MINUTES OF 320th MEETING OF REGISTRATION BOARD HELD ON 29th-31st AUGUST, 2022

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320th meeting of Registration Board was held on 29th, 30th & 31st September, 2022 in the Committee Room, Drug Regulatory Authority of Pakistan, G-9/4, Islamabad. The meeting was chaired by Dr. Obaidullah, Chairman Registration Board DRAP. The meeting started with recitation of the Holy Verses.

Dr. Obaidullah, Chairman Registration Board apprised the Board regarding appointment of newly appointed Secretary Registration Board Ch. Zeeshan Nazir Bajar, after the recent promotions within DRAP. All the Board members welcomed newly appointed Secretary Registration Board and hoped that their presence in Registration Board will help in efficient working of the Board. The Board also acknowledged the services of Ex-Secretary, Registration Board Mr. Abdullah and appreciated his commendable efforts for efficiently conducting the proceedings of Board.

Following members attended the meeting:

1.	Ch. Zeeshan Nazir Bajar, Additional Director (BE&R/PE&R), DRAP.	Member/ Secretary
2.	Lt.Gen.(R) Prof. Dr. Karamat A. Karamat (HI-M.SI-M), Former Surgeon General Pakistan.	Member
3.	Maj. Gen. (R) Dr. Tahir Mukhtar Sayed, Inspector General (Hospitals), Fauji Foundation, Rawalpindi	Member
4.	Dr. Qurban Ali, Ex-Director General, National Veterinary Laboratories, Islamabad	Member
5.	Ms. Aisha Irfan, Additional Director, Biological Evaluation & Research Division, DRAP	Member
6.	Mr. Iftikhar A. Choudhary, Hospital Pharmacist, Lahore	Member
7.	Mr. Muhammad Aslam, Deputy Draftsman-I, Ministry of law & Justice, Islamabad.	Member
8.	Mr. Ijaz Alvi, Director, DTL, Rawalpindi	Member
9.	Dr. Imran Khan, Director, DTL, Peshawar	Member
10.	Mr. Akhtar Abbas Khan, Representative of QA&LT Division	Member

Mr. Nadeem Alamgir (Pharma Bureau), Mr. Ali Raza & Mr. Jalal (PPMA) and Mr. Ziaulhaq (PCDA) attended the meeting as observers.

Director, BE&R was assisted by respective Add. Director and Assistant Directors for presentation of the agenda.

Item No. I: Confirmation of Minutes of 319th meetings of Registration Board.

319th meeting of Registration Board was held on 11th August, 2022. The draft minutes of Registration Board were circulated among the members of Board on 25th August, 2022 with the request for perusal/approval/comments (if any) by 26th August, 2022 at 10:00am. All members agreed the draft minutes.

Accordingly, fair minutes were processed to Chairman, Registration Board for perusal/approval. After approval from Chairman Registration Board, fair minutes of 319th meeting of Registration Board were circulated among concerned divisions/sections for implementation.

Decision: Registration Board confirmed the minutes of 319th meeting.

Item No. II Division of Pharmaceutical Evaluation & Registration

Pharmaceutical Evaluation Cell (PEC)

Sr. No	Name of Evaluator	Title
1.	Mr. Farooq Aslam	Evaluator PEC-I
2.	Mr. Ammar Ashraf Awan	Evaluator PEC-II
3.	Mr. Muhammad Haseeb Tariq	Evaluator PEC-III
4.	Mst.Farzana Raja	Evaluator PEC-IV
5.	Mst. Iqra Aftab	Evaluator PEC-V
6.	Mr. Muhammad Umar Latif	Evaluator PEC-VI
7.	Dr. Sidra Khalid	Evaluator PEC-VII
8.	Dr. Hanif Ullah	Evaluator PEC-IX
9.	Dr. Farhadullah	Evaluator PEC-XI
10.	Mr. Shahid Nawaz	Evaluator PEC-XIII
11.	Mr. Ahsan Hafiz	Evaluator PEC-XIV
12.	Mst. Saima	Evaluator PEC-XV
13.	Mr. Akbar Ali	Evaluator PEC-XVI
14.	Mr. Zia Ullah	Evaluator PEC-XVII
15.	Mr. Muneeb Ahmed Cheema	Evaluator PEC-XVIII
16.	Mr. Sarfraz Nawaz	Evaluator PE&R

Case No. 1: Applications submitted on Form 5 / 5-D requiring submission of stability data

It is submitted that various applications were received on Form 5 / 5-D which requires submission of stability study data for further processing. The list of such applications is available on official website of DRAP at https://www.dra.gov.pk/e-services/applications-for-pharmaceutical-drugs/. The stability study data for these applications is not yet submitted.

Decision: Registration Board deliberated the matter in detail and observed that these applications are pending for submission of stability data/product development data by the applicants since many years. Keeping in view the pendency, the Board deliberated the matter in detail and also took opinion of PPMA and then decided that the firms shall initiate the product development and stability studies of submitted applications and intimate to Pharmaceutical Evaluation Cell (PEC) regarding procuremne of raw material, initiation of product development and initiation of stability studies, by 31st December 2022. For all those applications for which Pharmaceutical Evaluation Cell will not receive any intimation regarding initiation of product development and stability studies, will be placed before the Board for decision.

Case No. 2: Review of Reference status of Cephradine for Injection:

Registration Board in its various meetings deferred the cases of Cephradine for Injection due to discontinued status of the said product by USFDA and non-availability of evidence of approval in other reference regulatory authorities.

Recently, the firm M/s GSK, Pakistan has submitted that they have contacted US FDA to seek confirmation on the reason of discontinuation of Cephradine (Velosef) Injections in US. They were advised to refer "US Federal Register" for the reason of discontinuation, wherein it has been declared that "*Cephradine (Velosef) Injections were discontinued by the manufacturer itself based on marketing reasons and that's why the dispensing of stocks was also allowed to continue till depletion of inventories or expiry of the stocks."*

The claim of the firm has been verified from Federal Register- The daily Journal of United States Government which notified that the Food and Drug Administration (FDA) has withdrawn the approval of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) listed in table below. The notification is elaborated as below:

"The holders of the applications listed in the table have informed FDA that these drug products are no longer marketed and have requested that FDA withdraw approval of the applications under the process described in § 314.150(c) (21 CFR 314.150(c)). The applicants have also, by their requests, waived their opportunity for a hearing. Withdrawal of approval of an application or abbreviated application under § 314.150(c) is without prejudice to refiling."

NDA No./ANDA No.	Drug	Applicant	Withdrawal date
NDA/50-501	Velosef Injection.	Bristol-Myers Squibb Co., P.O. Box 4000, Princeton, NJ 08543-6837.	April, 29, 2002
ANDA/061975	Cephradine Powder for Injection	Bristol-Myers Squibb Co., P.O. Box 4000, Princeton, NJ 08543.	September 7, 2018.

"Therefore, approval of the applications listed in the table, and all amendments and supplements thereto, is hereby withdrawn as of September 7, 2018. Introduction or delivery for introduction into interstate commerce of products without approved new drug applications violates section 301(a) and (d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(a) and (d)). Drug products that are listed in the table that are in inventory on September 7, 2018 may continue to be dispensed until the inventories have been depleted or the drug products have reached their expiration dates or otherwise become violative, whichever occurs first."

Hence it is evident from the above cited reference that the formulation of Cephradine injection had been discontinued only due to marketing reasons and no issues related to safety & efficacy have been reported by US FDA, because had there been any safety or efficacy issue, US FDA would have not allowed the dispensing of available stocks till the expiry or depletion of the inventory.

It is also pertinent to mention that other dosage forms of Cephradine i.e., Capsule & dry powder suspension are also available as of today in several reference regulatory authorities.

Following are the official website links for regulatory authorities:

Sr. No.	Website links	Regulatory authorities	Comments
1	https://cekbpom.pom.go.id//home/produk/pnkk3s5dhi2trjufaigklkt0qr/all/row/10/page/0/order/4/DESC/search/5/cefradine.	**Indonesian Food and Drug Supervisory Agency**	Confirms the registration of Cephradine 1gm/vial.
2	https://www.drugoffice.gov.hk/eps/do/en/consumer/search_drug_database2.html	**Pharmacy & Poisons Board of Hong Kong.**	Confirms the registration of Cephradine for Inj 500mg.
3	http://dgdagov.info/index.php/registered-products/allopathic	**Bangladesh Govt. - DGDA**	Confirms the registration of Cephradine 250mg/vial, 500mg/vial, 1gm/vial.
4	https://www.federalregister.gov/documents/2018/08/08/2018-16985/fougera-pharmaceuticals-inc-et-al-withdrawal-of-approval-of-27-abbreviated-new-drug-applications.	**Federal Register of US Govt.**	Confirms that Cephradine discontinued based on marketing reasons only. Hence allowed to dispense till the inventory deplete or stocks expired.
5	https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts.	**FDA Safety Alerts**	The non-availability of cephradine in said register confirms that there is no safety issue for market withdrawals.

Decision: Registration Board deliberated the matter in detail and acknowlwdged the fact that the "Cephradien injection" has not been withdrawan from US market due to safety & efficacy reasons as evident from the above cited notice published in US Federal Register. Hence, Registration Board decided to consider pending registration applications in the light of aforementioned position.

Case no. 03 Borrowing of APIs for performing Product Development, R&D & stability Testing:

DRAP Authority in its 133rd and 134th meeting considered the request of PPMA regarding borrowing of APIs for performing Product Development, R&D & stability Testing. The Authority in its 134th meeting decided as under:

The Authority reviewed its earlier decision taken in its 133rd meeting and decided as follows:

"The Authority deliberated that for product development / stability studies, the manufacturer need to purchase drug substance from a reliable source, however, in extraordinary circumstances beyond the control of manufacturer, the Authority acceded to the request of Pakistan Pharmaceutical Manufacturers Association (PPMA) to allow borrowing, except controlled drugs,

the requisite quantity of drug substance for product development / stability studies only to fulfill pre-requisite for submission of Form 5-F (CTD) from a licensed manufacturer having legitimate purchase evidence. However, all requirements of quality and traceability would be applicable in such cases and will be the responsibility of the borrower of the material. Further, the products so manufactured in NO case shall be allowed for commercial sale."

Decision: Registration Board considered decision of Authority and requested for guidance regarding processing of cases for borrowing of drug susbtances/materials for product development / stability studies of drug products on following points:

- **a.** Parameters to determine "extraordinary circumstances beyond the control of manufacturer".
- **b.** Whether borrowing will be permisable from manufacturer having registration of the products (containing same material) or will also be permisable for materials imported for experimental/ product development purposes by another manufacturer.
- **c.** Status of material after commercial import by registration holder (borrower).

On the basis of above cited decision of Board, instant case was referred for seeking guidance from the Authority. Subsequently Authority in its 140th meeting held on 28-29th June, 2022 has decided as under:

"The Authority, keeping in view of practical difficulties in implementation as highlighted by the Registration Board, reviewed its earlier decision taken in its 134th meeting held on 29th April, 2022, as under:

"The Authority deliberated that for product development / stability studies, the manufacturer need to purchase drug substance from a reliable source. Therefore, the Authority acceded to the request of Pakistan Pharmaceutical Manufacturers Association (PPMA) to allow borrowing the requisite quantity of drug substance, except controlled drugs, for product development / stability studies only to fulfill pre-requisite for submission of registration dossier from a licensed manufacturer having legitimate purchase evidence. However, all requirements of quality and traceability would be applicable in such cases and will also be the responsibility of the borrower of the material. Further, the products so manufactured in NO case shall be allowed for commercial sale."

Discussion & Decision:

Registration Board adopted the above cited decision of Authority and considered following cases:

1.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s. SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.**
	Name, address of Manufacturing site.	M/s Sami Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19160 dated :08-07-2021
	Details of fee submitted	PKR 30,000/-: Deposit slip #887056162198 PKR 120,000/-: Deposit slip #12835367 dated:20-01-2022

	The proposed proprietary name / brand name	**Mevulak MR 200mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Modified release Mebeverine HCl Pellets Equivalent to Mebeverine HCl ……. 200mg (Innovator's Specifications)
	Pharmaceutical form of applied drug	Modified Release Capsule
	Pharmacotherapeutic Group of (API)	Synthetic anticholinergics ATC Code: A03AA04
	Reference to Finished product specifications	Innovator's Specifications
	Proposed Pack size	10's, 20's, & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Colofac® MR. Modified release capsule by M/s MHRA Approved.
	For generic drugs (me-too status)	Mebever MR 200mg Capsule by M/s Getz Pharma,Registration No. 050747
	GMP status of the Finished product manufacturer	GMP Certificate issued date 11-08-2020 on the basis of inspection conducted on 28-08-2019
	Name and address of API manufacturer.	M/s RA Chem Pharma Limited (FDF) Plot No: A-19/C, A-23A 7 A-23B, Road No0 18, IDA Nancharam, Nancharm Village , Uppal Manda, Medchal- malkajgiri district, Hyderabad, Telegana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies of Drug substance	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches:(MBPJ16007,MBPJ16008,MBPJ16009,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls,

		impurities, individual impurity and total impurity, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Competitor that is Mebever MR® 200mg Tablets by M/s Getz Pharma by performing quality tests (Appearance, average weight, Assay, Dissolution, impurity profiling, Microbiological limit test). CDP has been performed against the same brand that is A Mebever MR® 200mg Tablets by M/s Getz Pharma in Acid media (pH 1.2-4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision (including intermediate precision, Repeatability), Robustness, specificity

STABILITY STUDY DATA

Manufacturer of API	M/s RA Chem Pharma Limited (FDF) Plot No: A-19/C, A-23A 7 A-23B, Road No0 18, IDA Nancharam, Nancharm Village , Uppal Manda, Medchal- malkajgiri district, Hyderabad, Telegana, India.		
API Lot No.	DMBPJ19049		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06th months Accelerated: 6th months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	2500 Capsules	2500 Capsules	2500 Capsules
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	14-07-2020	14-07-2020	14-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Reference of our last onsite panel inspection for instant dosage form conducted during last two years i.e. DELANZO DR (Dexlansoprazole) 30mg & 60mg Capsules which was presented in 281th meeting of the registration board & hence approved & registered by registration board

		Date of inspection: 02nd April, 2018.The inspection report confirms following points • The HPLC software is 21CFR Compliant • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML for M/s RA Chem Pharma Limited (FDF) (License No# 23/RR/AP/2007/F/R/CC, Dt:07/07/2013) issued by Drug Control Administration Government of Telegana, valid upto 26-10-2025 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Detail of Loan material from S.J & G Fazul Elahie (Pvt.) Karachi along with the Copy of form 3, form 7 & commercial invoice (Invoice# RATG/19-20/812 02-03- 2020 with received quantity i.e. 250 kg) for the purchase Mebeverine HCl SR Pellets by RA CHEM PHARMA LIMITED (FDF Division) with attestation of DRAP dated: 13 -02- 2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator(II):

Fee submitted PKR 120,000/-: Deposit slip #12835367, Dated: 20-01-2022

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.P.8	Clarify why you take loan of Pellets from S.J & G Fazul Elahie (Pvt.) Karachi instead of purchase from direct pellets maufacturer	Mebeverine HCL pellets of good quality could be sourced from good Indian manufacturers at reasonable rates. In order to conduct Stability Studies, we requested few manufacturers to supply required quantity of Mebeverine Hcl SR pellets to which they agreed. Unfortunately no Courier company was willing to lift sample quantity from India for delivery to us; copies of emails exchanged with them are annexed herewith.

			M/s S.J. & G Fazul Ellahie Pvt. Ltd. Karachi fortunately had sufficient stock of imported Mebeverine Hcl pellets and were willing to provide required quantity on loan. We accordingly obtained required quantity on loan from them.

Decision of 316th meeting: Deferred for further deliberation regarding regarding use of drug substance pellets by M/s Sami Pharmaceuticals (Pvt.) Ltd, for the manufacturing of stability batches, which had been procured and imported by M/s S.J. & G Fazul Ellahie Pvt. Ltd. Karachi.

Firm's response: Firm has submitted as under:

- Import of all material from India was banned vide SRO. 927 (I)/2019. dated 09-08-2019 issued by Ministry of Commerce & Textile however it was effectively operational only after Oct 2019 when DRAP Legal Affairs Division, vide its letter dated 17-10-2019 , requested Ministry of Commerce to issue the following clarification: ***(Annex A)***

  The words "therapeutic products" and "therapeutic good" carry the same meaning

- Due to this reason, all courier companies and postal authorities were not accepting any type of post and mail including letter, parcels and documents; copies of emails exchanged with FedEx, TCS(*UPS*) are annexed herewith ***(Annex B)***

- We contacted many leading USFDA, MHRA and EDQM Certified manufacturers of APIs and Pellets in India from whom we were procuring the material since last 10 years for obtaining samples but due to COVID surge in India, no courier service was accepting samples for delivery to Pakistan ***(Annex C)***

- Having been left with no other option, the material was received on "Loan" against an Understanding; as stated on Memo attached; from an established manufacturer viz., **M/s. S.J. &G. Fazul Ellahie (Pvt.) Ltd. Karachi** who had legally imported these Pellets from the same source viz., RA Chem Pharma Ltd**. It was assured to them that on obtaining drug registration, we will import commercial quantities from the same source and then return the material received on loan** ***(Annex D)***
- We have learnt that the DRAP Authpority has now allowed to take the material on loan as per following criteria:

  Material can be procured from one manufacturer to another for R&D purpose and commercial consignment then shall be obtained from the same source i.e. API supplier

Hence, in the light of above, it is earnestly requested to consider our case for favorable decision.

Moreover, firm has submitted memorandum of understanding between M/s Sami Pharma. & M/s S.J&G Fazul Ellahe regarding loan and return of the said drug substance. Firm has also submitted regarding use of the borrowed material for R&D purpose only.

Decision: Deferred till decision of Authority on borrowing of APIs for performing Product Development, R&D & stability Testing.

Decision of 320th meeting: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

2.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nabiqasim Industries Pvt Ltd. 17/24, Korangi Industrial Area, Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s Nabiqasim Industries Pvt Ltd. 17/24, Korangi Industrial Area, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 19-09-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of DML, declaring "Ear drop/Topical solution" section, whereas submitted GMP certificate mentions the "Cream/Ointment/Lotion section."
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10088 dated 31-03-2021
	Details of fee submitted	Rs.20,000/- dated 31-003-2021
	The proposed proprietary name / brand name	**Lidogel 2% Jelly**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml Contains: Lidocaine HCl……20mg
	Pharmaceutical form of applied drug	Topical spray solution
	Pharmacotherapeutic Group of (API)	Local Anaesthetic Jelly Sterile. For topical application only ***ATC Code***: N01BB02
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1gm x 1's
	Proposed unit price	MRP as per PRC
	The status in reference regulatory authorities	Xylocaine 2% Gel (Lidocaine HCl 2%) is registered and being marketed by OAK Pharms, USA (FDA approved).
	For generic drugs (me-too status)	M/s Barrett Hodgson Pakistan (Pvt) Ltd., b. Brand Name: Xylocaine 2% c. Strength: 2% Jelly Reg. No.: 009315
	Name and address of API manufacturer.	M/s **Gufic Group Testing Laboratories.** N.H.No.8, Near Grid AT & PO Kabilpore-39G 424, Navsari, Gujrat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 25°C ± 2°C / 60 ± 5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Xylocaine jelly 2%" of M/s Barret Hodgson has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA	
Manufacturer of APIs	M/s Shandong Boyuan Pharmaceutical Co., Ltd. Qiangjin Street, Jibei Economic Development Zone, Jinan, Shandong, China.
API Lot No.	190305TA
Description of Pack (Container closure system)	15gm Aluminium tube with an applicator cone in a unit carton.

Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	L001DS01	L001DS02	L001DS03
Batch Size	01 ltr.	01 ltr.	01 ltr.
Manufacturing Date	12-2019	12-2019	12-2019

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr.#	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm (if any)	--
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate (Certificate# 19081523) issued by Food & Drug Administration Gujarat, valid upto 06-08-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice issued in the name of M/s Surge Laboratories (Pvt.) Ltd. attested by AD I&E DRAP, Lahore has been submitted for import of Lidocaine HCl
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Invoice No.	**Quantity Imported**	**Date of approval by DRAP**
NBEXBD2021000188	600Kg	10-11-2020

Remarks of Evaluator(II):

Section	Observation	Firm's response
2.3	Table for literature references for the drug substance & drug product has not been submitted.	Submitted.
2.3. S.1.2	Submitted molar mass is not correct.	Corrected molar mass has now been submitted.
2.3. S.3.2	List of impurities is as per the USP monograph for Lidocaine HCl, whereas API manufacturer has declared the API of BP grade.	List of impurities as per BP monograph has now been submitted.
2.3. S.4.2	This section declares that "Lidocaine hydrochloride is tested as per the test procedures described in the US	Firm has submitted that the drug substance manufacturer has declared

	Pharmacopoeia", whereas section 2.3.S.4.1 declares the API of BP standard.	the drug substance of standard quality as per both USP & BP monograph.
3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	Submitted for the titration method as per BP monograph
3.2.S.4.4	Submit analytical record for the batch analysis of drug substance performed by the M/s Nabiqasim.	Firm has submitted analytical record for the analysis of drug substance according to which analysis has been performed as per BP monograph by way of potentiometric titration.
3.2.P.1	Clarification shall be submitted regarding label claim whether it is in term of "%age w/w" or "%age w/v".	Frim has submitted that the label claim is as per innovator i.e., %age w/v"
3.2.P.2.1.2	Quantities of preservatives used in formulation shall be justified for per unit dose with reference to the relevant guidelines/standards.	Firm has referred to the literature from Hand book of pharmaceutical excipients and reference limits from FDA IID database.
3.2.P.5.1	Test for content of antimicrobial preservative & efficacy of preservative, as recommended by ICH Q1 (R2) guidelines & USP chapter <51>, has not been included in the finished product specifications. You are advised to submit justification in this regard.	Firm has submitted that preservative efficacy test, preservative content test, initial testing and 01-month stability testing and has submitted reports now. Firm has also submitted revised specifications and finished drug product analytical procedure including the test for Methyl paraben & Propyl paraben.
3.2.P.8	• Submitted commercial invoice attested by AD DRAP I&E Karachi has been isuued in the name of M/s Surge Laborartories (Pvt.) Ltd. Justification shall be submitted in this regard. • Test for content of antimicrobial preservative & efficacy of preservative, as recommended by ICH Q1 (R2) guidelines, has not been performed during stability studies. You are advised to submit justification in this regard. • A white paper titled "Support for Title 21 CFR Part 11 ….." has been submitted from "Agilent open Lab" under the heading of "Compliance record of HPLC software 21 CFR & audit trail report on product testing", whereas submitted chromatograms establish that the analysis has been performed on Schimadzu HPLC.	• With reference to the subjected query, we would like to inform you that "M/s Surge Laboratories (Pvt.) Ltd" is the sister company of "M/s Nabiqasim Industries (Pvt.) Ltd." • Commercial invoice of Lidocaine HCl attested by AD DRAP issued in the name of M/s Surge Laboratories (Pvt.) Ltd because material is imported by Surge Laboratories (Pvt.) Limited. • Lidocaine HCl supplier to "Nabiqasim Industries (Pvt.) Ltd." is its sister company "Surge Laboratories (Pvt.) Ltd". • Moreover, testing of API and stability batches conducted by M/s Nabiqasim Industries (Pvt.) Ltd. and reports are enclosed for ready reference. • Firm has submitted that preservative efficacy test, preservative content test, initial testing and 01-month stability testing and has submitted reports now. Firm has also submitted revised specifications and finished drug product analytical

		procedure including the test for Methyl paraben & Propyl paraben. • Firm has now submitted Audit trail reports.
• You are advised to submit scientific rationale for claiming USP specifications for finished drug product while the Drug substance used is of BP specifications. • Clarification shall be submitted that in which section applied product will be manufactured along with the evidence of approval of required manufacturing facility/section for applied product, from the Licensing Division of DRAP.		• We would like to inform that as per dosage form definition in USP chapter (1151). Jelly can also be covered in the definition of Gels and can be manufactured in Semi solid (Gel) manufacturing area. • Nabiqasim has dedicated semi solid manufacturing area for cream, ointment and gel manufacturing. Nabiqasim has also registered gel dosage form i.e. Chlorhexidine Gluconate Gel for which product specific inspection has been conducted on 27.10.2020. Report of this inspection is attached for your ready reference. • The Panel has report as follows against the query of required manufacturing facility for manufacturing and filling of gels: "Firm has well equipped area for manufacturing of ointment, creams and gels. Along with creams and ointments one gel preparation (Acnicot Gel, Reg. No. 080660) is already manufactured in this area. Firm has already applied to the licensing division for the inclusion of gel in their layout vide letter No. NQIL/DRAP/06-20/027, dated 10-06-2020."

Decision of 316th meeting: Registration Board deferred the case for further deliberation regarding use of drug substance by M/s Nabiqasim Industries (Pvt.) Ltd., for the manufacturing of stability batches, which had been procured and imported by M/s Surge Laboratories (Pvt.) Ltd.

Firm's response: We in this regard, would like to clarify that since M/s. Surge Laboratories (Pvt) Ltd., Sheikhupura is our associated company which is under the control of common management. As M/s. Surge Laboratories is importing API "Lidocaine HCl USP" for the manufacturing of their registered drug "Lidoject 2% Injection" Reg # 057348. In order to save time, we had taken a loan of 15Kgs "Lidocaine HCl USP" from M/s. Surge Laboratories to conduct stability for our applied drug "Lidogel Gel 2%". Firm has submitted following documents.

- Mutual agreement between M/s Nabiqasim and M/s. Surge Laboratories.

Undertaking.

Decision: Deferred till decision of Authority on borrowing of APIs for performing Product Development, R&D & stability Testing.

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

3.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on 17-07-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 24-06-2019 which specifies Ophthalmic general section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 398 dated 05-01-2022
	Details of fee submitted	Rs.30,000/- dated 06-12-2021
	The proposed proprietary name / brand name	**Dorzil Eye drop**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains 22.26 mg of Dorzolamide hydrochloride equivalent to 20 mg Dorzolamide.
	Pharmaceutical form of applied drug	Eye Drops, Solution
	Pharmacotherapeutic Group of (API)	Dorzolamide: Carbonic anhydrase inhibitors ATC Code: S01EC03
	Reference to Finished product specifications	BP specification
	Proposed Pack size	1 x 5 ml
	Proposed unit price	--
	The status in reference regulatory authorities	USFDA Trusopt 20 mg/ml Eye drops, solution Santen pharmaceuticals Co., Ltd Japan
	For generic drugs (me-too status)	Trusopt Ophthalmic Drops 2% 5ml by OBS Pharma (Pvt) Karachi Ltd, Pakistan Regd. No. 021100 Pack size: 5 ml
	Name and address of API manufacturer.	**Dorzolamide** Dorzolamide from Neuland Laboratories Limited, Unit-1 Sy. No: 347, 473, 474, 490 / 2 Veerabhadraswamy temple road, Bonthapalli Village, Gummadidala Mandal, Sangareddy District - 502 313 Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	**Dorzolamide** Long-term stability studies were performed at a storage temperature of 30°C±2°C/65%±5% RH for 60 months. Accelerated stability studies were performed at a temperature of 40±2°C/75%±5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Trusopt sterile ophthalmic Solution" by Santen pharmaceuticals Co., Ltd. Imported by OBS pharma
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions.

STABILITY STUDY DATA	
Manufacturer of APIs	**Dorzolamide** Dorzolamide from Neuland Laboratories Limited, Unit-1 Sy. No: 347, 473, 474, 490 / 2 Veerabhadraswamy temple road, Bonthapalli Village, Gummadidala Mandal, Sangareddy District - 502 313 Telangana, India
API Lot No.	DZ10420013 (Dorzolamide)
Description of Pack (Container closure system)	Low density polyethylene bottle with insert-cap assembly, HDPE screw- cap over a LDPE nozzle with tamper–evident LDPE dustcover sealing the bottle cap.
Stability Storage Condition	Real time: 30^{o}C ± 2^{o}C / 35% HR ±5%

		Accelerated: 40°C ± 2°C / NMT 25% HR		
Time Period		Real time: 3 months Accelerated: 3 months		
Frequency		Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.		PDDN0012021	PDDN0022021	PDDN0032021
Batch Size		5 liter	5 liter	5 liter
Manufacturing Date		07/2021	07/2021	07/2021
DOCUMENTS / DATA PROVIDED BY THE APPLICANT				
#	**Documents To Be Provided**	**Status**		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Dorzolamide** Copy of GMP certificate in the name of Neuland Laboratories Limited, Unit-1 Sy. No: 347, 473, 474, 490 / 2 Veerabhadraswamy temple road, Bonthapalli Village, Gummadidala Mandal, Sangareddy District - 502 313 Telangana, India, valid upto 28-06-2022 issued by Drug Control Administration, Government of Telangana, India.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted. **Batch No.** / **Quantity Imported** / **Date of approval by DRAP** DZ10420013 (Dorzolamide) / 1 kg / 08-06-2021 The commercial invoice is in the name of M/s Pacific Pharmaceuticals Ltd., 30th KM, Multan Road, Lahore.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports on product testing.		
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)		
Remarks of Evaluator (II):				
Section#	**Observations**	**Firm's response**		
1.5.6	Drug product specifications have been referred to as Innovator's specifications	Firm has now claimed European Pharmacopoeia Specifications		

	whereas Pharmacopoeial monographs are available for applied product.	
Dorzolamide HCl		
3.2. S.4.1	• Drug substance manufacturer has declared drug substance as of Ph. Eur grade for related substances whereas the submitted Assay test is declared as per USP pharmacopoeia. • The analytical method for Assay submitted by drug product manufacturer is different form that proposed by the drug substance manufacturer. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.	• In BP/Ph. Eur there is potentiometric titration for API assay determination while in USP there is use of HPLC for Assay determination, which is better technique and equipment than the technique adopted by drug substance manufacturer. • Copies of analytical procedure submitted from drug product manufacturer.
3.2.P.5.1	• Submitted drug product specifications does not include test of "Preservative Effectiveness testing".	Microbial report for Preservative testing has been submitted now.
3.2. P.6	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted
3.2. P.8	Following shall be submitted: • Stability studies till 3rd month time point has been submitted only. • Analytical record i.e., HPLC chromatograms, raw data sheets & COAs shall be submitted for complete stability studies till 6th month time point.	• Firm has submitted 6 months stability data along woith analytical record.
2.3.R.1.1	• As per submitted BMRs terminal sterilization has not been performed. Justification shall be submitted in this regard. • The proposed batch size shall be justified against the minimum handling	• No terminal sterilization has been performed, for which firm has submitted that aseptic area manufacturing tank under LAF and aseptic blowing, filling/sealing multiple function cartage assembling 0.65µm+0.45µm+0.22µm in manufacturing for filtration of solution and 0.22 in filling BFS machine which already mention in BMR so our product is sterile by filtration and aseptic process.

	capacity of the formulation tank.	

Decision of 316th meeting: Registration Board deferred the case for further deliberation regarding use of drug substance by M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore, for the manufacturing of stability batches, which had been procured and imported by M/s Pacific Pharmaceuticals Ltd., 30th KM, Multan Road, Lahore.

Firm's response:

We Pacific Pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) have borrowed drug substance material used in the following products (Dorzil Eye drops, Glucozole-T Eye Drops, Pacilact-D IV Infusion 500ml, Pacilact-D IV Infusion 1000ml) for stability and validation purpose only from Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore (DML 000295).

The justification for the borrowing was based on the fact that commercial department dealing with procurement was common for both plants operating from the address 30th Km Multan Road, Lahore. However, we have already started using dedicated procurement for IV plant. We assure that all of our future procurement will be made by Pacific Pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) separately and dedicatedly.

Decision: Deferred till decision of Authority on borrowing of APIs for performing Product Development, R&D & stability Testing.

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

4.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on 17-07-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 24-06-2019 which specifies Ophthalmic (General) Section
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 24883 dated 08-09-2021
	Details of fee submitted	Rs.30,000/- dated 12-08-2021
	The proposed proprietary name / brand name	**Glucozole-T 5ml Eye Drops**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml Contains: Dorzolamide as Dorzolamide HCl ……. 20mg Timolol as Timolol Maleate …… 5mg
	Pharmaceutical form of applied drug	Eye drops, solution
	Pharmacotherapeutic Group of (API)	Dorzolamide Carbonic anhydrase inhibitors ATC Code: S01EC03 Timolol: nonselective beta-adrenergic receptor blocker ATC Code: S01ED01
	Reference to Finished product specifications	Innovator's Specs
	Proposed Pack size	5ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Cosopt sterile ophthalmic Solution Solution by: Santen pharmaceuticals Co., Ltd. Japan Regd. No. 025294 Pack size: 5 ml
	Name and address of API manufacturer.	**Dorzolamide HCl:** M/sNeuland Laboratories Limited, Unit-1 Sy. No: 347, 473, 474, 490 / 2 Veerabhadraswamy temple road, Bonthapalli Village, Gummadidala Mandal, Sangareddy District – 502 313 Telangana, India **Timolol maleate:** FDC Limited, 142-48, Swami Vivekananda Road Jogeshwari (West) Mumbai-400 102.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	**Dorzolamide HCl:** Long-term stability studies were performed at a storage temperature of 30°C±2°C/65%±5% RH for 36months.

		Accelerated stability studies were performed at a temperature of 40±2°C/75%±5% RH for 6 months. **Timolol maleate:** Long-term stability studies were performed at a storage temperature of 30°C±2°C/65%±5% RH for 36months. Accelerated stability studies were performed at a temperature of 40±2°C/75%±5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Cosopt" of M/s Santen Pharmaceuticals.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA			
Manufacturer of APIs	**Dorzolamide HCl:** M/s Neuland Laboratories Limited, Unit-1 Sy. No: 347, 473, 474, 490 / 2 Veerabhadraswamy temple road, Bonthapalli Village, Gummadidala Mandal, Sangareddy District – 502 313 Telangana, India **Timolol maleate:** FDC Limited, 142-48, Swami Vivekananda Road Jogeshwari (West) Mumbai-400 102.		
API Lot No.	Dorzolamide HCl: DZI0420013 Timolol maleate: 021D026		
Description of Pack (Container closure system)	Low Density Polyethylene Bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 35% ± 5%RH Accelerated: 40°C ± 2°C / NMT 25% RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TD0109O	TD0209O	TD0309O
Batch Size	10 liters	10 liters	10 liters
Manufacturing Date	09/2019	11/2019	11/2019

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**N/A**

<table>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Dorzolamide HCl:
Copy of GMP certificate in the name of M/s Neuland Laboratories Limited valid upto 28-06-2022 issued by DCA Tealngana.
Timolol maleate:
Copy of GMP certificate (certificate#NEW-WHO-GMP/CERT/KD/72416/2018/11/24412) in the name of M/s FDC Limited valid upto 08-08-2021 issued by FDA Maharashtra.</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted.<table><tr><th>Batch No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>011909031</td><td>5875</td><td>03-10-2019</td></tr></table>Firm has submitted that Invoice stated the address Mis Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore</td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>N/A</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
<tr><td colspan="3">Remarks of Evaluator (II):
In response to the following shortcomings communicated to firm vide letter no. F.1-1/2020/PEC-DRAP (AD PEC-II), firm has submitted that due to some errors in our previous data we have submitted the updated stability batches data along with 6 months stability report. Kindly consider this updated data and withdraw or neglect our previous data at the date of submission of dossier.
Details of revised stability data are as under:</td></tr>
<tr><td colspan="3">STABILITY STUDY DATA</td></tr>
<tr><td colspan="2">Manufacturer of APIs</td><td>Dorzolamide HCl: M/s Neuland Laboratories Limited, Unit-1 Sy. No: 347, 473, 474, 490 / 2 Veerabhadraswamy temple road, Bonthapalli Village, Gummadidala Mandal, Sangareddy District – 502 313 Telangana, India
Timolol maleate: FDC Limited, 142-48, Swami Vivekananda Road Jogeshwari (West) Mumbai-400 102.</td></tr>
<tr><td colspan="2">API Lot No.</td><td>Dorzolamide HCl: DZI0420013
Timolol maleate: 021D026</td></tr>
<tr><td colspan="2">Description of Pack
(Container closure system)</td><td>Low Density Polyethylene Bottle</td></tr>
<tr><td colspan="2">Stability Storage Condition</td><td>Real time: 30°C ± 2°C / 35% ± 5%RH
Accelerated: 40°C ± 2°C / NMT 25% RH</td></tr>
<tr><td colspan="2">Time Period</td><td>Real time: 6 months
Accelerated: 6 months</td></tr>
<tr><td colspan="2">Frequency</td><td>Accelerated: 0, 3, 6 (Months)
Real Time: 0, 3, 6 (Months)</td></tr>
</table>

<table>
<tr><td colspan="2">Batch No.</td><td>PDEN0012021</td><td>PDEN0022021</td><td>PDEN0032021</td></tr>
<tr><td colspan="2">Batch Size</td><td>5 liters</td><td>5 liters</td><td>5 liters</td></tr>
<tr><td colspan="2">Manufacturing Date</td><td>12-07-2021</td><td>12-07-2021</td><td>12-07-2021</td></tr>
<tr><td colspan="5">DOCUMENTS / DATA PROVIDED BY THE APPLICANT</td></tr>
<tr><td>#</td><td>Documents to be provided</td><td colspan="3">Status</td></tr>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td colspan="3">N/A</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td colspan="3">Dorzolamide HCl:
Copy of GMP certificate in the name of M/s Neuland Laboratories Limited valid upto 28-06-2022 issued by DCA Telangana.
Timolol maleate:
Copy of GMP certificate (Certificate#NEW-WHO-GMP/CERT/KD/72416/2018/11/24412) in the name of M/s FDC Limited valid upto 08-08-2021 issued by FDA Maharashtra.</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td colspan="3">Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted.
<table>
<tr><th>API</th><th>Batch No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>Dorzolamide</td><td>DZT0420013</td><td>1Kg</td><td>08-06-2021</td></tr>
<tr><td>Timolol</td><td>1386/186</td><td>0.025gm</td><td>08-06-2021</td></tr>
</table>
Submitted invoices are in the name of M/s Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore.</td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td colspan="3">Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td colspan="3">N/A</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td colspan="3">Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
<tr><td colspan="5">
<table>
<tr><th>Section#</th><th>Observations</th><th>Firm’s response</th></tr>
<tr><td>1.5.6</td><td>Drug product specifications have been referred to as Innovator’s specifications whereas Pharmacopoeial monographs are available for applied product.</td><td>It was a typographic error. Product is according to the European pharmacopoeial monographs.</td></tr>
<tr><td colspan="3">Dorzolamide HCl</td></tr>
<tr><td>3.2. S.4.1</td><td>• Drug substance manufacturer has declared drug substance as of Ph. Eur grade, whereas the submitted Assay method is as per USP pharmacopoeia.</td><td>• In BP/Ph. Eur there is potentiometric titration for API assay determination while in USP there is use of HPLC for Assay determination, which is better technique</td></tr>
</table>
</td></tr>
</table>

	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.	and equipment than the technique adopted by drug substance manufacturer. • Copies of analytical procedure submitted from drug product manufacturer.
3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	Submitted.
3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture.	Submitted.
3.2. S.7	Drug substance stability data as per Zone IV a condition shall be submitted.	Submitted as per Zone-IVa.
Timolol maleate		
3.2. S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.	Submitted
3.2. S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	Submitted
3.2. S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture.	Submitted.
3.2. S.7	Submitted stability reports are not readable.	Submitted
3.2. P.3.5	Process validation protocol shall be submitted.	Submitted
3.2. P.5.3	Analytical method verification studies performed by drug product manufacturer shall be submitted.	Analytical method verification studies have been submitted for Dorzolamide only.
3.2. P.6	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted
3.2. P.8	Following shall be submitted:	

	• Complete batch manufacturing record of stability trial batches. • Documents for the procurement of API with approval from DRAP (in case of import). • Record of Digital data logger for temperature & humidity monitoring of stability chambers • Submitted analytical record reflect that chromatographic conditions for the Assay analysis of Dorzolamide have not been performed as per recommendations of USP monograph, since the gradient run time as per monograph is of 30 minutes while the firm has run HPLC chromatogram, for about 12 minutes only.	• BMR for three trial batches have been submitted • No terminal sterilization has been performed, for which firm has submitted that aseptic area manufacturing tank under LAF and aseptic blowing, filling/sealing multiple function cartage assembling 0.65µm+0.45µm+0.22µm in manufacturing for filtration of solution and 0.22 in filling BFS machine which already mention in BMR so our product is sterile by filtration and aseptic process. • Firm has applied "Solution preparation tank" of 100 litres for the manufacturing of 5 litre batch size stating that design capacity of active manufacturing tank ranges from 5 litres to 100 litres so, 5 litres batch can be easily processed. • Submitted HPLC chromatograms reflect that the chromatographic conditions for the Assay test have not been complied as per USP monograph in terms of the run time for which firm has replied that although the injection run time is 30minute but the peaks separation of Dorzolamide is about 12 minutes. In the chromatograms sample run time is about 20minute but there is no any further peak found. So, it Is not big issue, in future will follow up to 30minutes.

Firm has submitted fee of Rs. 30,000/- for revision of stability data as per following details:
Rs. 7,500/- vide deposit slip#5349893974 dated 01-03-2022
Rs. 22500/- vide deposit slip#92601467 dated 09-03-2022

Decision of 316th meeting: Registration Board deferred the case for further deliberation regarding use of drug substance by M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore, for the manufacturing of stability batches, which had been procured and imported by M/s Pacific Pharmaceuticals Ltd., 30th KM, Multan Road, Lahore.

Firm's response:

We Pacific Pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) have borrowed drug substance material used in the following products (Dorzil Eye drops, Glucozole-T Eye Drops, Pacilact-D IV Infusion 500ml, Pacilact-D IV Infusion 1000ml) for stability and validation purpose only from Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore (DML 000295).

The justification for the borrowing was based on the fact that commercial department dealing with procurement was common for both plants operating from the address 30th Km Multan Road, Lahore.

However, we have already started using dedicated procurement for IV plant. We assure that all of our future procurement will be made by Pacific Pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) separately and dedicatedly.

Decision: Deferred till decision of Authority on borrowing of APIs for performing Product Development, R&D & stability Testing.

Decision of 320th meeting: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
5.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore**
	Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sunder Industrial Estate, Raiwind Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 29420 dated 28-10-2021
	Details of fee submitted	Rs.20,000/- dated 25-02-2021
	The proposed proprietary name / brand name	**Pacilact-D IV Infusion 500ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml Contains: Sodium Chloride…….0.60g Potassium Chloride…….0.03g Calcium Chloride Dihydrate…….0.02g Sodium Lactate …… 0.31gram Dextrose Monohydrate Eq. to Anhydrous Dextrose…….4.3g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolyte
	Reference to Finished product specifications	USP
	Proposed Pack size	500ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Lactated Ringer's and 5% Dextrose Injection of M/s Medipak Limited (Reg.no: 008242)
	GMP status of the Finished product manufacturer	New DML issued on 24-06-2019
	Name and address of API manufacturer.	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac Bioquimica SA, BarcelonaSpain

		Dextrose: M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module-III (Drug Product):	Firm has submitted relevant information against the Module III, including, Process validation protocol, Finished product analytical method verification report & stability studies data.
	Remarks: Firm has submitted Pharmaceutical equivalence studies against the reference product of 5% DEXTROSE in LACTATED RINGER'S INJECTION of M/s B Braun.	

STABILITY STUDY DATA

Manufacturer of API	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac, Spain **Dextrose:** M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.		
API Lot No.	**Sodium Chloride:** 0801209 **Calcium Chloride Dihydrate:** 20190826 **Potassium Chloride:** 190815 **Sodium Lactate:** 1904001735 **Dextrose:** 201906001		
Description of Pack (Container closure system)	Low Density Polyethylene film bags.		
Stability Storage Condition	Real time: 30°C ± 2°C / 35% ± 5%RH Accelerated: 40°C ± 2°C / NMT 25% RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RN0111O	RN0211O	RN0311O
Batch Size	4000 litres	4000 litres	4000 litres
Manufacturing Date	15/10/2019	16/10/2019	17/10/2019
No. of Batches	03		

Details of Documents submitted

1.	Reference of previous approval of applications with stability study data of the firm (if any)	--
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (Certificate# HE20190013) in the name of M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China valid upto 02-02-2024 issued by HEBEI Dug Administration.

		Sodium Chloride: Firm has submitted copy of GMP certificate in the name of M/s Dominion Salt Ltd., 89, totara street, Mount Maunganui, NewZeland valid upto 29-03-2021 issued by Ministry of Health, Newzeland. **Calcium Chloride Dihydrate:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Potassium Chloride:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Sodium Lactate:** Firm has submitted Eudra GMP certificate (Certificate# ***NCF-II/1817/001/CAT***) is valid till April 2021. **Dextrose anhydrous:** Firm has submitted copy of GMP certificate (Certificate# HE20190013) in the name of M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China valid upto 02-02-2024 issued by HEBEI Dug Admiistration.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sodium Lactate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore, **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** dated 21-10-2019 specifying the quantity of 800Kgs of Sodium lactate (60%). **Calcium Chloride Dihydrate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 21-10-2019, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1MTS. **Potassium Chloride:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 21-10-2019, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1MTS. **Dextrose anhydrous:** Firm has submitted copy of commercial invoice (Invoice#. 20ST27003) attested by AD DRAP I&E Lahore, dated 03-10-2019, in the name of **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** specifying the quantity of 5000Kgs of Dextrose anhydrous (Batch# 201906001) from M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Sr. No.	Section #.	Deficiencies	Firm's response
		Calcium Chloride	
1.	***3.2. S.2.1***	• Address of drug substance manufacturer mentioned in this section is different from that mentioned on the COA from drug substance manufacturer.	• It was a typographic error, the said section has been revised.
2.	***3.2.S.4. 4***	• The drug substance COA from drug substance manufacturer declare it of BP grade, whereas COA from drug product manufacturer declare it as of USP grade.	• It was a typographic error, we have rectified the error. Our COA is also as BP grade.
		Sodium Lactate	
3.	***3.2.S.4***	• The Assay limits in the COA of drug substance manufacturer is 59% -61%, whereas the Assay limits in the COA of drug product manufacturer is 95.0% - 110.0%. • The Assay results in the COA of drug substance manufacturer is 60.1%, whereas the Assay limits in the COA of drug product manufacturer is 101.28%.	According to USP monograph, Sodium Lactate Solution is an aqueous solution containing not less than 50.0 percent, by weight, of monosodium lactate. It contains not less than 98.0 percent and not more than 102.0 percent of labeled amount of $C_3H_5NaO_3$.We have overlooked the COA of drug substance. This was typographical error from supplier we have intimated the supplier and will provide you correct COA later. However, Assay limits in the COA of drug product manufacturer is 101.28% according to specifications.
4.	***1.5.2 & 3.2. P.1***	• The reference product contains Dextrose monohydrate = 5gm/100ml, while firm has applied for Dextrose anhydrous = 4.3gm/100ml. • You are advised to justify the variation in formulation from reference product or else submit revised composition as per reference product along with relevant fee as per Notification No. F.7-11f2012-B&A/DRAP dated 07th May, 2021.	• According to Martindale Anhydrous glucose 900 mg is equivalent to about 1 g of glucose monohydrate. 50g/litre of glucose monohydrate is (equivalent to about 45 g/litre of anhydrous glucose).
5.	***3.2. P.5.2***	• Evidence of availability of atomic absorption spectrophotometer and flame photometry, as required by	Firm has submitted calibration certificate for atomic absorption spectrophotometer.

		the USP monograph of applied product, shall be submitted	List of equipment including Flame photometer has been submitted.
6.	***3.2. P.3.3***	• You are advised to submit justification for applying sterilization conditions other than the standard conditions for terminal sterilization by moist heat i.e., temperature 121oC & Time > 15 min.	• We have followed Sterilization process by super-heated water showering at 109ºC for 85 minutes. • 121ºC & Time ≥ 15 min, this temperature is used for machine sterilization before running product
7.	• The date of manufacturing of three stability batches i.e., RN0111O, RN0211O, RN0311O, as per submitted BMR is 15/10/2019,16/10/2019 & 17/10/2019 respectively, whereas commercial invoice submitted for Potassium chloride & Calcium chloride is attested by AD DRAP I&E Lahore dated 21-10-2019. • Justify the quantities of Dextrose anhydrous dispensed for batch manufacturing considering the proposed label claim OF Dextrose anhydrous 4.3gm/100ml. • Justify the dispensed quantity of Sodium Lactate dispensed for batch manufacturing considering the Assay percentage of drug substance declared in the submitted COA from Pacific Pharma. • Submit analytical record for the analysis of Potassium, Sodium & Calcium for the stability studies. • Submit reconciliation record for the imported quantity of 1 MTS each of Potassium chloride & Sodium chloride.		• We have purchased the material from Medipak Limited for sample. Attested invoice by AD DRAP I&E Lahore dated 21-10-2019 was after manufacturing of RN0111O, RN0211O, RN0311O batches. This material was imported for commercial manufacturing of other products which is not used in these batches. The Correct invoice is attached. • The quantity of dextrose anhydrous dispensed for batch manufacturing considering the proposed label claim of Dextrose anhydrous is 4.5g/100ml. (As per submitted BMR Dextrose anhydrous has been dispensed as per 5gm/100ml which is not as per reference product.) • We have used sodium lactate (as sodium lactate solution (60% w/v) as label claim. (Dispensed quantity is not as per the percentage purity of sodium lactate determined by the Pacific pharma) • We have purchased the material from Medipak Limited for sample. Attested invoice by AD DRAP I&E Lahore dated 21-10-2019 was after manufacturing of RN0111O, RN0211O, RN0311O batches. This material was imported for commercial manufacturing of other products which is not used in these batches.

Decision of 307th meeting: Registration Board deferred the case for submission of following:
• Revised label claim for Dextrose monohydrate as per the innovator's product, along with submission of relevant fee.
• Legal provision of utilizing Drug substances purchased from another DML holder i.e., M/s Medipak Limited.

Firm's response: Firm has submitted new stability studies data on 28-10-2021, along with correction in label claim of Dextrose monohydrate. Fee for the submission of new stability data has not been submitted. Details of new stability data are as under:

Name, address of Applicant / Marketing Authorization Holder	**M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore**

Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384 Sundar industrial Estate, Raiwind Road, Lahore
Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
GMP status of the firm	GMP certificate issued on 17-07-2020
Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 24-06-2019 which specifies Large volume parental section.
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
Dy. No. and date of submission	Dy. No. 29420 dated 28-10-2021
Details of fee submitted	Rs. 30,000/- vide deposit slip# 516358736
The proposed proprietary name / brand name	**Pacilact-D IV Infusion 500ml**
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml Contains: Sodium Chloride…….0.60g Potassium Chloride…….0.03g Calcium Chloride Dihydrate…….0.02g Sodium Lactate …… 0.31gram Dextrose Monohydrate Eq. to Anhydrous Dextrose…….5g
Pharmaceutical form of applied drug	Intravenous Infusion
Pharmacotherapeutic Group of (API)	Electrolyte
Reference to Finished product specifications	USP
Proposed Pack size	500ml
Proposed unit price	As per SRO
The status in reference regulatory authorities	Approved by US FDA
For generic drugs (me-too status)	Lactated Ringer's and 5% Dextrose Injection of M/s Medipak Limited (Reg.no: 008242)
Name and address of API manufacturer.	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac Bioquimica SA, BarcelonaSpain **Dextrose:** M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.

Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions duration of Stability studies)	Real time: 30°C ± 2°C / 35% ± 5%RH Accelerated: 40°C ± 2°C / NMT 25% RH
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted Pharmaceutical equivalence studies against the reference product of 5% DEXTROSE in LACTATED RINGER'S INJECTION of M/s B Braun.
Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions.
STABILITY STUDY DATA (Currently Submitted)	
Manufacturer of APIs	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac Bioquimica SA, BarcelonaSpain **Dextrose:** M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.
API Lot No.	Sodium chloride: 08012019 Potassium chloride: 200413 Sodium lactate: 1909000241 Calcium chloride: 20200625 Dextrose: 201906001
Description of Pack (Container closure system)	Low Density Polyethylene film bags.

Stability Storage Condition		Real time: 30°C ± 2°C / 35% ± 5%RH Accelerated: 40°C ± 2°C / NMT 25% RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		LANB0012020	LANB0022020	LANB0032020
Batch Size		4 liter	4 liter	4 liter
Manufacturing Date		09/2020	09/2020	09/2020
DOCUMENTS / DATA PROVIDED BY THE APPLICANT				
#	**Documents To Be Provided**	**Status**		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	PACILACT-RL 500 ml IV INFUSION approve in 297 DRB		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Sodium Chloride:** Firm has submitted copy of GMP certificate in the name of M/s Dominion Salt Ltd., 89, totara street, Mount Maunganui, NewZeland valid upto 29-03-2021 issued by Ministry of Health, Newzeland. **Calcium Chloride Dihydrate:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Potassium Chloride:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Sodium Lactate:** Firm has submitted Eudra GMP certificate (Certificate# ***NCF-II/1817/001/CAT***) is valid till April 2021. **Dextrose anhydrous:** Firm has submitted copy of GMP certificate (Certificate# HE20190013) in the name of M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China valid upto 02-02-2024 issued by HEBEI Dug Admiistration.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sodium Lactate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore, **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** dated 07-07-2020 specifying the quantity of 800Kgs of Sodium lactate (60%). **Calcium Chloride Dihydrate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 09-09-2020, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1 MTS. **Potassium Chloride:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 09-09-2020, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1 MTS. **Dextrose anhydrous:** Firm has submitted copy of commercial invoice (Invoice#. 20ST27003) attested by AD DRAP I&E Lahore, dated 03-10- 2019, in the name of **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** specifying the quantity of 5000Kgs of Dextrose anhydrous (Batch# 201906001) from M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China.		

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not applicable
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator(II):

Decision of 316th meeting: Registration Board deferred the case for further deliberation regarding use of drug substance by M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore, for the manufacturing of stability batches, which had been procured and imported by M/s Pacific Pharmaceuticals Ltd., 30th KM, Multan Road, Lahore.

Firm's response:

We Pacific pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) have borrowed drug substance material used in the following products (Dorzil Eye drops, Glucozole-T Eye Drops, Pacilact-D IV Infusion 500ml, Pacilact-D IV Infusion 1000ml) for stability and validation purpose only from Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore (DML 000295).

The justification for the borrowing was based on the fact that commercial department dealing with procurement was common for both plants operating from the address 30th Km Multan Road, Lahore.

However, we have already started using dedicated procurement for IV plant. We assure that all of our future procurement will be made by Pacific pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) separately and dedicatedly.

Decision: Deferred till decision of Authority on borrowing of APIs for performing Product Development, R&D & stability Testing.

Decision of 320th meeting: Approved. Registration Board further decided that registration letter will be issued after submission of full fee that is Rs. 30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

6.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore**
	Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sunder Industrial Estate, Raiwind Road,

		Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 8507 dated 16-03-2021
	Details of fee submitted	Rs.20,000/- dated 25-02-2021
	The proposed proprietary name / brand name	**Pacilact-D IV Infusion 1000ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml Contains: Sodium Chloride…….0.60g Potassium Chloride…….0.03g Calcium Chloride Dihydrate…….0.02g Sodium Lactate …… 0.31gram Dextrose Monohydrate Eq. to Anhydrous Dextrose…….4.3g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolyte
	Reference to Finished product specifications	USP
	Proposed Pack size	1000ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Lactated Ringer's and 5% Dextrose Injection of M/s Medipak Limited
	GMP status of the Finished product manufacturer	New DML issued on 24-06-2019
	Name and address of API manufacturer.	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac Bioquimica SA, BarcelonaSpain **Dextrose:** M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module-III (Drug Product):	Firm has submitted relevant information against

		the Module III, including, Process validation protocol, Finished product analytical method verification report & stability studies data.		
	Remarks: Firm has submitted Pharmaceutical equivalence studies against the reference product of 5% DEXTROSE in LACTATED RINGER'S INJECTION of M/s B Braun.			
STABILITY STUDY DATA				
Manufacturer of API		**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac, Spain **Dextrose:** M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.		
API Lot No.		**Sodium Chloride:** 0801209 **Calcium Chloride Dihydrate:** 20190826 **Potassium Chloride:** 190815 **Sodium Lactate:** 1904001735 **Dextrose:** 201906001		
Description of Pack (Container closure system)		Low Density Polyethylene film bags.		
Stability Storage Condition		Real time: 30˚C ± 2˚C / 35% ± 5%RH Accelerated: 40˚C ± 2˚C / NMT 25% RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		RD0111O	RD0211O	RD0311O
Batch Size		4000 litres	4000 litres	4000 litres
Manufacturing Date		15/10/2019	14/10/2019	14/10/2019
No. of Batches		03		
Details of Documents submitted				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	--		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (Certificate# HE20190013) in the name of M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China valid upto 02-02-2024 issued by HEBEI Dug Administration.		
		Sodium Chloride: Firm has submitted copy of GMP certificate in the name of M/s Dominion Salt Ltd., 89, totara street, Mount Maunganui, NewZeland valid upto 29-03-2021		

		issued by Ministry of Health, Newzeland. **Calcium Chloride Dihydrate:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Potassium Chloride:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Sodium Lactate:** Firm has submitted Eudra GMP certificate (Certificate# ***NCF-II/1817/001/CAT***) is valid till April 2021. **Dextrose anhydrous:** Firm has submitted copy of GMP certificate (Certificate# HE20190013) in the name of M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China valid upto 02-02-2024 issued by HEBEI Dug Admiistration.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sodium Lactate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore, **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** dated 21-10-2019 specifying the quantity of 800Kgs of Sodium lactate (60%). **Calcium Chloride Dihydrate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 21-10-2019, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1MTS. **Potassium Chloride:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 21-10-2019, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1MTS. **Dextrose anhydrous:** Firm has submitted copy of commercial invoice (Invoice#. 20ST27003) attested by AD DRAP I&E Lahore, dated 03-10-2019, in the name of **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** specifying the quantity of 5000Kgs of Dextrose anhydrous (Batch# 201906001) from M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China.
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Sr. No.	Section #.	Deficiencies	Firm's response
		Calcium Chloride	
1.	***3.2. S.2.1***	• Address of drug substance manufacturer mentioned in this section is different from that mentioned on the COA from drug substance manufacturer.	• It was a typographic error, the said section has been revised.
2.	***3.2.S.4 .4***	• The drug substance COA from drug substance manufacturer declare it of BP grade, whereas COA from drug product manufacturer declare it as of USP grade.	• It was a typographic error, we have rectified the error. Our COA is also as BP grade.
		Sodium Lactate	
3.	***3.2.S.4***	• The Assay limits in the COA of drug substance manufacturer is 59% - 61%, whereas the Assay limits in the COA of drug product manufacturer is 95.0% - 110.0%.gmail • The Assay results in the COA of drug substance manufacturer is 60.1%, whereas the Assay limits in the COA of drug product manufacturer is 101.28%.	According to USP monograph, Sodium Lactate Solution is an aqueous solution containing not less than 50.0 percent, by weight, of monosodium lactate. It contains not less than 98.0 percent and not more than 102.0 percent of labeled amount of $C_3H_5NaO_3$.We have overlooked the COA of drug substance. This was typographical error from supplier we have intimated the supplier and will provide you correct COA later. However, Assay limits in the COA of drug product manufacturer is 101.28% according to specifications.
4.	***1.5.2 & 3.2. P.1***	• The reference product contains Dextrose monohydrate = 5gm/100ml, while firm has applied for Dextrose anhydrous = 4.3gm/100ml. • You are advised to justify the variation in formulation from reference product or else submit revised composition as per reference product along with relevant fee as per Notification No. F.7-11f2012-B&A/DRAP dated 07th May, 2021.	• According to Martindale Anhydrous glucose 900 mg is equivalent to about 1 g of glucose monohydrate. 50g/litre of glucose monohydrate is (equivalent to about 45 g/litre of anhydrous glucose).

5.	***3.2. P.5.2***	• Evidence of availability of atomic absorption spectrophotometer and flame photometry, as required by the USP monograph of applied product, shall be submitted	Firm has submitted calibration certificate for atomic absorption spectrophotometer. List of equipment including Flame photometer has been submitted.
6.	***3.2. P.3.3***	• You are advised to submit justification for applying sterilization conditions other than the standard conditions for terminal sterilization by moist heat i.e., temperature 121oC & Time ≥ 15 min.	• We have followed Sterilization process by super-heated water showering at 109ºC for 85 minutes. • 121ºC & Time ≥ 15 min, this temperature is used for machine sterilization before running product
7.	• The date of manufacturing of three stability batches i.e., RN0111O, RN0211O, RN0311O, as per submitted BMR is 15/10/2019,16/10/2019 & 17/10/2019 respectively, whereas commercial invoice submitted for Potassium chloride & Calcium chloride is attested by AD DRAP I&E Lahore dated 21-10-2019. • Justify the quantities of Dextrose anhydrous dispensed for batch manufacturing considering the proposed label claim OF Dextrose anhydrous 4.3gm/100ml. • Justify the dispensed quantity of Sodium Lactate dispensed for batch manufacturing considering the Assay percentage of drug substance declared in the submitted COA from Pacific Pharma. • Submit analytical record for the analysis of Potassium, Sodium & Calcium for the stability studies. • Submit reconciliation record for the imported quantity of 1 MTS each of Potassium chloride & Sodium chloride.	• We have purchased the material from Medipak Limited for sample. Attested invoice by AD DRAP I&E Lahore dated 21-10-2019 was after manufacturing of RN0111O, RN0211O, RN0311O batches. This material was imported for commercial manufacturing of other products which is not used in these batches. The Correct invoice is attached. • The quantity of dextrose anhydrous dispensed for batch manufacturing considering the proposed label claim of Dextrose anhydrous is 4.5g/100ml. (As per submitted BMR Dextrose anhydrous has been dispensed as per 5gm/100ml which is not as per reference product.) • We have used sodium lactate (as sodium lactate solution (60% w/v) as label claim. (Dispensed quantity is not as per the percentage purity of sodium lactate determined by the Pacific pharma) • We have purchased the material from Medipak Limited for sample. Attested invoice by AD DRAP I&E Lahore dated 21-10-2019 was after manufacturing of RN0111O, RN0211O, RN0311O batches. This material was imported for commercial manufacturing of other products which is not used in these batches.

Decision of 307th meeting: Registration Board deferred the case for submission of following:

• Revised label claim for Dextrose monohydrate as per the innovator's product, along with submission of relevant fee.

• Legal provision of utilizing Drug substances purchased from another DML holder i.e., M/s Medipak Limited.

Firm's response: Firm has submitted new stability studies data on 28-10-2021, along with correction in label claim of Dextrose monohydrate. Fee for the submission of new stability data has not been submitted. Details of new stability data are as under:

Name, address of Applicant / Marketing Authorization Holder	M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384,Sundar industrial Estate, Raiwind Road, Lahore
Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384,Sundar industrial Estate, Raiwind Road, Lahore
Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
GMP status of the firm	GMP certificate issued on 17-07-2020
Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 24-06-2019 which specifies Large volume parental section.
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
Dy. No. and date of submission	Dy. No.29421 dated 28-10-2021
Details of fee submitted	Rs. 30,000 vide deposit slip# 3015188420
The proposed proprietary name / brand name	**Pacilact-D IV Infusion 1000ml**
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml Contains: Sodium Chloride……0.60g Potassium Chloride…….0.03g Calcium Chloride Dihydrate…….0.02g Sodium Lactate …… 0.31gram Dextrose Monohydrate Eq. to Anhydrous Dextrose…….5g
Pharmaceutical form of applied drug	Intravenous Infusion
Pharmacotherapeutic Group of (API)	Electrolyte
Reference to Finished product specifications	USP
Proposed Pack size	1000ml
Proposed unit price	As per SRO
The status in reference regulatory authorities	Approved by US FDA
For generic drugs (me-too status)	Lactated Ringer's and 5% Dextrose Injection of M/s Medipak Limited
Name and address of API manufacturer.	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac Bioquimica SA, BarcelonaSpain

	Dextrose: M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions duration of Stability studies)	Real time: 30°C ± 2°C / 35% ± 5%RH Accelerated: 40°C ± 2°C / NMT 25% RH
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted Pharmaceutical equivalence studies against the reference product of 5% DEXTROSE in LACTATED RINGER'S INJECTION of M/s B Braun.
Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions.
STABILITY STUDY DATA (Currently Submitted)	
Manufacturer of APIs	**Sodium Chloride:** Dominion Salt Limited, 89 Totara Street, Mount Maunganui, New Zealand. **Calcium Chloride Dihydrate:** Hebei Huachen Pharmaceuticals. Ltd. **Potassium Chloride:** Hebei Huachen Pharmaceuticals Ltd., Economic Devleopment zone. Hebei, China **Sodium Lactate:** Corbion Purac Bioquimica SA, BarcelonaSpain **Dextrose:** M/s CSPC Shengxue Glucose Co., Ltd, No.48 Shengxue Road, Luancheng District, China-051430 Shijiazhuang City, Hebei Province.
API Lot No.	Sodium chloride: 08012019 Potassium chloride: 200413 Sodium lactate: 1909000241

		Calcium chloride: 20200625 Dextrose: 201906001		
Description of Pack (Container closure system)		Low Density Polyethylene film bags.		
Stability Storage Condition		Real time: 30°C ± 2°C / 35% ± 5%RH Accelerated: 40°C ± 2°C / NMT 25% RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		LANA0012020	LANA0022020	LANA0032020
Batch Size		4 liter	4 liter	4 liter
Manufacturing Date		09/2020	09/2020	09/2020
DOCUMENTS / DATA PROVIDED BY THE APPLICANT				
#	**Documents To Be Provided**	**Status**		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	PACILACT-RL 1000 ml IV INFUSION approve in 297 DRB		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Sodium Chloride:** Firm has submitted copy of GMP certificate in the name of M/s Dominion Salt Ltd., 89, totara street, Mount Maunganui, NewZeland valid upto 29-03-2021 issued by Ministry of Health, Newzeland. **Calcium Chloride Dihydrate:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Potassium Chloride:** Firm has submitted GMP certificate (Certificate# HE20180030) issued by Hebei food & Drug administration valid till 22-04-2023. **Sodium Lactate:** Firm has submitted Eudra GMP certificate (Certificate# ***NCF-II/1817/001/CAT***) is valid till April 2021. **Dextrose anhydrous:** Firm has submitted copy of GMP certificate (Certificate# HE20190013) in the name of M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China valid upto 02-02-2024 issued by HEBEI Dug Admiistration.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sodium Lactate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore, **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** dated 07-07-2020 specifying the quantity of 800Kgs of Sodium lactate (60%). **Calcium Chloride Dihydrate:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 09-09-2020, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1 MTS. **Potassium Chloride:** Firm has submitted copy of invoice attested by AD DRAP I&E Lahore dated 09-09-2020, **M/s Pacific Pharmaceuticals Ltd., Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore** specifying the quantity of 1 MTS. **Dextrose anhydrous:** Firm has submitted copy of commercial invoice (Invoice#. 20ST27003) attested by AD DRAP I&E Lahore,		

		dated 03-10- 2019, in the name of **M/s Pacific Pharmaceuticals Ltd., 30 Km, Multan Road, Lahore** specifying the quantity of 5000Kgs of Dextrose anhydrous (Batch# 201906001) from M/s CSPC SHENGXUE Glucose Co., Ltd., No. 48 Shengxue Road, Luancheng District, Shijiazhuang City, Hebei province, China.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data pf stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not applicable
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Decision of 316th meeting: Registration Board deferred the case for further deliberation regarding use of drug substance by M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore, for the manufacturing of stability batches, which had been procured and imported by M/s Pacific Pharmaceuticals Ltd., 30th KM, Multan Road, Lahore.

Firm's response:

We Pacific pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) have borrowed drug substance material used in the following products (Dorzil Eye drops, Glucozole-T Eye Drops, Pacilact-D IV Infusion 500ml, Pacilact-D IV Infusion 1000ml) for stability and validation purpose only from Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore (DML 000295).

The justification for the borrowing was based on the fact that commercial department dealing with procurement was common for both plants operating from the address 30th Km Multan Road, Lahore.

However, we have already started using dedicated procurement for IV plant. We assure that all of our future procurement will be made by Pacific pharmaceuticals Ltd. Ravi Lane Plot No. 384, Sundar Industrial Estate, Raiwind Lahore (DML 000902) separately and dedicatedly.

Decision: Deferred till decision of Authority on borrowing of APIs for performing Product Development, R&D & stability Testing.

Decision of 320th meeting: Approved. Approved. Registration Board further decided that registration letter will be issued after submission of full fee that is Rs. 30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Agenda of Evaluator PEC-I

Case No. I: Registration applications of Local Manufacturing submitted on Form 5F (New Section/New License)

Deferred Cases:

M/s Jaskan Pharmaceuticals (Pvt) Ltd., 50-Sundar Industrial Estate, Lahore was granted additional section "Injectable vial (General)" vide letter No.F.1-16/2006-Lic(Vol-I) dated 12th March, 2021.

Sr. No.	No. of molecules	No. of product
1	02	02

7.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26351 dated 22/09/2021
	Details of fee submitted	PKR 30,000/-: dated 16/09/2021
	The proposed proprietary name / brand name	Moxica 400mg Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Eacxh vial contains: Moxifloxacin as HCl……400mg
	Pharmaceutical form of applied drug	Solution for Infusion
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	In-house
	Proposed Pack size	1's (250ml)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Avelox 400mg/250mL infusion MHRA Approved.
	For generic drugs (me-too status)	Mofest 400mg/250mL Infusion by M/s Sami Pharmaceuticals Pvt. Ltd. Reg. No. 53227
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 10/2021-DRAP(FID-797667-1346) dated 18/02/2021 issued on the basis of inspection conducted on 26/10/2020.

	Name and address of API manufacturer.	M/s Vital Laboratories Pvt. Ltd. Plant No. II, plot No. 1710 & A1/2208, GIDC estate, Phase III, Vapi-396195 Gujrat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months for 3 batches (MOXPB112001, MOXPB112002, MOXPB112003) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 02 batches (MOXPB001, MOXPB001)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence studies have been conducted against Mofest Infusion 400mg/250mL Batch 041G By M/s Sami Pharmaceuticals.
	Analytical method validation/verification of product	

STABILITY STUDY DATA

Manufacturer of API	M/s Vital Laboratories Pvt. Ltd. Plant No. II, plot No. 1710 & A1/2208, GIDC estate, Phase III, Vapi-396195 Gujrat, India.
API Lot No.	MOX2010023
Description of Pack	Type I glass vial with rubber stopper and flip off aluminium seal.

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	KN-01	KN-02	KN-03
Batch Size	100 vials	100 vials	100 vials
Manufacturing Date	03/2021	03/2021	03/2021
Date of Initiation	17-03-2021	17-03-2021	17-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted against this point.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of drug manufacturing license number License Retention/Vital/2019/63520 valid till 2024 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No. HHM/2021/00377 (Diary No. 1447/2021/DRAP) dated 26/01/2021 is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of digital data logger.

Remarks OF Evaluator:

Observations	Response
Please provide analytical method used by drug product manufacturer for the routine analysis of drug substance.	The firm has submitted method of analysis for drug substance used for routine analysis as per USP.
Submit analytical method verification studies including specificity, accuracy and precision performed by drug product manufacturer for drug substance.	Analytical method verification studies for drug substance including specificity, precision and accuracy is submitted.
Since the excipients used in the applied formulation are different from the excipients used in manufacturing of reference product,	Not submitted.

therefore, provide compatibility studies of excipients with the drug substance.	
The stability summary sheets for drug substance are from M/s Vital Health Care Pvt. Ltd. (VAPI) Plot No. 1416-18 & 1507, GIDC Phase III, Vapi 396195 Gujrat, India while the address of manufacturer of drug substance as mentioned on DML and Form 5F is different, please clarify.	The firm could not clarify the difference of the address of drug substance manufacturer mentioned in license, form 5F and stability summary sheets.
Clarification is required since pharmaceutical equivalence is established against Mofest 400mg/250mL infusion by M/s Sami Pharmaceuticals while the studies should be carried out against the reference/innovator's product.	The firm has submitted pharmaceutical equivalence data against another product Avelox Infusion 400mg/250mL (B: BXJE602) by M/s Bayer AG Pharmacutical pvt ltd.
Please provide detailed calculations for quantity to be dispensed per vial considering the actual potency of Moxifloxacin HCl since "loss on drying" has not been considered.	The firm has stated that without considering LOD factor, the assay results are well in limits. The firm has further stated that in future they would consider this factor.
The stability data is submitted till 3rd month time point, please provide stability studies till 6th month time point.	The firm has submitted the stability studies till 6th month's time point.
Provide documents confirming import of the drug substance used in the manufacturing of trial batches.	Invoice No. HHM/2021/00377 dated 15/01/2021 (Diary No. 1447/2021/DRAP dated 26/01/2021) is submitted.

Decision of 316th meeting:

Deferred for clarification of variation in the address of drug substance manufacturer as mentioned in Drug Manufacturing License, Form 5F and stability summary sheets of the drug substance.

Submission by the firm:

The firm has stated that M/s Vital Laboratories Pvt. Ltd., India (Previously known as Vital Health Care Pvt. Ltd., has 3 manufacturing plants. Earlier, DML of plant II was submitted erroneously. Their latest DML of plant I is submitted, which has same address as on stability summary sheets of the drug substance.

- Plant I: Plot No. 1416 to 1421 & 1507 /1 & 2, 1601, GIDC Phase III Vapi 396195 Gujrat India.
- Plant II: Plot No. 1710 & A1/2208, GIDC Estate, Phase III, Vapi 396195 Gujarat India.
- Plant III: Plot No. 1302/3, GIDC Estate, Phase III, Vapi 396195 Gujarat India.

The firm has stated that the API used for product development is from plant I. Copy of Retention of License (No. G/28/1117) is submitted. The license is valid till20/02/2027.

Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

New Cases:

M/s Jaskan Pharmaceuticals (pvt) Ltd. was granted New Section "Injectable (vial) General Section" vide letter No. F.1-16/2006-Lic (Vol-I) dated 12/03/2021 title of which was corrected

in 283rd meeting of Licensing Board as "Injectable (Vial) (General) (LVP) Section" vide even letter No. dated 18/111/2021.

Injectable (Vial) (General) (LVP) Section:

The firm has applied for:

Sr. No.	No. of Molecules	No. of products
1	01	01

8.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10949 dated 30/04/2022
	Details of fee submitted	PKR 30,000/-: dated 03-04-2022
	The proposed proprietary name / brand name	Tramak Infusion 1000mg /100ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100 ml Vial contains: Paracetamol ……. 1000mg
	Pharmaceutical form of applied drug	Liquid for Infusion
	Pharmacotherapeutic Group of (API)	Analgesic; antipyretic.
	Reference to Finished product specifications	Manufacturer's specs
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved
	For generic drugs (me-too status)	Provas I.V Infusion 1000 mg M/s Sami Pharmaceuticals Pvt Ltd. Karachi Pakistan, Reg. No. 053223
	GMP status of the Finished product manufacturer	Certifictae No.10/2021-DRAP (FID-797667-1346) issued by DRAP valid till 25/10/2022.
	Name and address of API manufacturer.	Pharmagen Limited Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing

		process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (Lab Experiment/001/2016, Lab Experiment/002/2016, Lab Experiment/003/2016)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established Provas I.V Infusion 1000mg Infusion by M/S Sami Pharmaceuticals Pvt Ltd. Karachi Pakistan, Reg. No. 053223 by performing quality tests. The results of all the tests of both products fall within the specifications and are comparable.
	Analytical method validation/verification of product	Firm has submitted reports of verification studies of analytical method for the drug substance. Firm has also submitted reports of validation of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore.
API Lot No.	00510911-01/002/2021
Description of Pack	Colorless glass vial (Type II) with aluminium foil seal and a transparent white rubber stopper as closure.

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	LC 01	LC 02	LC 03
Batch Size	100 vials	100 vials	100 vials
Manufacturing Date	09-08-2021	09-08-2021	09-08-2021
Date of Initiation	11-08-2021	11-08-2021	11-08-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted against this point
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML certificate No. 000325 and GMP Certificate No. 06-2019-DRAP(AD/607409-530, both issued by DRAP.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying Local Procurement of Paracetamol Invoice No 2129 dated 10-02-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted the compliance record of HPLC 21CFR software audit trail report for the applied product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

The drug substance is manufactured according to B.P but the data submitted by the finished product manufacturer shows that USP method is used for routine analysis of Paracetamol drug substance. However, the method used for analysis of finished product is In-House.

Sr. No	Observations	Response by the firm
1	As per available literature, the manufacturer of the reference product has included the test for Osmolality in the finished product specifications while you have not performed any such test, please clarify.	The firm has submitted the results of osmolality test. The test was performed on 16/07/2022.

2	Cysteine Hydrochloride is used as an anti-oxidant in the reference product but you have not used any excipient having a role as anti-oxidant, please clarify.	The firm has provided reference of another product "Paracetamol Panpharma 10mg/ml solution for infusion" approved in France where no anti-oxidant is used in the formulation. http://agence-prd.ansm.sante.fr/php/ecodex/frames.php?specid=63069892&typedoc=R&ref=R0378034.htm (Accessed on 25/07/2022)
3	Clarification is required since the performance of pharmaceutical equivalence is performed against Provas infusion by M/s Sami Pharma but not against the reference / innovator's product.	"The innovator's product is not available in Pakistan"
4	Please provide detail of calculations for potency adjustment considering the purity of drug substance as per COA.	The firm has provided complete calculations.
5	Justify the stability studies without the performance of Bacterial Endotoxin and Sterility testing.	The firm has submitted revised stability summary sheets containing the results of sterility testing and Bacterial endotoxin test without any clarification regarding previously submitted sheets without these tests.

Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7.500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

M/s Jaskan Pharmaceuticals (Pvt) Ltd., 50-Sundar Industrial Estate, Lahore was granted additional section "DRY POWDER FOR INJECTION (CEPHALOSPORIN)" vide letter No.F.1-16/2006-Lic(Vol-I) dated 12th March, 2021.

DRY POWDER FOR INJECTION (CEPHALOSPORIN):

After consideration of 02 more applications, the total number of considered molecules/product will be:

Sr. No.	No. of molecules	No. of product
1	01	06

9.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7368 dated 16/03/2022
	Details of fee submitted	PKR 30,000/-: dated 18/02/2022
	The proposed proprietary name / brand name	Jaxone Dry Powder for Solution for IV Injection 250mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone as sodium……250mg
	Pharmaceutical form of applied drug	Powder for solution for
	Pharmacotherapeutic Group of (API)	Cephalosporin
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone for injection 1g, MHRA Approved.
	For generic drugs (me-too status)	Rocephin 500mg Injection by M/s MartinDow
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 10/2021-DRAP(FID-797667-1346) dated 18/02/2021 issued on the basis of inspection conducted on 26/10/2020.
	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukhshwla, 34 km Ferozepur road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.

	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (00241/007/2006, 00241/00/2006, 00241/009/2006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is performed against Oxidil 250mg Injection by M/s Sami by performing the quality tests. (B:013G).
	Analytical method validation/verification of product	The firm has submitted analytical method verification studies including certain testing parameters such as accuracy, precision and specificity for drug product and substance performed by drug product manufacturer.

STABILITY STUDY DATA

Manufacturer of API	M/s Pharmagen Ltd., Kot Nabi Buksh wala, 34-km, Ferozepur road, Lahore.		
API Lot No.	00421/002/2021		
Description of Pack (Container closure system)	Type I glass vial (15ml) with rubber stopper and grey flip off aluminium cap		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	KG-1	KG-2	KG-3
Batch Size	100 vials	100 vials	100 vials
Manufacturing Date	03/2021	03/2021	03/2021
Date of Initiation	25-03-2021	25-03-2021	25-03-2021
No. of Batches	03		

Administrative Portion

7.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted against this point.

8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate No. 06/2019-DRAP(AD/607409-530) dated 11/01/2019 issued on the basis of inspection conducted on 08/01/2019.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	The drug substance is locally procured.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of digital data logger.

Remarks OF Evaluator:

Sr. no.	Observations	Response
1	Justify the performance of stability studies without the performance of Bacterial Endotoxin and Sterility testing.	The firm has submitted revised stability summary sheets containing the results of sterility testing and Bacterial endotoxin test without any clarification regarding previously submitted sheets without these tests.
2	The quantity to be dispensed as per submitted dossier is 299.96mg/vial, please submit the detail with justification for dispensed quantity.	The firm has submitted the calculations. The actual quantity to be dispensed should be 300.854mg per vial.
3	Provide invoice confirming the procurement of Ceftriaxone Sodium.	The firm has submitted copy of invoice No. 2268 dated 24/02/2021 from M/s Pharmagen Limited.
4	Oxidil Injection by M/s Sami Pharma is used for pharmaceutical equivalence testing while the said studies are required to be performed against innovator's/reference product, please clarify.	"Rocephin 250mg is not available in Pakistan"

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

10.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7369 dated 16/03/2022
	Details of fee submitted	PKR 30,000/-: dated 18/02/2022
	The proposed proprietary name / brand name	Jaxone Dry Powder for Solution for IV Injection 500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone as sodium……500mg
	Pharmaceutical form of applied drug	Powder for solution for
	Pharmacotherapeutic Group of (API)	Cephalosporin
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone for injection 1g, MHRA Approved.
	For generic drugs (me-too status)	Rocephin 500mg Injection by M/s MartinDow
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 10/2021-DRAP(FID-797667-1346) dated 18/02/2021 issued on the basis of inspection conducted on 26/10/2020.
	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukhshwla, 34 km Ferozepur road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications,

		analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (00241/007/2006, 00241/00/2006, 00241/009/2006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is performed against Rocephin 500mg Injection 1g by M/s MartinDow by performing the quality tests. (B:B0067).
	Analytical method validation/verification of product	The firm has submitted analytical method verification studies including certain testing parameters such as accuracy, precision and specificity for drug product and substance performed by drug product manufacturer.

STABILITY STUDY DATA

Manufacturer of API	M/s Pharmagen Ltd., Kot Nabi Buksh wala, 34-km, Ferozepur road, Lahore.		
API Lot No.	00421/002/2021		
Description of Pack (Container closure system)	Type I glass vial (15ml) with rubber stopper and green flip off aluminium cap		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	KG-1	KG-2	KG-3
Batch Size	100 vials	100 vials	100 vials
Manufacturing Date	03/2021	03/2021	03/2021
Date of Initiation	25-03-2021	25-03-2021	25-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted against this point.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate No. 06/2019-DRAP(AD/607409-530) dated 11/01/2019 issued on the basis of inspection conducted on 08/01/2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The drug substance is locally procured.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of digital data logger.

Remarks OF Evaluator:

Sr. No.	Observations	Response
1	Justify the stability studies without the performance of Bacterial Endotoxin and Sterility testing.	The firm has submitted revised stability summary sheets containing the results of sterility testing and Bacterial endotoxin test without any clarification regarding previously submitted sheets without these tests.
2	Justify the dispensed quantity (599.91mg/vial) of Ceftriaxone Sodium keeping in view the moisture content as per the certificate of analysis from drug product manufacturer.	The firm has submitted the calculations. The actual quantity to be dispensed should be 601.685mg per vial.
3	Provide invoice confirming the procurement of Ceftriaxone Sodium.	The firm has submitted copy of invoice No. 2268 dated 24/02/2021 from M/s Pharmagen Limited.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

M/s Jaskan Pharmaceuticals (Pvt) Ltd., 50-Sundar Industrial Estate, Lahore was granted additional section "Injectable (Ampoule) General Section" vide letter No.F.1-16/2006-Lic(Vol-I) dated 12th March, 2021.

Injectable (Ampoule) General Section:

01 product and 01 molecules is considered by the board already. The firm has applied for 02 more product and after consideration of two more products the detail of total number of molecules/products will be:

No. of Molecules		No. of products
02		03
11.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19357 dated 01/07/2022
	Details of fee submitted	PKR 30,000/-: dated 26/05/2021
	The proposed proprietary name / brand name	Aqua J 10ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains: Sterile Water for injection…..10ml
	Pharmaceutical form of applied drug	Clear, colorless water for injection
	Pharmacotherapeutic Group of (API)	Water for injection/diluent/solvent
	Reference to Finished product specifications	B.P
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Sterile water for injection 10ml glass ampoule by M/s Hameln Pharma Ltd, MHRA Approved.
	For generic drugs (me-too status)	Water for injection 10ml by M/s Healthtek, Reg. No. 076482
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 10/2021-DRAP(FID-797667-1346) dated 18/02/2021 issued on the basis of inspection conducted on 26/10/2020. Dry powder
	Name and address of API manufacturer.	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility,

		physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of the product.
	Module III (Drug Substance)	Firm has submitted detailed data of drug substance related to nomenclature, structure, general properties, solubilities, description of manufacturing process and controls, specifications, analytical procedures, batch analysis and justification of specification and container closure system.
	Stability studies	N/A
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	The firm has submitted pharmaceutical equivalence testing data against WFI 10ml injection by M/s Healthtek by performing all the quality tests (027H).
	Analytical method validation/verification of product	N/A

STABILITY STUDY DATA

Manufacturer of API	N/A		
API Lot No.	N/A		
Description of Pack (Container closure system)	Glass AMpoule		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	KV-01	KV-02	KV-03
Batch Size	1000 injection	1000 ampoules	1000 ampoules
Manufacturing Date	March, 2021	March, 2021	March, 2021
Date of Initiation	30/03/2021	30/03/2021	30/03/2021

No. of Batches	03	
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Aqua J 5ml Injection approved in 313th meeting.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	N/A
3.	Documents for the procurement of API with approval from DRAP (in case of import).	N/A
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted stability study data of 3 batches along with water loss test at each time point. Firm has submitted analytical report at each stability testing interval.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of digital data logger.
Remarks OF Evaluator-I:		
Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
12.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 9331 dated 12/04/2022
	Details of fee submitted	PKR 30,000/-: dated 06-10-2021
	The proposed proprietary name / brand name	JD-3 Injection 5mg/mL IM/Oral

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Ampoule (1mL) contains: Cholecalciferol 5mg
	Pharmaceutical form of applied drug	Solution for IM Injection/Oral
	Pharmacotherapeutic Group of (API)	Vitamin
	Reference to Finished product specifications	Innovator's Specs
	Proposed Pack size	1ml(1x1,s)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vitamin D3 Bon 200000 IU /1mL Solution for injection, ANSM France Approved.
	For generic drugs (me-too status)	Indrop D Injection M/s Neutro Pharmaceutical Pvt Ltd Pakistan., Reg. No. 023170
	GMP status of the Finished product manufacturer	New Section Approval granted on 12-03-2021 (Injectable General Ampoule & Injectable General vials) section approved.
	Name and address of API manufacturer.	Sichuan Yuxin Pharmaceutical Co. Ltd No 51 West Section Of Changjiang Road Shifang Economic Delopment Zone Southern District) Sichuan China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH The firm has submitted stability data of cholecalciferol in different container closure with the following details

		• Packed under vacuum in glass ampoule (36months real time and 6 months accelerated) B: CHL0408020, CHL0408021, CHL0408022 • Packed in LDPE bag under vacuum (36months real time and 6 months accelerated) B: CHL0411028, CHL0411029, CHL0411030 • Packed in aluminium bottle under inert gas (36months real time and 6 months accelerated) B: CHL040802, CHL0408021, CHL0408022
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the brand leader that is Indrop D Injection M/s Neutro Pharmaceutical Pvt Ltd Pakistan. B. No. HP933, by performing quality tests.
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Sichuan Yuxin Pharmaceutical Co. Ltd No 51 West Section Of Changjiang Road Shifang Economic Development Zone (Southern District) Sichuan China.		
API Lot No.	VD3210701		
Description of Pack (Container closure system)	Clear glass USP type 1 in unit carton (1×1's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	DK 01	DK 02	DK 03
Batch Size	100 Ampoule	100 Ampoule	100 Ampoule
Manufacturing Date	14-09-2021	14-09-2021	14-09-2021
Date of Initiation	16-09-2021	16-09-2021	16-09-2021

No. of Batches	03	
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML No. 20160429 valid till 1/10/2025 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of AD attested invoice No. XS21804581 dated 21/08/2021 dy. No. 3571/2021-DRAP dated 09/09/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Observations	Response
1	Please submit the Compliance Record of HPLC software 21CFR & audit trail reports on product testing	"We are using EZ chrome light software for our testing which is in 21CFR compliance". The firm has submitted the audit trail report.
2	Provide analytical method validation/verifications studies including specificity, precision and accuracy for Drug substance along with the method of analysis used for routine analysis of drug substance.	Analytical verification studies for drug substance from drug product manufacturer are submitted including specificity, accuracy and precision.
3	The submitted stability data for the applied product is till 3rd month time point, please submit stability data till 6 months. Moreover, justification is required is require for not performing the tests for sterility and bacterial endotoxins in stability studies.	The applicant has submitted stability data at 6th month time for all the 03 batches for accelerated and real time stability studies. The tests for sterility and BET are included at 6th month time point testing.
4	Provide documents confirming the import/procurement of drug substance used for the development of applied product.	Copy of ADC attested invoice No. XS21804581 dated 21/08/2021 dy. No. 3571/2021-DRAP dated 09/09/2021.
5	Provide complete calculations for potency adjustment.	Calculations for potency adjustment is submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot has been granted with Drug Manufacturing License vide letter No. F.1-5/2017-Lic dated 17/09/2021.

Dry Powder Injectable Section (Cephalosporin):

The firm has applied for 01 molecule and 07 product in Dry Powder Injectable Section (Cephalosporin).

13.	Name, address of Applicant / Marketing Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17593: 16/06/2022
	Details of fee submitted	PKR 30,000/-: 13/05/2022
	The proposed proprietary name / brand name	QXON 250mg Injection IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……250mg
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)

	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. 1% lignocaine hydrochloride injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Oxidil 250mg Injection of M/s Sami Pharmaceuticals.

	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/039/2021		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	30-10-2021	30-10-2021	30-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying purchase of 10Kg Ceftriaxone sodium (sterile) dated 28-09-2021 lot number 00421/039/2021 from Pharmagen Limited.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	Firm has submitted report of verification studies of the analytical method of drug substance performed by Qadir Pharmaceuticals.
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	Justify why pharmaceutical equivalence is not conducted against the innovator product for 250mg Injection	Firm has submitted that since the reference product is not available in market therefore we have used comparator product for pharmaceutical equivalence studies.
5.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
6.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies different analytical method for each strength.	Firm has submitted that we have performed verification studies for all strengths and route of administration. Firm has submitted verification studies for each product.
7.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
14.	Name, address of Applicant / Mar keting Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17594: 16/06/2022
	Details of fee submitted	PKR 30,000/-: 15/05/2022
	The proposed proprietary name / brand name	QXON 500mg Injection IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……500mg
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized

		information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. 1% lignocaine hydrochloride injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Rocephin 500mg Injection of M/s Martin Dow Ltd Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.
STABILITY STUDY DATA		

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/039/2021		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	30-10-2021	30-10-2021	30-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.

	procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	Firm has submitted report of verification studies of the analytical method of drug substance performed by Qadir Pharmaceuticals.
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
5.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies different analytical method for each strength.	Firm has submitted that we have performed verification studies for all strengths and route of administration. Firm has submitted verification studies for each product.
6.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

15.	Name, address of Applicant / Mar keting Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17597: 16/06/2022
	Details of fee submitted	PKR 30,000/-: 13/05/2022
	The proposed proprietary name / brand name	QXON 1g Injection IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……1g
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities,

		physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. 1% lignocaine hydrochloride injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Rocephin 1g Injection of M/s Martin Dow Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
API Lot No.	00421/039/2021
Description of Pack (Container closure system)	Glass vials
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	29-10-2021	29-10-2021	29-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both	Firm has submitted report of verification studies of the analytical method of drug substance performed by Qadir Pharmaceuticals.

	compendial as well as non-compendial drug substance(s) shall be submitted".	
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
5.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies different analytical method for each strength.	Firm has submitted that we have performed verification studies for all strengths and route of administration. Firm has submitted verification studies for each product.
6.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

16.	Name, address of Applicant / Mar keting Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17592: 16/06/2022
	Details of fee submitted	PKR 30,000/-: 13/05/2022
	The proposed proprietary name / brand name	QXON 250mg Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……250mg
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real

		time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. water for injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Oxidil 250mg Injection of M/s Sami Pharma.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/039/2021		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	30-10-2021	30-10-2021	30-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	Firm has submitted report of verification studies of the analytical method of drug substance performed by Qadir Pharmaceuticals.
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	Justify why pharmaceutical equivalence is not conducted against the innovator product for 250mg Injection	Firm has submitted that since the reference product is not available in market therefore we have used comparator product for pharmaceutical equivalence studies.

5.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
6.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies different analytical method for each strength.	Firm has submitted that we have performed verification studies for all strengths and route of administration. Firm has submitted verification studies for each product.
7.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

17.	Name, address of Applicant / Marketing Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17595: 16/06/2022
	Details of fee submitted	PKR 30,000/-: 13/05/2022

	The proposed proprietary name / brand name	QXON 500mg Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……500mg
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control,

		process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. water for injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Rocephin 500mg Injection of M/s Martin Dow Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/039/2021		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	30-10-2021	30-10-2021	30-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg

		Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	Firm has submitted report of verification studies of the analytical method of drug substance performed by Qadir Pharmaceuticals.
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
5.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies	Firm has submitted that we have performed verification studies for all strengths and route of administration.

	different analytical method for each strength.	Firm has submitted verification studies for each product.
6.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

18.	Name, address of Applicant / Mar keting Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17596 16/06/2022
	Details of fee submitted	PKR 30,000/-: 13/05/2022
	The proposed proprietary name / brand name	QXON 1g Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……1g
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. water for injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator

		i.e. Rocephin 1g Injection of M/s Martin Dow Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/039/2021		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	29-10-2021	29-10-2021	29-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of	Firm has submitted record of digital data logger for temperature and humidity

	stability chambers (real time and accelerated)	monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	Firm has submitted report of verification studies of the analytical method of drug substance performed by Qadir Pharmaceuticals.
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
5.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies different analytical method for each strength.	Firm has submitted that we have performed verification studies for all strengths and route of administration. Firm has submitted verification studies for each product.
6.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the**

commitment submitted in the registration application.		
19.	Name, address of Applicant / Mar keting Authorization Holder	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Name, address of Manufacturing site.	M/s Qadir Pharmaceuticals, Veerum Fateh Garh Sahuwala Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000944) by way of formulation dated 14-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 which specifies Dry powder injectable (Cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17598 : 16/06/2022
	Details of fee submitted	PKR 30,000/-: 13/05/2022
	The proposed proprietary name / brand name	QXON 2g Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……2g
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical

		procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. water for injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Oxidil 2g Injection of M/s Sami Pharma.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
API Lot No.	00421/039/2021
Description of Pack (Container closure system)	Glass vials

Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	29-10-2021	29-10-2021	29-10-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Qadir Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 02-09-2020. The GMP certificate was granted based on inspection dated 22-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from both API manufacturer as well as Qadir Pharmaceuticals.
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document	Firm has submitted report of verification studies of the analytical

	approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	method of drug substance performed by Qadir Pharmaceuticals.
3.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2.S.5.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	USP monograph specifies two different sample solutions as well as two different analysis, calculation formula and acceptance criteria for assay test, while your specifications does not specify two different tests and acceptance criteria for assay and you have released your batches with only 1 type of assay results. Justify why your specifications, analytical method and practices of batch release are not aligned with USP monograph recommendations.	Firm has submitted that we have performed both these tests as per USP but at different stages. As our drug product is constituted solution therefore we have used the test of constituted solution (sample solution 2) at finished product stage. The other test specified in USP (Sample solution 1) was performed at drug substance stage before filling in the drug product.
5.	Justify how a single validation studies are used for all strengths of ceftriaxone injection since USP monograph specifies different analytical method for each strength.	Firm has submitted that we have performed verification studies for all strengths and route of administration. Firm has submitted verification studies for each product.
6.	Provide documents for the procurement of relevant lot(s) of API used in the manufacturing of 3 batches of drug product for which stability studies data is submitted in section 3.2.P.8.3.	API is locally procured from M/s Pharmagen.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

New Section

M/s Ferozsons Laboratories Ltd, Amangarh Nowshera was granted additional Tablet General section vide letter no.F.3-14/2004-Lic(Pt) dated 09/04/2020.

The firm has applied for 04 products and 02 molecules.

20.	Name, address of Applicant / Marketing Authorization Holder	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Status of the applicant	☑ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☑ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☑ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 18581 dated 27/06/2022
	Details of fee submitted	PKR 30,000/- dated 10/05/2022
	The proposed proprietary name / brand name	Vonesta 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan as fumarate……10mg
	Pharmaceutical form of applied drug	Round, Film coatedTablet
	Pharmacotherapeutic Group of (API)	PPIs
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	10's, 14's, 20's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablets (10mg+20mg) approved by PMDA
	For generic drugs (me-too status)	Vonozan 10mg by Getz Pharma
	GMP status of the Finished product manufacturer	GMP certificate No. F.11-6/2019-DRAP -06 granted on 29-01-2019 valid upto 25-01-2022. Tablet section (General) approved vide letter No.F.3-14\2004-Lic Dated: 08-04-2015 is submitted
	Name and address of API manufacturer.	M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP road, At & Post: Karakhadi 391450 Taluka Padra, District Vadodara Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity (I, II, III, IV, V, VI) individual

		impurities, specifications, analytical procedures for assay of drug substance and content of Fumaric Acid along with the verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (VPF/RD/31800819, VPF/RD/31810819, VPD/RD/31820819)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure for active and related substances and relevant verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The applicant has established pharmaceutical equivalence against Takecab Tablet 10mg (B: 517929) manufactured by M/s Takeda Pharamceuticals, PMDA Japan. Comparative dissolution profile against the innovator's product (Takecab 10mg, B:571929) in all the 03 media (0.1N HCl, acetate Buffer, Phosphate Buffer) is submitted. F2 values are more than 50.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP road, At & Post: Karakhadi 391450 Taluka Padra, District Vadodara Gujarat, India.		
API Lot No.	VPF/30021020		
Description of Pack (Container closure system)	03 Alu-pvdc blisters of 10 tablets packed in cardboard box (30 tablets)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	VFTTab-001	VFTTab-002	VFTTab-003
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	08/2021	08/2021	08/2021
Date of Initiation	17/08/2021	17/08/2021	17/08/2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empagen tablet 10mg Approved in 294th meeting of RB Inspection date: 25/10/20219 Asp per report, the HPLC system is 21CFR compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 22043267 issued on the basis of inspection conducted on 04-05/04/2022 valid till 17/04/2025 issued by food & Drugs Control Administration Gujarat.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice No. EXP/1/21-22/0108 dated 07/06/2021 (Dy. No. 1771 dated 24/06/2021).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	submitted
Remarks by PEC-I:		
Sr. No.	**Observations**	**Response**
1	As per the unit formula the final quantity of Vonoprazan fumarate to be dispensed is 13.563mg, please justify considering the assay value 98.2% (as is basis).	The firm has submitted revised calculations for potency adjustment. The amount of API to be dispensed is 13.605mg while 13.563mg was dispensed without considering w.c (water content). The difference is 0.31%.
2	Please justify the selection of dissolution parameters that is dissolution medium, dissolution apparatus, rpm etc.	The firm has stated that dissolution data is not available in any reference regulatory authority nor the drug product is pharmacopoeial, however following justification is provided. • 6.8 Phopshate Buffer (Medium), The durg substance is found to be highly soluble in all physiological pH ranges. • USP type II apparatus (as per USP <1092> • 50rpm-lowest rpm for paddle apparatus • 900mL volume • 15mins sampling time-on the basis of CDP
Decision: The Board was apprised that the calculations for potency adjustment are not appropriate. The Board discussed the matter in detail and decided to approve the case with the directions that the applicant will adopt the correct calculations for potency adjustment for commercial manufacturing.		

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
21.	Name, address of Applicant / Marketing Authorization Holder	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Status of the applicant	☑ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☑ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☑ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 18582 dated 27/06/2022
	Details of fee submitted	PKR 30,000/- dated 10/05/2022
	The proposed proprietary name / brand name	Vonesta 20mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan as fumarate……20mg
	Pharmaceutical form of applied drug	Round, Film coatedTablet
	Pharmacotherapeutic Group of (API)	PPIs
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	10's, 14's, 20's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablets (10mg+20mg) approved by PMDA
	For generic drugs (me-too status)	Vonozan 20mg by Getz Pharma
	GMP status of the Finished product manufacturer	GMP certificate No. F.11-6/2019-DRAP -06 granted on 29-01-2019 valid upto 25-01-2022. Tablet section (General) approved vide letter No.F.3-14\2004-Lic Dated: 08-04-2015 is submitted
	Name and address of API manufacturer.	M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP road, At & Post: Karakhadi 391450 Taluka Padra, District Vadodara Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity (I, II, III, IV, V, VI) individual impurities, specifications, analytical procedures for assay of drug substance and content of Fumaric Acid along with the verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (VPF/RD/31800819, VPF/RD/31810819, VPD/RD/31820819)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure for active and related substances and relevant verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The applicant has established pharmaceutical equivalence against Vonozan 20mg (B: 006FF9) manufactured by M/s Getz Pharma. Comparative dissolution profile against the innovator's product (Vonozan 20mg (B: 006FF9) manufactured by M/s Getz Pharma/) in all the 03 media (0.1N HCl, acetate Buffer, Phosphate Buffer) is submitted. F2 values are more than 50.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP road, At & Post: Karakhadi 391450 Taluka Padra, District Vadodara Gujarat, India.
API Lot No.	VPF/30021020

Description of Pack (Container closure system)	03 Alu-pvdc blisters of 10 tablets packed in cardboard box (30 tablets)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	VFTTab-001	VFTTab-002	VFTTab-003
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	08/2021	08/2021	08/2021
Date of Initiation	17/08/2021	17/08/2021	17/08/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empagen tablet 10mg Approved in 294th meeting of RB Inspection date: 25/10/20219 Asp per report, the HPLC system is 21CFR compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 22043267 issued on the basis of inspection conducted on 04-05/04/2022 valid till 17/04/2025 issued by food & Drugs Control Administration Gujarat.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice No. EXP/1/21-22/0108 dated 07/06/2021 (Dy. No. 1771 dated 24/06/2021).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	submitted

Remarks by PEC-I:

Sr. No.	Observations	Response
1	As per the unit formula the final quantity of Vonoprazan fumarate to be dispensed is 27.127mg, please justify considering the assay value 98.2% (as is basis).	The firm has submitted revised calculations for potency adjustment. The amount of API to be dispensed is 27.210mg while 27.127mg was dispensed without considering w.c. The difference is 0.305%.
2	Please justify the selection of dissolution parameters that is	The firm has stated that dissolution data is not available in any reference regulatory authority

	dissolution medium, dissolution apparatus, rpm etc.	nor the drug product is pharmacopoeial, however following justification is provided. • 6.8 Phopshate Buffer (Medium), The durg substance is found to be highly soluble in all physiological pH ranges. • USP type II apparatus (as per USP <1092> • 50rpm-lowest rpm for paddle apparatus • 900mL volume • 15mins sampling time-on the basis of CDP
3	Pharmaceutical equivalence testing and CDP have been performed against Vonozan by Getz Pharma while the said testing should be performed against the innovator's / reference product, please clarify.	The firm has submitted the required data of CDP and pharmaceutical equivalence against the reference product that is Takecab 20mg tablet (B:517196) PMDA Japan approved.
Decision: The Board was apprised that the calculations for potency adjustment are not appropriate. The Board discussed the matter in detail and decided to approve the case with the directions that the applicant will adopt the correct calculations for potency adjustment for commercial manufacturing. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
22.	Name, address of Applicant / Marketing Authorization Holder	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Status of the applicant	☑ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☑ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☑ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8301 dated 30/03/2022
	Details of fee submitted	PKR 30,000/- dated 20/01/2022
	The proposed proprietary name / brand name	XIna 2.5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Apixaban……..2.5mg
	Pharmaceutical form of applied drug	Round, immediate release, film coated tablet

	Pharmacotherapeutic Group of (API)	Anti-thormbotic agent
	Reference to Finished product specifications	Innovator's specs
	Proposed Pack size	10's, 14's, 20's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Eliquis (2.5 & 5mg) Tablet, USFDA Approved.
	For generic drugs (me-too status)	Zilero 2.5mg tablet by M/s Pharmevo Reg. No. 105254
	GMP status of the Finished product manufacturer	GMP certificate No. F.11-6/2019-DRAP -06 granted on 29-01-2019 valid upto 25-01-2022. Tablet section (General) approved vide letter No.F.3-14\2004-Lic Dated: 08-04-2015 is submitted
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Fengxin 330700, Jiangxi Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities and residual solvents, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	It is classified as BCS class II drug. No official monograph is available. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures for assay of drug substance and content of Fumaric Acid along with the verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (20180201Y, 20180202Y, 20180203Y)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure for active and related substances and

		relevant verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Comparative dissolution profile is submitted agaisnt the innovator's product Eliquis 2.5mg tablet by M/s Bristol Mayors Squib, USFDA Approved in all the 03 media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer. (B:ABB2239). Pharmaceutical equivalence is established against the innovator's product (Eliquis 5mg Tablet) by performing all the quality tests B:ABB6690.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Fengxin 330700, Jiangxi Province, China.		
API Lot No.	10200301Y		
Description of Pack (Container closure system)	Alu-Pvdc blister, Packed in outer (secondary) cardbox.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ADTab-001	ADTab-002	ADTab-003
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	03/21	03/21	03/21
Date of Initiation	05/04/2021	05/04/2021	05/04/2021
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Empagen tablet 10mg Approved in 294th meeting of RB Inspection date: 25/10/20219 Asp per report, the HPLC system is 21CFR compliant.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Pharmaceutical Production License No. GAN20160125 is submitted which is valid till 26/11/2025 issued by provincial Medical Products Administration.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice is submitted (Dy. No. 5160 dated 30/12/2020, DRAP Peshawar).

10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	submitted
Remarks by PEC-I:		
Sr. No.	**Observations**	**Response**
1	Please provide the reference for adaptation of dissolution specifications including paddle speed (75rpm).	The firm has provided reference from USFDA dissolution data base and provided the following weblink. https://www.accessdata.fda.gov/scripts/cder/dissolution/dsp_SearchResults.cfm
2	Provide justification of all the specifications in the relevant section (3.2.P.5.6).	The firm has provided justification for specification for drug product is submitted.
3	Calculations for potency adjustment.	The difference in the calculation for potency adjustment is 0.596%.
Decision: The Board was apprised that the calculations for potency adjustment are not appropriate. The Board discussed the matter in detail and decided to approve the case with the directions that the applicant will adopt the correct calculations for potency adjustment for commercial manufacturing. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
23.	Name, address of Applicant / Marketing Authorization Holder	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Limited P.O Ferozsons, Amangarh, Nowshera, Khyber Pakhtunkhwa-Pakistan
	Status of the applicant	☑ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☑ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☑ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8302 dated 30/03/2022

	Details of fee submitted	PKR 30,000/- dated 20/01/2022
	The proposed proprietary name / brand name	XIna 5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Apixaban……..5mg
	Pharmaceutical form of applied drug	Round, immediate release, film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-thormbotic agent
	Reference to Finished product specifications	Innovator's specs
	Proposed Pack size	10's, 14's, 20's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Eliquis (2.5 & 5mg) Tablet, USFDA Approved.
	For generic drugs (me-too status)	Zilero 5mg tablet by M/s Pharmevo Reg. No. 105255
	GMP status of the Finished product manufacturer	GMP certificate No. F.11-6/2019-DRAP -06 granted on 29-01-2019 valid upto 25-01-2022. Tablet section (General) approved vide letter No.F.3-14\2004-Lic Dated: 08-04-2015 is submitted
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Fengxin 330700, Jiangxi Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities and residual solvents, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	It is classified as BCS class II drug. No official monograph is available. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures for assay of drug substance and content of Fumaric Acid along with the verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months of 3 batches

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (20180201Y, 20180202Y, 20180203Y)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure for active and related substances and relevant verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Comparative dissolution profile is submitted against the innovator's product Eliquis 5mg tablet by M/s Bristol Mayors Squib, USFDA Approved in all the 03 media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer. (B:ABB6690). Pharmaceutical equivalence is established against the innovator's product (Eliquis 5mg Tablet) by performing all the quality tests B:ABB6690.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Fengxin 330700, Jiangxi Province, China.		
API Lot No.	10200301Y		
Description of Pack (Container closure system)	Alu-Pvdc blister, Packed in outer (secondary) cardbox.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ADTab-004	ADTab-005	ADTab-006
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	03/21	03/21	03/21
Date of Initiation	05/04/2021	05/04/2021	05/04/2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empagen tablet 10mg Approved in 294th meeting of RB Inspection date: 25/10/20219 Asp per report, the HPLC system is 21CFR compliant.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Pharmaceutical Production License No. GAN20160125 is submitted which is valid till 26/11/2025 issued by provincial Medical Products Administration.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice is submitted (Dy. No. 5160 dated 30/12/2020, DRAP Peshawar).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	submitted
Remarks by PEC-I:		
Sr. No.	**Observations**	**Response**
1	Please provide the reference for adaptation of dissolution specifications including paddle speed (75rpm).	The firm has provided reference from USFDA dissolution data base and provided the following weblink. https://www.accessdata.fda.gov/scripts/cder/dissolution/dsp_SearchResults.cfm
2	Provide justification of all the specifications in the relevant section (3.2.P.5.6).	The firm has provided justification for specification for drug product is submitted.
3	Calculations for potency adjustment.	The difference in the calculation fir potency adjustment is 0.596%.
Decision: The Board was apprised that the calculations for potency adjustment are not appropriate. The Board discussed the matter in detail and decided to approve the case with the directions that the applicant will adopt the correct calculations for potency adjustment for commercial manufacturing. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		

Case No. II: Cases of local manufacturing submitted on Form 5F

24.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare Pvt., Ltd., Plot # 33, Sundar Industrial Estate Lahore.
	Name, address of Manufacturing site.	M/s Horizon Healthcare Pvt., Ltd., Plot # 33, Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29987 dated 03-11-2021
	Details of fee submitted	PKR 30,000/-: dated 27-10-2021
	The proposed proprietary name / brand name	Azilsartan Medoxomil 40mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Azilsartan Medoxomil as Potassium…….40mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-Hypertensive
	Reference to Finished product specifications	In-House
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Edarbi Tablet (40mg, 80mg) by Arbor Pharms LLC, USFDA Approved.
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 103/2020-DRAP (AD-1998036-5147) issued on the basis of inspection conducted on 18/06/2020 Is submitted,
	Name and address of API manufacturer.	M/s CTX Life Sciences Pvt. Ltd., Block No: 251/P, 252/P, 253 to 255, 256/P, 258/P, 276/P, 277, 278/P, 279 to 282, 283/P, 284/P, GIDC Sachin, Surat-394 230 Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, impurity testing for impurity A-G, analytical procedure and its

		verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 72 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months B: AK180002, AK180003, AK180004
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Comparative dissolution profile is submitted against Edarbi 40mg tablet in 0.1N HCl, Phosphate Buffer and Acetate Buffer. The values of F2 are in acceptable range (B: 483822). Pharmaceutical equivalence is established against Edarbi 40mg tablet (B: 483822) by performing all the quality tests.
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s CTX Life Sciences Pvt. Ltd., Block No: 251/P, 252/P, 253 to 255, 256/P, 258/P, 276/P, 277, 278/P, 279 to 282, 283/P, 284/P, GIDC Sachin, Surat-394 230 Gujarat, India.		
API Lot No.	19AK00013		
Description of Pack (Container closure system)	Aluminium blisters integrated with desiccant.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	MAM-001	MAM-002	MAM-001
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	04-2022	04-2022	04-2022
Date of Initiation	08/04/2020	18/04/2020	21/04/2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate No. 19061470 valid till 01/07/2022 issued by Food & Drugs Control Administration. Copy of retention of License to Manufacture No. G/25/1723 valid till 23/01/2026 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice No. EI/3092100609 dated 23/09/2019 (Dy. No. 1572/2020-DRAP dated 27/01/2020) is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide the documents (invoice etc) confirming import of drug substance for product development.	The firm has submitted copy of attested invoice no. E1/3092100609 dated 23/09/2019 dy. No. 1572/2020-DRAP dated 27/01/2020.
2	Please provide CoA of drug substance for the batch used for product development from the drug product manufacturer along with the analytical procedures used for routine analysis of drug substance.	COA from drug product manufacturer is submitted for the relevant batch that is used for development of the applied product (B:19AK00013)
3	In section 3.2.P.5.6, please provide justification for the specifications of the applied product.	Submitted.
4	Provide complete calculations for potency adjustment considering the assay value of the drug substance, salt factor etc.	Factor: 1.067 Assay (Anhydrous): 100.06% Loss on drying: 0.37% Assay As-is: 99.69% Batch size: 1500 tab Quantity to be dispensed: 42.813mg / tab For 1500 tablets: 64.219g

Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/-for revision of specifications

and differential fee of Rs. 45,000/- since the applied product is new drug as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
25.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare Pvt., Ltd., Plot # 33, Sundar Industrial Estate Lahore.
	Name, address of Manufacturing site.	M/s Horizon Healthcare Pvt., Ltd., Plot # 33, Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29988 dated 03-11-2021
	Details of fee submitted	PKR 30,000/-: dated 27-10-2021
	The proposed proprietary name / brand name	Azilsartan Medoxomil 80mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Azilsartan Medoxomil as Potassium…….80mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-Hypertensive
	Reference to Finished product specifications	In-House
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Edarbi Tablet (40mg, 80mg) by Arbor Pharms LLC, USFDA Approved.
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 103/2020-DRAP (AD-1998036-5147) issued on the basis of inspection conducted on 18/06/2020 Is submitted,
	Name and address of API manufacturer.	M/s CTX Life Sciences Pvt. Ltd., Block No: 251/P, 252/P, 253 to 255, 256/P, 258/P, 276/P, 277, 278/P, 279 to 282, 283/P, 284/P, GIDC Sachin, Surat-394 230 Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, impurity testing for impurity A-G, analytical procedure and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 72 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months B: AK180002, AK180003, AK180004
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Comparative dissolution profile is submitted against Edarbi 80mg tablet in 0.1N HCl, Phosphate Buffer and Acetate Buffer. The values of F2 are in acceptable range (B: 483803). Pharmaceutical equivalence is established against Edarbi 40mg tablet (B: 483803) by performing all the quality tests.
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s CTX Life Sciences Pvt. Ltd., Block No: 251/P, 252/P, 253 to 255, 256/P, 258/P, 276/P, 277, 278/P, 279 to 282, 283/P, 284/P, GIDC Sachin, Surat-394 230 Gujarat, India.
API Lot No.	19AK00013
Description of Pack	Aluminium blisters integrated with desiccant.

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	HAM-001	HAM-002	HAM-001
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	04-2022	04-2022	04-2022
Date of Initiation	08/04/2020	18/04/2020	21/04/2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate No. 19061470 valid till 01/07/2022 issued by Food & Drugs Control Administration. Copy of retention of License to Manufacture No. G/25/1723 valid till 23/01/2026 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice No. EI/3092100609 dated 23/09/2019 (Dy. No. 1572/2020-DRAP dated 27/01/2020) is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide the documents (invoice etc) confirming import of drug substance for product development.	The firm has submitted copy of attested invoice no. E1/3092100609 dated 23/09/2019 dy. No. 1572/2020-DRAP dated 27/01/2020.
2	Please provide CoA of drug substance for the batch used for product development from the drug product	COA from drug product manufacturer is submitted for the relevant batch that is used

	manufacturer along with the analytical procedures used for routine analysis of drug substance.	for development of the applied product (B:19AK00013)
3	In section 3.2.P.5.6, please provide justification for the specifications of the applied product.	Submitted.
4	Provide complete calculations for potency adjustment considering the assay value of the drug substance, salt factor etc.	Factor: 1.067 Assay (Anhydrous): 100.06% Loss on drying: 0.37% Assay As-is: 99.69% Batch size: 1500 tab Quantity to be dispensed: 85.63mg / tab For 1500 tablets: 128.438g

Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/-for revision of specifications and differential fee of Rs. 45,000/- since the applied product is new drug as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

26.	Name, address of Applicant / Marketing Authorization Holder	M/s NovaMed Pharmaceuticals (pvt) ltd., 28-km, Ferozepur road, Lahore.
	Name, address of Manufacturing site.	M/s NovaMed Pharmaceuticals (pvt) ltd., 28-km, Ferozepur road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1083 dated 20-10-2021
	Details of fee submitted	PKR 30,000/-: dated 08-10-2021
	The proposed proprietary name / brand name	Empozin 12.5/850mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….12.5mg Metformin HCl……...850mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Drugs used in diabetics (Combination of oral blood glucose lowering drugs)
	Reference to Finished product specifications	In-House
	Proposed Pack size	10’s, 14’s

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy Tablet (5/850, 5/1000, 12.5/500, 12.5/850, 12.5/1000), EMA approved.
	For generic drugs (me-too status)	Adrance-M Tablet 12.5mg + 850mg by M/s Atco Laboratories, Reg. No. 095147
	GMP status of the Finished product manufacturer	Last inspection report dated 06/08/2021 is submitted.
	Name and address of API manufacturer.	Empagliflozin: Jiangsu Yongan Pharmacetuical Co., Limited, No. 18 237 provincial road, economic development zone, Huaian Jiangsu, China. Metformin HCl: Aarti Drugs Limited, Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, 396 155 Dist.: Valsad, Gujarat, INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substances and drug product is submitted.
	Module III (Drug Substance)	Empagliflozin and Metformin are classified as BCS class III drugs. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substances that is Empagliflozin and Metformin.
	Stability studies	Empagliflozin: • 36 months real time stability studies conducted at 30°C ± 2°C / 65% ± 5%RH of 03 batches. • 06 months accelerated stability studies conducted at 40°C ± 2°C / 75% ± 5%RH of 03 batches Batches: 130701, 13702, 130801 Metformin HCl:

		• 60 months real time stability studies conducted at 30°C ± 2°C / 65% ± 5%RH of 03 batches. • 06 months accelerated stability studies conducted at 40°C ± 2°C / 75% ± 5%RH of 03 batches Batches: MET10040109, MET10040110 & MET10040111
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence by performing all the quality tests against the reference product Synjardy 12.5/850mg Batch No. 04891. Comparative dissolution profile is submitted against the reference product Synjardy (B:04891) in all the 03 media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer. The values of F2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Empagliflozin: Jiangsu Yongan Pharmacetuical Co., Limited, No. 18 237 provincial road, economic development zone, Huaian Jiangsu, China. Metformin HCl: Aarti Drugs Limited, Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, 396 155 Dist.: Valsad, Gujarat, INDIA.		
API Lot No.	4500-202003001 (Empagliflozin) MEF/11020379 (Metfromin)		
Description of Pack (Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	RD/PR21-059/T1/S1	RD/PR21-059/T1/S2	RD/PR21-059/T1/S3

Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	28-05-2021	28-05-2021	28-05-2021
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any response	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificates; Empagliflozin: Copy of GMP certificate issued by Huaian Pharmaceutical Industry association is submitted valid till 14-01/2024. Metformin HCl: Copy of GMP certificate No. 6096236 valid till 01-11-2021 issued by FDA Maharashtra, India.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of ADC attested invoice No. ZY20052001G/W dated 20/05/2020 dy. No. 7093/2020-DRAP dated 09/06/2020 is submitted for Empagliflozin. Copy of invoice no. EXP/3236/20-21 dated 05/03/2021 dy. No 4485/2021-DRAP dated 26/03/2021 for Metformin is submitted.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	
Remarks of Evaluator-I:			
Sr. No.	**Observations**	**Response**	
1.	Provide GMP certificate / drug manufacturing license of Empagliflozin drug substance manufacturer issued by the relevant authority. The submitted copy of GMP certificate is neither verifiable nor it is issued by relevant authority, conversely the submitted certificate is issued by Industry Association.	Copy of DML no. SU2016324 valid till 06-12-2025 issued by Jiangsu medical products administration.	
2.	Submitted data of analytical method validation studies for Empagliflozin drug substance does not contain the test	The Firm has provided the details of specificity testing for analytical method validation studies for Empagliflozin drug	

	for Specificity parameter performed by drug product manufacturer. Please provide the required data. Moreover, clarification is required regarding the criteria / basis of naming the dilutions (as 60%, 80%, 100% 160% etc) for performing the accuracy and linearity tests.	substance performed by drug product manufacturer.
3.	USP-43 describes the HPLC assay method for analysis of Metformin HCl but you have performed the required studies for drug substance including analytical method validation / verification studies using titration method, please clarify.	"we have tested Metformin as per USP 42 where assay is given by titration method. Accordingly, we have performed validation of the method". The firm has not performed the analysis as per USP 43 (HPLC method) for estimation of Metformin.
4.	The detail of capsule filling machine is provided in 3.2.P.3 while detail regarding tablet manufacturing facility is required.	Revised manufacturing process is submitted.
5.	As per submitted dossier, the manufacturing method is not in detail, it provides a very brief details of different steps involved in the manufacturing of the applied product. Please provide detailed manufacturing method with the detail of each step including wet granulation.	The firm has provided the manufacturing method.
6.	Justify the dissolution that is 80% in 30 minutes while as per the available literature the innovator has specified 20 minutes for achieving the required dissolution limit.	"After reviewing the dissolution release trend in CDP report it is evident that more than 80% drug is released in 20 minutes so we are revising our current acceptance specification limit to NLT 80% in 20 minutes instead of 30minute". The firm has submitted the revised specifications without performing the dissolution test according to new specs on any of the batch.
7.	Justification regarding the performance of specificity parameter of method validation studies for drug product is required where the test is performed without spiking by taking the blank solution as reference.	"ICH Q2R1, specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix etc". "We have rub placebo containing matrix and there is no interference observed in analytical method validation of product".
8.	The submitted stability data is till 3rd month time point while the required data should be till 6th month time point, please submit the remaining data.	The firm has submitted stability data till 6th month time point.
9.	Please provide documents confirming the import of drug substances (Empagliflozin and Metformin) (e.g. invoice) along with the relevant COAs	Copy of ADC attested invoice No. ZY20052001G/W dated 20/05/2020 dy. No. 7093/2020-DRAP dated 09/06/2020 is submitted for Empagliflozin.

	from drug substance manufacturers as well as from the finished product manufacturer.	Copy of invoice no. EXP/3236/20-21 dated 05/03/2021 dy. No 4485/2021-DRAP dated 26/03/2021 for Metformin is submitted.
10.	Provide detail of container-closure of the applied product since container-closure is described very briefly and little information is presented in the submitted dossier.	Alu-Alu blister, each containing white colored, oval shaped film coated tablets having break line on one side and the other side is plain. 10's, 20's, 30's, 14's, 28's.
Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **For commercial manufacturing, the manufacturer will perform analytical testing for Metformin as per USP 43.**		
27.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (pvt) Ltd. plot No. 204-205, Industrial Triangle, Kahuta road, Islamabad.
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (pvt) Ltd. plot No. 204-205, Industrial Triangle, Kahuta road, Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26922 dated 29-09-2021
	Details of fee submitted	PKR 30,000/-: dated 24-09-2021
	The proposed proprietary name / brand name	Myotan 40mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Azilsartan Medoximil as Potassium…….40mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-Hypertensive
	Reference to Finished product specifications	In-House
	Proposed Pack size	14's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	**4** Edarbi Tablet (40mg, 80mg) by Arbor Pharms LLC, USFDA Approved.
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	GMP certificate No. F.3-16/2018-Addl.Dir.(QA&LT) dated 24/12/2018.
	Name and address of API manufacturer.	M/s Ami Life Sciences Private limited, Block No. 82/B, ECP road, At & Post: Karakhadi-391450, Taluka: Padra, District Vadodara Gujrrat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months B: AZP/50031216, AZP/50041216, AZP50051216
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against Edarbi Tablet 40mg, USFDA Approved B. No. 11701856, by performing quality tests. Comparative Dissolution Testing is performed against the same brand.

	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.	
STABILITY STUDY DATA			
Manufacturer of API	M/s Ami Life Sciences Private limited, Block No. 82/B, ECP road, At & Post: Karakhadi-391450, Taluka: Padra, District Vadodara Gujarat, India.		
API Lot No.	AZP/50180920		
Description of Pack (Container closure system)	Alu-Alu blister in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	ST21B043	ST21B044	ST21B045
Batch Size	3000 tablets	3000 tablets	3000 tablets
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	21-04-2021	21-04-2021	21-04-2021
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML No. 20160429 valid till 1/10/2025 is submitted.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC attested invoice No. EXP/20-21/0539 dated 16/01/2021 Dy. No. 405 dated 28/01/2021.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	
Remarks of Evaluator-I:			

Sr. No.	Observations	Response
1	The specifications of Drug Substance do not include particle size determination test while the innovator has performed the said test for drug substance, please clarify.	"We have just based the particle size estimation on sieve analysis at vendor sample whose result is attached".
2	Since the drug product does not contain any antimicrobial preservative as well as it does not possess inherent anti-microbial activity nor any such data which supports the microbial inhibitory property of the drug product is provided with the submitted dossier, therefore, as per ICH guidelines (Q6A) microbial limits' acceptance criteria and testing should have been performed. As per available literature of the innovator's product (Edarbi tablet), the manufacturer has established the microbial limits and performed the microbial testing on the commercial batches.	"R&D batches are no true replica of commercial batches as these batches are not sometime manufactured in strict environmental conditions, so the microbial testing results of these R&D batches will not be the actual picture of manufacturing controls conditions that is why we omit this test". "In general practices we are performing the microbial testing on commercial batches. In this case we will also adopt this practice.
3	In section 3.2.P.5.6, please provide justification for the specifications of the applied product.	The firm has submitted justification for the specifications in section 3.2.P.5.6.
4	The submitted stability data is till 3rd month time point, please provide 6 month stability data.	Submitted.
5	Provide documents (invoice) for the procurement of API with approval from DRAP (in case of import).	ADC attested invoice No. EXP/20-21/0539 dated 16/01/2021 Dy. No. 405 dated 28/01/2021.
6	Provide GMP certificate of drug substance manufacturer is required along with the last inspection report/GMP certificate of finished product manufacturer.	Copy of GMP certificate no. 22043267 valid till 17/04/2025 is submitted.
7	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is required while you have submitted the compliance assessment report.	Submitted.

Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/-for revision of specifications and differential fee of Rs. 45,000/- since the applied product is new drug as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

28.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (pvt) Ltd. plot No. 204-205, Industrial Triangle, Kahuta road, Islamabad.
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (pvt) Ltd. plot No. 204-205, Industrial Triangle, Kahuta road, Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26923 dated 29-09-2021
	Details of fee submitted	PKR 30,000/-: dated 24-09-2021
	The proposed proprietary name / brand name	Myotan 80mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Azilsartan Medoxomil as Potassium…….80mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-Hypertensive
	Reference to Finished product specifications	In-House
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Edarbi Tablet (40mg, 80mg) by Arbor Pharms LLC, USFDA Approved.
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	GMP certificate No. F.3-16/2018-Addl.Dir.(QA&LT) dated 24/12/2018.
	Name and address of API manufacturer.	M/s Ami Life Sciences Private limited, Block No. 82/B, ECP road, At & Post: Karakhadi-391450, Taluka: Padra, District Vadodara Gujrrat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies

		of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months B: AZP/50031216, AZP/50041216, AZP50051216
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against Edarbi Tablet 80mg, USFDA Approved B. No. 483829, by performing quality tests. Comparative Dissolution Testing is performed against the same brand.
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API			
API Lot No.	AZP/50180920		
Description of Pack (Container closure system)	Alu-Alu blister in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	ST21B047	ST21B048	ST21B049
Batch Size	3000 tablets	3000 tablets	3000 tablets
Manufacturing Date	02-2021	02-2021	02-2021

Date of Initiation	21-04-2021	21-04-2021	21-04-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML No. 20160429 valid till 1/10/2025 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC attested invoice No. EXP/20-21/0539 dated 16/01/2021 Dy. No. 405 dated 28/01/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Observations	Response
1	The specifications of Drug Substance do not include particle size determination test while the innovator has performed the said test for drug substance, please clarify.	"We have just based the particle size estimation on sieve analysis at vendor sample whose result is attached".
2	Since the drug product does not contain any antimicrobial preservative as well as it does not possess inherent anti-microbial activity nor any such data which supports the microbial inhibitory property of the drug product is provided with the submitted dossier, therefore, as per ICH guidelines (Q6A) microbial limits' acceptance criteria and testing should have been performed. As per available literature of the innovator's product (Edarbi tablet), the manufacturer has established the microbial limits and performed the microbial testing on the commercial batches.	"R&D batches are no true replica of commercial batches as these batches are not sometime manufactured in strict environmental conditions, so the microbial testing results of these R&D bacthes will not be the actual picture of manufacturing controla conditions that is why we omit this test". "In general practices we are performing the microbial testing on commercial batches. In this case we wll alsoadopt this practice.

3	In section 3.2.P.5.6, please provide justification for the specifications of the applied product.	The firm has submitted justification for the specifications in section 3.2.P.5.6.
4	The submitted stability data is till 3rd month time point, please provide 6 month stability data.	Submitted.
5	Provide documents (invoice) for the procurement of API with approval from DRAP (in case of import).	ADC attested invoice No. EXP/20-21/0539 dated 16/01/2021 Dy. No. 405 dated 28/01/2021.
6	Provide GMP certificate of drug substance manufacturer is required along with the last inspection report/GMP certificate of finished product manufacturer.	Copy of GMP certificate no. 22043267 valid till 17/04/2025 is submitted.
7	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is required while you have submitted the compliance assessment report.	Submitted.

Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/-for revision of specifications and differential fee of Rs. 45,000/- since the applied product is new drug as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. II: Import (Human) cases of Form 5F
New Cases:

29.	Name, address of Applicant / Importer	M/s Pfizer Pakistan Limited, B-2, S.I.T.E Karachi.
	Details of Drug Sale License of importer	License No: 030 Address: Pfizer Pakistan Ltd., B-2 SITE Krachi. Address of Godown: 12 Dockyard road West Wharf Karachi C-II-D, SITE Karachi. Validity: 25-02-2023 Status: Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.
	Name, address of manufacturer(s)	M/s Pfizer manufacturing Deutschland GmbH, Betriebsstatte Freiburg, Mooswaldalle 1 79090 Frieburg, Germany.
	Name of exporting country	Germany
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Firm has submitted original, legalized COPP certificate (No. 05/21/157659) dated 28/05/2021 issued by EMA. The applied product is available for free sale in the market of exporting region.	

	The facilities and operations conform to WHO-GMP. • Embassy attested GMP certificate No. De_BW_01_GMP_2021_006 issued on the basis of inspection conducted on 07/10/2020.	
	Details of letter of authorization / sole agency agreement: • Letter of authorization is submitted whereby the MAH has authorized M/s Pfizer Pakistan Limited for MAH activities in Pakistan for the applied product.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 1045 dated 26-10-2021
	Details of fee submitted	PKR 75,000/-: dated 25-08-2021
	The proposed proprietary name / brand name	Ibrance film coated tablet 75mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Palbociclib…….75mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-neoplastic /Protein kinase Inhibitor
	Reference to Finished product specifications	Innovator's specs
	Proposed Pack size	Pack of 21 tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ibrance tablet (75mg, 100mg, 125mg), USFDA Approved.
	For generic drugs (me-too status)	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.

	Name, address of drug substance manufacturer	M/s Pfizer Ireland Pharmaceuticals, Ringaskiddy API plant Ribgaskiddy County Cork, Ireland.
	Module-III Drug Substance:	The drug substance belongs to BCS class II drugs. Crystalline anhydrous form a is the most thermodynamically stable form used in the manufacturing. Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25^{o}C±2 and 60%RH±5% for 36 months of 3 batches • Accelerated stability study is conducted at 40^{o}C±2 and 75%RH±5% for 6 months of 3 batches Batches: E010014100, E010014102, GR06107
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	N/A
	Analytical method validation/verification of product	Analytical validations studies for drug substance as well as for drug product are submitted.
	Container closure system of the drug product	Polyvinylchloride / Oriented Polyamide / Aluminium foil / Polyvinylchloride (PVC/OPA/Al/PVC/Al) blister with aluminium foil lidding card containing 7 tablets. Each pack contains 3 blisters.
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30oC±2 and 75%RH±5% for 24 months of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches

		• Batches: H000013329 S83543, H000013329 S83544, H000013329 S83545 • Shelf life: 2 years
Evaluation by PEC-I: **Indications:** Palbociclib is a kinase inhibitor indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women or in men; or • fulvestrant in patients with disease progression following endocrine therapy		
Sr. No.	**Observations**	**Response**
1	As per the submitted dossier, the manufacturer of Drug Substance is M/s Pfizer Ireland Pharmaceuticals while the provided stability data is from another manufacturer, please clarify.	*"M/s Pfizer limited, Sandwich, UK is a Pfizer R&D site and was sed to manufacture the DSregistration stability batches. An additional Supportive batch was manufactured at Pfizer Inc USA which is another Pfizer R&D site".* The firm has submitted Stability data of 03 batches manufactured at M/s Pfizer Ireland Pharmaceuticals with the following details; • Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 36 motnhs of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches Batches: J11579, J14939, J14940
2	Provide stability study data (Real Time & Accelerated) according to the conditions of zone IV-A of 03 batches till claimed shelf life.	• Real time stability studies have been conducted at 30oC±2 and 75%RH±5% for 24 months of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches Batches: H000013329 S83543, H000013329 S83544, H000013329 S83545
Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.		
30.	Name, address of Applicant / Importer	M/s M/s Pfizer Pakistan Limited, B-2, S.I.T.E Karachi.
	Details of Drug Sale License of importer	License No: 030 Address: Pfizer Pakistan Ltd., B-2 SITE Krachi. Address of Godown: 12 Dockyard road West Wharf Karachi C-II-D, SITE Karachi. Validity: 25-02-2023 Status: Drug License by way of Wholesale

	Name and address of marketing authorization holder (abroad)	M/s Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.
	Name, address of manufacturer(s)	M/s Pfizer manufacturing Deutschland GmbH, Betriebsstatte Freiburg, Mooswaldalle 1 79090 Frieburg, Germany.
	Name of exporting country	Germany
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Firm has submitted original, legalized COPP certificate (No. 05/21/157660) dated 28/05/2021 issued by EMA. The applied product is available for free sale in the market of exporting region. The facilities and operations conform to WHO-GMP. • Embassy attested GMP certificate No. De_BW_01_GMP_2021_006 issued on the basis of inspection conducted on 07/10/2020.	
	Details of letter of authorization / sole agency agreement: • Letter of authorization is submitted whereby the MAH has authorized M/s Pfizer Pakistan Limited for MAH activities in Pakistan for the applied product.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 1044 dated 26-10-2021
	Details of fee submitted	PKR 75,000/-: dated 25-08-2021
	The proposed proprietary name / brand name	Ibrance film coated tablet 100mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Palbociclib…….100mg
	Pharmaceutical form of applied drug	Film coated immediate release tablet
	Pharmacotherapeutic Group of (API)	Anti-neoplastic / Protein kinase Inhibitor
	Reference to Finished product specifications	Innovator's specs
	Proposed Pack size	Pack of 21 tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ibrance tablet (75mg, 100mg, 125mg), USFDA Approved.
	For generic drugs (me-too status)	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information

		related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.
	Name, address of drug substance manufacturer	M/s Pfizer Ireland Pharmaceuticals, Ringaskiddy API plant Ribgaskiddy County Cork, Ireland.
	Module-III Drug Substance:	The drug substance belongs to BCS class II drugs. Crystalline anhydrous form a is the most thermodynamically stable form used in the manufacturing. Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25^{o}C±2 and 60%RH±5% for 36 months of 3 batches • Accelerated stability study is conducted at 40^{o}C±2 and 75%RH±5% for 6 months of 3 batches Batches: E010014100, E010014102, GR06107
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	N/A
	Analytical method validation/verification of product	Analytical validations studies for drug substance as well as for drug product are submitted.
	Container closure system of the drug product	Polyvinylchloride / Oriented Polyamide / Aluminium foil / Polyvinylchloride (PVC/OPA/Al/PVC/Al) blister with aluminium

		foil lidding card containing 7 tablets. Each pack contains 3 blisters.
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30oC±2 and 75%RH±5% for 24 months of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches • Batches: H000013330 S80563, H000013330 S80564, H000013330 S80565 • Shelf life: 2 years

Evaluation by PEC-I:

Indications:

Palbociclib is a kinase inhibitor indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

• an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women or in men; or

• fulvestrant in patients with disease progression following endocrine therapy

Sr. No.	Observations	Response
1	As per the submitted dossier, the manufacturer of Drug Substance is M/s Pfizer Ireland Pharmaceuticals while the provided stability data is from another manufacturer, please clarify.	*"M/s Pfizer limited, Sandwich, UK is a Pfizer R&D site and was sed to manufacture the DSregistration stability batches. An additional Supportive batch was manufactured at Pfizer Inc USA which is another Pfizer R&D site".* The firm has submitted Stability data of 03 batches manufactured at M/s Pfizer Ireland Pharmaceuticals with the following details; • Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 36 motnhs of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches Batches: J11579, J14939, J14940
2	Provide stability study data (Real Time & Accelerated) according to the conditions of zone IV-A of 03 batches till claimed shelf life.	• Real time stability studies have been conducted at 30oC±2 and 75%RH±5% for 24 months of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches Batches: H000013330 S80563, H000013330 S80564, H000013330 S80565

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

31.	Name, address of Applicant / Importer	M/s Pfizer Pakistan Limited, B-2, S.I.T.E Karachi.

	Details of Drug Sale License of importer	License No: 030 Address: Pfizer Pakistan Ltd., B-2 SITE Krachi. Address of Godown: 12 Dockyard road West Wharf Karachi C-II-D, SITE Karachi. Validity: 25-02-2023 Status: Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.
	Name, address of manufacturer(s)	M/s Pfizer manufacturing Deutschland GmbH, Betriebsstatte Freiburg, Mooswaldalle 1 79090 Frieburg, Germany.
	Name of exporting country	Germany
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Firm has submitted original, legalized COPP certificate (No. 05/21/157661) dated 28/05/2021 issued by EMA. The applied product is available for free sale in the market of exporting region. The facilities and operations conform to WHO-GMP. • Embassy attested GMP certificate No. De_BW_01_GMP_2021_006 issued on the basis of inspection conducted on 07/10/2020.	
	Details of letter of authorization / sole agency agreement: • Letter of authorization is submitted whereby the MAH has authorized M/s Pfizer Pakistan Limited for MAH activities in Pakistan for the applied product.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 1043 dated 26-10-2021
	Details of fee submitted	PKR 75,000/-: dated 25-08-2021
	The proposed proprietary name / brand name	Ibrance film coated tablet 125mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Palbociclib…….125mg
	Pharmaceutical form of applied drug	
	Pharmacotherapeutic Group of (API)	Anti-neoplastic / Protein kinase Inhibitor
	Reference to Finished product specifications	Innovator's specs

	Proposed Pack size	Pack of 21 tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ibrance tablet (75mg, 100mg, 125mg), USFDA Approved.
	For generic drugs (me-too status)	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.
	Name, address of drug substance manufacturer	M/s Pfizer Ireland Pharmaceuticals, Ringaskiddy API plant Ribgaskiddy County Cork, Ireland.
	Module-III Drug Substance:	The drug substance belongs to BCS class II drugs. Crystalline anhydrous form a is the most thermodynamically stable form used in the manufacturing. Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25^{o}C±2 and 60%RH±5% for 36 months of 3 batches • Accelerated stability study is conducted at 40^{o}C±2 and 75%RH±5% for 6 months of 3 batches Batches: E010014100, E010014102, GR06107
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	N/A
	Analytical method validation/verification of product	Analytical validations studies for drug substance as well as for drug product are submitted.
	Container closure system of the drug product	Polyvinylchloride / Oriented Polyamide / Aluminium foil / Polyvinylchloride (PVC/OPA/Al/PVC/Al) blister with aluminium foil lidding card containing 7 tablets. Each pack contains 3 blisters.
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30oC±2 and 75%RH±5% for 24 months of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches • Batches: H000013331 S78147, H000013331 S78148, H000013331 S78149 • Shelf life: 2 years

Evaluation by PEC-I:

Indications:

Palbociclib is a kinase inhibitor indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

• an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women or in men; or

• fulvestrant in patients with disease progression following endocrine therapy

Sr. No.	Observations	Response
1	As per the submitted dossier, the manufacturer of Drug Substance is M/s Pfizer Ireland Pharmaceuticals while the provided stability data is from another manufacturer, please clarify.	*"M/s Pfizer limited, Sandwich, UK is a Pfizer R&D site and was sed to manufacture the DSregistration stability batches. An additional Supportive batch was manufactured at Pfizer Inc USA which is another Pfizer R&D site".* The firm has submitted Stability data of 03 batches manufactured at M/s Pfizer Ireland Pharmaceuticals with the following details; • Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 36 motnhs of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches Batches: J11579, J14939, J14940
2	Provide stability study data (Real Time & Accelerated) according to the conditions of zone IV-A of 03 batches till claimed shelf life.	• Real time stability studies have been conducted at 30oC±2 and 75%RH±5% for 24 months of 03 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 03 batches

		Batches: H000013331 S78147, H000013331 S78148, H000013331 S78149
Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.		
32.	Name, address of Applicant / Importer	M/s AJ Mirza Pharma (Pvt.) Ltd., 1st Floor, Shafi Court, Merewether Road, Civil Lines, Karachi. Pakistan.
	Details of Drug Sale License of importer	**License No: 043** **Address:** 1st Floor, Shafi Court, Civil Lines, Merewether Road, Karachi, Pakistan. **Address of Godown:** 2nd Floor, Shafi Court, Civil Lines, Merewether Road, Karachi, Pakistan. **Validity:** 22.12.2022. **Status:** License to sell drugs as distributor **Renewal:** Renewed
	Name and address of marketing authorization holder (abroad)	M/s Cipla Ltd, S-103 to S-105 S-107 to S-112, L- 138 L-147, L-147/1 to L-147/3, & L-147/A, & L-147/A, L-150 Verna Industrial Estate Verna Goa.
	Name, address of manufacturer(s)	M/s Cipla Ltd.,S-103 to 105, S-107 to S-112, L-138, L-147, L-147/1 to L-147/3 & L-147/A, L-150, Verna Industrial Estate, Verna Goa, India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate) • Firm has submitted original, legalized CoPP certificate (No. 789/MFG/WHO-GMP/DFDA/2020/143(4)) valid up to 19-05-2022 issued by Directorate of Food & Drug Administration, India the Applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP.	
	Details of letter of authorization / sole agency agreement • Copy of Letter of Authorization is attached. M/s Cipla Ltd. Cipla house, Peninsula Business Park, Gantaptrao Kadam Marg, Lower Parel, Mumbai India authorizes M/s A.J. Miza Pharma (Pvt) Ltd., 1st Floor Shafi Court, Merewether Road, Civil Lines Karachi to register, Import & Distribute Erlotinib 25mg Tablets. The authorization letter is valid till 22-02-2022.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import

		☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. NA : NA
	Details of fee submitted	PKR 100,000/-: 13-08-2018
	The proposed proprietary name / brand name	Erlocip 25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains:- Erlotinib HCl eq. to Erlotinib ……..25mg
	Pharmaceutical form of applied drug	Tablets
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In house
	Proposed Pack size	10 Tablets in a blister Pack, 10/30 Tablets in a container pack
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Tarceva 25mg Tablet **(USFDA** Approved).
	For generic drugs (me-too status)	Tarceva 25mg Tablet of Roche Pakistan Ltd. (Reg # 043001)
	Module-II (Quality Overall Summary)	Submitted
	Name, address of drug substance manufacturer	M/s Cipla Ltd.,S-103 to 105, S-107 to S-112, L-138, L-147, L-147/1 to L-147/3 & L-147/A, L-150, Verna Industrial Estate, Verna Goa, India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$. The stability study data is till 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard

		or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has submitted pharmaceutical equivalence performed against Tarceva 25mg tablet approved by USFDA by performing quality tests and comparative dissolution profile in all the 3 media (B:M0004B05) with values of F2 factor in acceptable range.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Alu-lidding foil and clear pvc at one side.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30^{o}C ±2^{o}C / 75% ± 5% RH. The real time stability study data of 3 batches is for 24 months.

Evaluation by PEC:

Sr. no.	**Observations**	**Response**
1	Data of product development including manufacturing process development and Drug Product specifications data in the light of decision of Registration Board in the light of the decision of 267th meeting.	The firm has submitted the detail of product development and presented the relevant data in section 3.2.P.2.1 to 3.2.P.6 in detail along with the detail of finished drug specifications, testing method and justification of specifications in relevant sections along with the method validation studies for all the parameters.
3	Submission of product specific letter of authorization.	Copy of letter of authorization is submitted whereby M/s Cipla Limited has authorized AJ
4	Original legalized and valid CoPP mentioning the free sale status of the applied product.	Firm has submitted original, legalized CoPP certificate (No. 789/MFG/WHO-GMP/DFDA/2020/143(4)) valid up to 19-05-2022 issued by Directorate of Food & Drug Administration, India the Applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP.
5	Stability studies according to zone IV-A till shelf life.	• Real time stability studies for 03 batches till 24 months at 30^{o}C ±2^{o}C / 75% ± 5% RH • Accelerated stability data of 03 batches till 6 months time point at 40^{o}C ±2^{o}C / 75% ± 5% RH B: GJ60992, GJ60993, GJ70116

6	Detail of pack size is required.	10 tablets in a blister, 10/30 tablets in a container pack.

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

Deferred cases:

33.	Name, address of Applicant / Importer	M/s AJM Pharma (Pvt) Ltd. 1st Floor, Shafi Court, Civil Lines Merewether Road, , Karachi. Address of the godown: Address1: Ground floor, Plot no. 44 Sector 27, Korangi Industrial Area, Karachi Address2: Shed No. F-9, PI.No.S1, Survey No.230 Sector – 02, Road 4000, Korangi Industrial area, Karachi.
	Details of Drug Sale License of importer	Address: 1st Floor Shafi Court Civil Lines, Merewether Road, Karachi Validity: 23-02-2023 Status: Drug license by the way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Jiangsu Hengrui Medicine Co. Ltd. 38 Huanghe Road, economic and technological development zone, Lianyungang, Jiangsu 222047, P.R.China
	Name, address of manufacturer(s)	M/s Jiangsu Hengrui Medicine Co. Ltd. 38 Huanghe Road, economic and technological development zone, Lianyungang, Jiangsu 222047, P.R.China.

	Name of exporting country	CHINA
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: Firm has submitted Original Valid CoPP (Certificate#MTMU-9M53) issued by United States Food And Drug Administration for Carmustine 100mg For Injection. The CoPP confirms free sale status of the product in the exporting country as well as GMP status of the manufacturing site through periodic inspection once in a year. The certificate is valid till 08.09.2023. Copy of GMP certificate No : JS20180922 Valid till 18-10-2023 is submitted issued by China food and drug Adminstration
	Details of letter of authorization / sole agency agreement	Firm has submitted a copy of letter of authorization M/s Jiangsu Hengrui Medicine Co. Ltd. 38 Huanghe Road, economic and technological development zone, Lianyungang, Jiangsu 222047, P.R. China. According to the letter, the firm authorizes M/s AJM Pharma (Pvt) Ltd. with registered address at 1st floor, Shafi Court, Merewether Road, Civil Lines, Karachi -75520, Pakistan to apply for registration of applied product manufactured by M/s Jiangsu Hengrui Medicine Co. Ltd. for importation and distribution in the territory of Pakistan. The letter was issued on 04-07-2019 and it is valid for five years from date of issue.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy.No. 15879 dated 27-08-2019
	Details of fee submitted	PKR 50,000/-: 27-08-2019
	The proposed proprietary name / brand name	Carmus 100mg/Vial For Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Carmustine…..100 mg
	Pharmaceutical form of applied drug	Sterile lyophilized pale-yellow granule or congealed mass for intravenous infusion after reconstitution

	Pharmacotherapeutic Group of (API)	Alkylating antineoplastic agent
	Reference to Finished product specifications	USP
	Proposed Pack size	1 Vial with 1 Vial of Sterile Diluent 3 mL of Dehydrated Alcohol Injection
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	BiCNU (carmustine for injection) under NDA 017422 held by Emcure Pharmaceuticals Ltd. Was approved by FDA
	For generic drugs (me-too status)	NA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Name, address of drug substance manufacturer	Jiangsu Hengrui Medicine Co., Ltd. 22 Jinqiao Road, Dapu Industrial Park Lianyungang, Jiangsu 222002, China Contact: Lin Li, Ph.D.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated and real time conditions. The real time stability data were conducted at 5±3oC for 36 months and accelerated stability data were conducted at 25°C ± 2°C, RH: 60% ± 5% for 2 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, description of

		manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is established against Carmustine for injection Batch No# CDAA608 BiCNU (Carmustine for injection) under NDA 017422 held by Emcure Pharmaceuticals Ltd. Was approved by FDA.
	Analytical method validation/verification of product	The firm has submitted validation results of assay method, related substances, of Carmus Injection 100mg.
	Container closure system of the drug product	Glass Vial: 30 mL vial made of neutral borosilicate glass tubing, Type I clear, amber and siliconized glass. Stopper: 20 mm rubber stopper for lyophilization, V9154/FM257 Aluminum Flip-off Seal: 20 mm*7.2 mm, blue flip-off seals without logo
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches with upright and inverted orientation: Batch No. | Batch Size | Mfg. Date 170803AB | 4254 Vials | 24-08-2017 170830AB | 4557 Vials | 21-09-2017 170909AB | 4522 Vials | 21-09-2017 The firm has performed Real time stability study at 2oC – 8 oC for 18 months and accelerated stability study at 25 oC±2 oC/60%±5%RH for 06 months. In-use stability study at 2oC – 8 oC for 24hours

Evaluation by PEC:

S.No	Section	Shortcomings Communicated	Reply
	1.3.3.	Importer shall provide Certificate of Pharmaceutical Product (CoPP) / Free Sale certificate issued by relevant regulatory authority in the country of origin and name of exporting country.	Not submitted.
	1.4.1.	Generic Drug Product (GDP mentioned while fee of Rs: 50000/- submitted.	Firm submitted fee of Rs: 50000/- deposit slip No:72513093 , Dated:12-11-2021
	3.2.S.7	Submit Stability Studies data of Drug Substance.	In Drug substance accelerated stability studies terminated after 2months due to the result of 2-chloroethanol was out of specification for two of three batches,
	3.2.P.2 P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established	Details of RLD including brand name, manufacturer etc. not submitted

		with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed	

2nd letter 26th November, 2021

S.No	Section	Shortcomings Communicated	Reply
	1.3.3.	Importer shall provide Certificate of Pharmaceutical Product (CoPP) / Free Sale certificate issued by relevant regulatory authority in the country of origin and name of exporting country.	COPP from United states submitted
	3.2.S.7	In Drug substance if accelerated stability studies terminated after 2months due to the result of 2-chloroethanol was out of specification for two of three batches, then how finished product was manufactured.	According to IC Q1A 2.1.7.2. Drug substances intended for storage in a refrigerator: "If significant change occurs between 3 and 6 months' testing at the accelerated storage condition, the proposed re-test period should be based on the real time data available at the long term storage condition. If significant change occurs within the first 3 months' testing at the accelerated storage condition, a discussion should be provided to address the effect of short term excursions outside the label storage condition, e.g., during shipping or handling. This discussion can be supported, if appropriate, by further testing on a single batch of the drug substance for a period shorter than 3 months but with more frequent testing than usual It is considered unnecessary to continue to test a drug substance through 6 months when a significant change has occurred within the first 3 months." More over the short term Excursion stability data for drug substance could address the effect of short term excursion outside the label storage condition (between 2oC –and 8 oC) during the finished product was manufactured. The short term excursion stability study was conducted at 25°C ± 2°C/60% RH ± 5% RH for three batches of drug substance, and the testing results

			obtained up to 30 days for drug substance meet the acceptance criteria in the specification and show no significant changes during the storage, which could support short term excursion during shipping or handling
	3.2.P.2 P.2.2.1	Submit details of RLD including brand name, manufacturer etc.	BiCNU (carmustine for injection) under NDA 017422 held by Emcure Pharmaceuticals Ltd. Was approved by FDA

Decision of 316th meeting: Deferred for following:

• Justification regarding submitted COPP, since country of origin of applied product is China, whereas submitted COPP has been issued by the United States Food And Drug Administration.

• Scientific rationale for formulating drug product with a drug substance having accelerated stability studies of only two months.

Submission by the firm:

The firm has stated that:

1. The applied product is approved by USFDA and marketed in USA, therefore, the CoPP issued by USFDA is submitted along with the dossier. Moreover, due to commercial reasons the applied product is not marketed in china.

2.

- The limit for 2-chloroethylamine (Impurity) is included in the release and stability specifications of the finished product and could confirm that the results of the content of the impurity is within the specified limit.
- Moreover, As per ICH Q1A2.1.7.2. the drug substance intended for storage in refrigerator, if significant change occurs within first 3 months then a discussion should be provided to address the effect of short term excursions outside the labelled storage conditions e.g. during shipping or handling. This discussion can be supported, if appropriate, by further testing on a single batch of the drug substance for a period less than 3 months with more frequent testing than usual. It is unnecessary to continue to test a drug substance through 6 months when a significant change occurs.

  "Significant change for a drug substance is defined as failure to meet it specification". (2.1.7)
- The short term excursion stability data for drug substance could address the affect of short term excursions outside the label storage condition during finished product manufacturing.
- The short term excursion stability data is provided in 3.2.S.7.3 in DMF, which could support short term excursion during shipping. The temperature of the drug substance is controlled between 2-8^{o}C during the transportation to the finished product manufacturing site. During the manufacturing of finished product, the temperature is the controlled parameter during compounding, lyophilization and complete stoppering as well as the holding periods are also controlled as the critical parameters.

Indications:

Carmstine is a nitrosourea indicated as palliative therapy as a single agent or in established combination therapy with other approved chemotherapeutic agents in the following:

• Brain tumors glioblastoma, brainstem glioma, medulloblastoma, astrocytoma, ependymoma, and metastatic brain tumors

• Multiple myeloma-in combination with prednisone

• Relapsed or refractory Hodgkin's lymphoma in combination with other approved drugs

• Relapsed or refractory Non-Hodgkin's lymphomas in combination with other approved drugs

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

34.	Name, address of Applicant / Importer	M/s GHAZALI BROTHERS 19-SR-7, Campbel Street, Azzainab Court, 1st Floor, Karachi- Pakistan
	Details of Drug Sale License of importer	**License No:** 050 **Address:** 19-SR-7, Campbel Street, Azzainab Court, 1st Floor, Karachi- Pakistan **Validity:** 27th Oct 2021 **Status:** Drug License by the way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Shandong luoxin pharmaceutical group stock co., ltd, Luoqi road, linyi high and new technology industries Development zone shandong province, pr China.
	Name, address of manufacturer(s)	M/s Shandong luoxin pharmaceutical group stock co., ltd, Luoqi road, linyi high and new technology industries Development zone shandong province, PR China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • The firm has submitted Original legalized CoPP (certificate No. Shandong20200016(5) for Calcium Folinate for Injection 100mg issued by Shandong Drug Administration valid till 31/12/2020. The applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP. • CCPIT legalized barcode: 201100B0/040270 Dated: 02/July/2020 • Drug manufacturing license No. Lu20160194 valid till 31/12/2020. • Copy of GMP certificate No. SD20191020 valid till 10/12/2024.	
	Details of letter of authorization / sole agency agreement • Firm has submitted Exclusive Distribution Agreement wherein M/s SHANDONG LUOXIN PHARMACEUTICAL GROUP STOCK CO. LTD Luoqi Road, Linyi National High and New Technology Industries Development Zone, Shandong Province, PR China authorized M/s GHAZALI BROTHERS 19-SR-7, Campbel Street, Azzainab Court, 1st Floor, Karachi- Pakistan for marketing and selling for Calcium folinate injection 100mg..	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 7594 : 05-08-2020
	Details of fee submitted	PKR 100,000/- : 05-08-2020

	The proposed proprietary name / brand name	CALFOLINATE for Injection 100mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains : Folinic Acid as calcium folinate pentahydrate.....100mg
	Pharmaceutical form of applied drug	Off-white to yellow loose cake or powder (lyophilized) for solution for IV/IM injection
	Pharmacotherapeutic Group of (API)	Detoxifying agents for antineoplastic treatment
	Reference to Finished product specifications	Chinese Pharmacopeia
	Proposed Pack size	1's
	Proposed unit price	As per DRAP's pricing policy
	The status in reference regulatory authorities	Leucovorin Calcium 100mg base/vial by M/s Teva Pharms USA, USFDA Approved.
	For generic drugs (me-too status)	CALFONATE INJECTION 100MG by M/s GHAZALI BROTHERS, Reg. No. 70936
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and Drug Product.
	Name, address of drug substance manufacturer	M/s Zhejiang Davi Pharmaceutical Co., Ltd. No.818 Xinzhu Road, Economic Development Area, Huzhou City, Zhejiang Province 313000, The People's Republic of China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 24 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: CAN161201, CAN161202, CAN161203

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not submitted.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Injection vials made of low borosilicate glass tubing, bromobutyl rubber stopper for sterile powder for injection and aluminum-plastics combination caps for injection vials
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 36 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: 514082033, 514082043, 514082053

Evaluation by PEC:

Calcium folinate equivalent to Folinic acid 100mg is the actual quantity of base used in the formulation while in section 2.3.P.3.2 under batch formula, Calcium Folinate (calculates as folic acid) and in section 3.2.P.3.2 under Batch Formula is written. Since Folic Acid and Folinic Acid are two different chemical compounds therefore you are required to rectify the mistake and submit the information under relevant sections.	**Shandong Luoxin Response:** We apologize for the mistakes of the names shown in batch formula. The mistakes have been rectified following your comments, please find the revised Section 2.3.P.3.2 and 3.2.P.3.2 in Attachment 1 and 2. The name claimed in the label and carton is also revised following your comments. The firm has submitted relevant sections with correct label claims and batch formulas.
The submitted real time stability studies for drug product are conducted at 25^{o}C±2 and 60%RH±5% while real time stability studies of 03 batches till claimed shelf life according to the conditions of Zone IV-A (30^{o}C±2 and 65%RH±5%) are required.	The firm has submitted stability data of 03 batches with the following details; • Real time stability studies have been conducted at 30oC±2 and 65%RH±5% for 24 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: 518042042, 518102041, 518102042
Pharmaceutical equivalence of the applied product should be established by performing all the quality tests against the innovator's product and should be presented in the relevant sections.	Pharmaceutical equivalence is submitted against Leucovorin Calcium by M/s Westward-Hikma, USA by performing all the quality tests. (Batch: 1909A01).
The official monograph for C (Leucovorin Calcium) is present in USP while the testing of the applied product is done according to In-	The firm has submitted a comparison of specifications of Chinese Pharmacopoeia and

House standard/Chinese Pharmacopoeia, please justify scientifically by comparing the specifications & methods described in USP with the methods & specifications of In-House standard since the methods of analyses used are different.	USP. Limits are same in both monographs but the method used are different. USP describes the tests of 7 impurities for separately while Chinese pharmacopoeia does not describe individual impurities but it gives total impurity limit NMT 2.5% which is similar to USP. Moreover, the limit for unspecified impurity in USP is 0.5% while according to C.P. is 1%.
The test for specificity parameter of validation/verification of analytical method is performed by performing the tests on the sample solution against placebo solution, please refer the guideline for the procedure adopted while the specificity test is performed by spiking with appropriate level of impurities or exposing the drug product sample to relevant stress conditions as recommended by USP.	"The difference of excipient and brand of reagents used in the testing were taken into account during the verification of analytical procedure, the specificity was verified by comparing the interference on the sample solution against placebo".

Decision of 313rd meeting: The Board deferred the case for;

- Submission of impurity profiling according to USP for the applied product.
- Submission of Drug-excipient compatibility studies.
- Confirmation of the area where the applied product would be manufactured.

Firm's response: Firm has submitted following:

- The firm has submitted revised specifications for the applied product according to USP and submitted comparison of specifications of USP and In-house specs. Moreover, the firm has submitted COAs of 03 batches which have been tested against USP specification along with the results of tests of all the impurities. The results of impurities are in the limits as specified by USP.
  Batches: CAN200105, CAN200102, CAN200101
- The applicant has submitted drug-excipient compatibility studies. The tests have been performed by preparing binary and tertiary solutions and placing the solution under different conditions including high temperature that is 60°C/high humidity strong light irradiation etc for 10 days.
- Firm has submitted copy of GMP certificate (Certificate no. SD20191021) valid till 10-12-2024, issued by Shandong Food & Drug Administration in name of M/s Shandong Luoxin Pharmaceutical Group Stock Co., Ltd., wherein Scope of inspection has been declared as "Lyophilized Powder for injection."

Decision: Approved with USP specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

35.	Name, address of Applicant / Importer	M/s Adcare Pharma, House No. D-145, 5th road, Satelite town Rawalpindi.
	Details of Drug Sale License of importer	License No: 01-374-0177-028459D Address: Adcare Pharma, House No. D-145, 5th road, Satelite town Rawalpindi. Godown: House No. D-145, 5th road, satellite town, Rawalpindi. Validity: 24/03/2022 Status: Drug License by way of Wholesale

	Name and address of marketing authorization holder (abroad)	M/s Lunan Better Pharamceutical Co., Ltd., No. 243, Yingueshan road, Linyi city, Shandong province, China.
	Name, address of manufacturer(s)	M/s Lunan Better Pharamceutical Co., Ltd., No. 243, Yingueshan road, Linyi city, Shandong province, China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized GMP certificate (NO. SD20180814) is submitted with validity of 25/11/2023. • Original legalized CoPP (certificate No. 20200106) issued by Shandong Food and Drug Administration, China on 11/12/2020. The product is not available for free sale in the exporting country. The facilities and operation conform to WHO-GMP.	
	Details of letter of authorization / sole agency agreement: • Copy of letter of authorization is submitted	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.31904 : 01/12/2020
	Details of fee submitted	PKR 100,000/- : 01/12/2020
	The proposed proprietary name / brand name	Sevocare 250mL for Inhalation
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 250mL bottle contains: Sevoflurane……..100% (250mL)
	Pharmaceutical form of applied drug	Liquid for inhalation.
	Pharmacotherapeutic Group of (API)	General Anesthetics
	Reference to Finished product specifications	In-House
	Proposed Pack size	250mL
	Proposed unit price	Rs. 19980/- per 250mL
	The status in reference regulatory authorities	Sevoflurane 100% Inhalation Vapour, liquid (250mL type III amber colored glass bottle), MHRA Approved.
	For generic drugs (me-too status)	Sevorance Volatile Liquid For Inhalation by M/s Abbot, Reg. No. 27374

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, detail of impurities and validations studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.
	Name, address of drug substance manufacturer	M/s Shandong New Time Pharmaceutical Co., Ltd., No. 1 North Outer Ring road, Feixian County, Shandong 273400, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 36 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (100100, 1001002, 1001003)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, compatibility studies of excipients with drug substance manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures for the product along with the impurities, validation of analytical procedures, detail of impurities and the validation studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	
	Analytical method validation/verification of product	The firm has submitted analytical method verification studies including specificity, linearity and accuracy for drug product, drug substance and impurities as well.
	Container closure system of the drug product	250mL amber colored type III glass bottle sealed by an aluminium screw cap with a low density polyethylene liner.

	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30oC±2 and65%RH±5% for 36 months of 3 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (090301, 090302, 090303)

Evaluation by PEC:

- The applicant holds the registration of "Isofurane Inhalant" 100ml bottle with registration no. 045727 from the same manufacturer that is M/s Lunan Better Pharmaceutical Co., Ltd., China.
- As per the submitted CoPP the applied product is not available for free sale in the exporting country.

Observations	Response
Submission of valid copy of drug sale license is required.	The firm has submitted valid copy of DSL with the following details. License No: 01-374-0177-028459D Address: Adcare Pharma, House No. D-145, 5th road, Satelite town Rawalpindi. Godown: House No. D-145, 5th road, satellite town, Rawalpindi. Validity: 24/03/2022 Status: Drug License by way of Wholesale
Submit filled, signed and stamped Form 5F with the relevant details which should be provided along with., since the submitted Form 5F does not contain any information regarding the registration application.	The firm has submitted form 5F with the relevant documents.
Product specific sole agency agreement between the product license holder and the applicant is required.	
Since you are already granted the registration for Isoflurane 100ml bottle, therefore the application for 250ml bottle shall be submitted, please submit revised form 5F along with the applicable fee.	The firm has stated that they have been granted the registration of 100mL sevoflurane and now they are applying for 250mL. The firm has submitted relevant documents for 250mL sevoflurane.
The submitted data is for 100mL bottle while the registration for 100mL bottle is already granted by the Board. Therefore, you are required to provide the relevant data.	Submitted.
Provide evidence of approval of the applied formulation by reference regulatory authorities (with same filled volume/strength) which were adopted by Registration Board in its 275th meeting.	Sevoflurane 100% Inhalation Vapour, liquid (250mL type III amber colored glass bottle), MHRA Approved.
Pharmaceutical equivalence data is not submitted.	

Decision of 316the meeting:

- Submission of Free sale certificate in the country of origin i.e., China for the applied product in fill volume of 250ml, issued by relevant regulatory authority or else Free sale certificate in any of the reference regulatory authorities of the applied product from the

same finished drug product manufacturer i.e., M/s Lunan Better Pharamceutical Co., Ltd., No. 243, Yingueshan road, Linyi city, Shandong province, China.

- Submission of Pharmaceutical equivalence studies against the innovator product.

Submission by the firm:

- Initially the firm had applied for two filled volumes of Sevoflurane for Inhalation that is 100mL and 250mL and submitted relevant data. Upon communication the firm requested to consider 250mL bottle for registration against the submitted application. 250mL was not available for free sale in china as per submitted CoPP. The firm then requested to considered 100mL glass bottle.
- The case was deferred in 316th meeting for submission of free sale certificate/CoPP and pharmaceutical equivalence.
- The firm has now submitted original, legalized and valid CoPP for 100mL filled volume with the following detail;
  Certificate No.; Shandong20200105(5)
  Free Sale: YES
  Facilities and operations conform to WHO-GMP
  Manufacturer / Product License Holder: M/s Lunan Better Pharmaceutical Co. Ltd., No. 243 Yiqueshan road, Linyi city, Shandong province, China.
- Pharmaceutical equivalence is established against Ultane (B:1114338) approved by USFDA by performing all the quality tests.
- Pack size and Price: 1's & 9600/-.

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that the applicant will submit full fee that is Rs. 150,000/- before issuance of registration letter for change of filled volume.

36.	Name, address of Applicant / Importer	M/s AMGOMED Office # 4, First Floor Ghausia Plaza, Jinnah Avenue Blue area Islamabad Pakistan
	Details of Drug Sale License of importer	License No: DSL-002-ICT/2013 Address: Amgomed office # 4, First floor Ghausia Plaza, Jinnah Avenue Blue area Islamabad Address of Godown: Office number 5, First floor Rose-I plaza, I-8, Markaz Islamabad. Validity: 30/01/2022 Status: Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s DEVA Holding A.S., Halkali Merkez Mah. Basin Ekspres Cad. No:1 34303 Kucukcekmece – Istanbul/Turkey.
	Name, address of manufacturer(s)	M/s DEVA Holding A.S. Çerkezköy Organize Sanayi Bölgesi, Karaagaç Mah. Fatih Bulvarı No: 26, Kapaklı - TEKIRDAG/TURKEY.
	Name of exporting country	Turkey
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Copy of GMP certificate No.TR/GMP/2019/31 dated 28/01/2019 issued by Turkish Medicines and Medical Devices Agency. (Dosage form: SVP / Special requirements: Anticancer (oncologic) liquid injectable vials / Activities: manufacturing at sterile liquid oncologic (anticancer) manufacturing site). • Firm has submitted original, legalized COPP certificate (No. 2020/1390) dated 22-05-2020 issued by Republic of TURKEY MEDICINE AND MEDICAL DIVICES AGENCY For Carbodex 150mg/15mL solution for IV infusion.	

The applied product is available for free sale in the market of exporting country.
The facilities and operations conform to WHO-GMP.
The COPP is valid till 03-06-2022.

Details of letter of authorization / sole agency agreement:

- Copy of letter of authorization is submitted whereby M/s DEVA Holding A.S., Turkey authorized M/s AMgomed to apply for registration, for marketing, distribution and sale of below mentioned product;
  Carbodex 150mg/15ml solution fir IV injection.
  The authorization letter is valid till 15-06-2022.

Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
Dy. No. and date of submission	Dy. No.17502 : 23/06/2021
Details of fee submitted	PKR 100,000/- : 30-09-2020
The proposed proprietary name / brand name	Carbodex 150mg/15ml Solution for IV Infusion
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Carboplatin……10mg
Pharmaceutical form of applied drug	Solution for IV infusion
Pharmacotherapeutic Group of (API)	Antineoplastic agent
Reference to Finished product specifications	Present in BP (in-house applied)
Proposed Pack size	1's
Proposed unit price	As per SRO
The status in reference regulatory authorities	Carboplatin 150mg/15ml, concentrate for solution for infusion by M/s Accord Healthcare Limited, MHRA Approved.
For generic drugs (me-too status)	Carboplat 150mg/15ml solution for injection by M/s Rotex Pharma pvt ltd.
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications,

		analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.
	Name, address of drug substance manufacturer	Manufacturer: M/s Sicor De Mexico S.A de C.V Av. San Rafael No. 35 Parque Industrial Lerma, Edo. De Mexico C.P 52000, Mexico. DMF Holder: Teva Pharmaceutical Industries Ltd. 5 /Basel Street, P.O. Box 3190 Petah Tiqva 4951033, Israel.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 60 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (03CBP02A-0CH, 97CBP01A-OC, 97CBP02A-OC)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is established against DBL Carboplatin 150mg/15ml by M/s Hospira by performing
	Analytical method validation/verification of product	Not submitted.
	Container closure system of the drug product	Amber colored type I glass ampoule
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30oC±2 and65%RH±5% for 36 months of 3 batches

		• Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (A035176, A035177, A035178)
Evaluation by PEC-I:		
Observations		**Response**
Official monograph for Carboplatin drug substance is present in USP/BP while the testing is done according to in-house standard, please clarify.		No response is submitted against this observation.
Analytical method verification studies performed by drug product manufacturer for drug substance along with the complete method for routine analysis is required.		Analytical verification studies performed by drug product manufacturer are submitted according to In-House specifications.
Stability study data including accelerated and real time for 03 batches is required till shelf life/retest period for the drug substance should be submitted.		No response is submitted against this observations.
Since the official monograph for Carboplatin injection is present in B.P while the applied product is developed according to In-House standards. Provide scientific justification and comparison of BP and In-House specifications or provide complete analysis of all parameters for applied product as described in B.P along with the submission analytical method verification studies including accuracy, specificity and precision.		The has not provided a comparison of In-House and B.P specifications and no clarification is submitted as well regarding the In-House specifications.
Decision: The Board deferred the case for submission of; • **Clarification since the official monograph of the Carboplatin drug substance present in USP/BP while the testing is done according to in-house standard** • **Submission of Stability study data including accelerated and real time for 03 batches is required till shelf life/retest period for the drug substance.** • **Since the official monograph for Carboplatin injection is present in B.P while the applied product is developed according to In-House standards. Provide scientific justification and comparison of BP and In-House specifications or provide complete analysis of all parameters for applied product as described in B.P along with the submission analytical method verification studies including accuracy, specificity and precision**.		
37.	Name, address of Applicant / Importer	M/s Organ Pharma office no. 2, Second floor, Plot # 50-D Khayaban-e-Ittehad, DHA Phase 6, Karachi Pakistan
	Details of Drug Sale License of importer	**License No:** 514 **Address:** Organs Pharma, plot No. V-98, first floor, 6FKorangi Mehran town, I.A.K Kyc, Karachi. **Validity:** 09/11/2022 **Status:** Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Adamed Pharma S.A. Pienkow ul. Mariana Adamkiewicza 6A 05-152 Czosnow Poland
	Name, address of manufacturer(s)	M/s Adamed Pharma S.A., Ul. Marszalka Jozefa Pilsudskiego 5 95-200 Pabianice Poland

	Name of exporting country	Poland
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate number 692/20) certified by Chief pharmaceutical Inspector, 12 Senatorska street, 00-082 Warsaw, Poland on 10/08/2020. The product is present in the market of exporting country for free sale. The facilities and operations conform to WHO-GMP.	
	Details of letter of authorization / sole agency agreement • Notarized supply and distribution agreement is submitted whereby M/s Adamed Pharma S.A. authorized M/s Organs Life Science FZC, Sharjah UAE for the applied product (100mg and 200mg). • Another notarized letter of authorization is submitted by the firm whereby M/s Organs life sciences, Sharjah, UAE authorized M/s Organs Pharma, Karachi Pakistan for distribution, registration, promotion, import etc for the applied product. • Legalized CEP certificate for API is submitted.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 21789 Dated 24-10-2019
	Details of fee submitted	Rs. 100,000/- dated 21-08-2019
	The proposed proprietary name / brand name	LUTEINA 100mg vaginal tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vaginal tablet contains: Progesterone…..100mg
	Pharmaceutical form of applied drug	Round, biconvex, white to off-white in colour, Vaginal Tablet
	Pharmacotherapeutic Group of (API)	Hormone
	Reference to Finished product specifications	In-house
	Proposed Pack size	30 tablets per pack
	Proposed unit price	Rs. 1536/- Per Pack
	The status in reference regulatory authorities	Lutigest 100 mg vaginal tablets by M/s Ferring Pharmaceuticals, MHRA Approved. Lutinus 100mg Vaginal Tablets by M/s Ferring Ireland Limites, HPRA Ireland Approved
	For generic drugs (me-too status)	Could not be confirmed
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information

		related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.
	Name, address of drug substance manufacturer	M/s Zhejiang Shenzhou Pharmaceutical Co., Ltd. 14 Chuancheng Nan Road China-317300 Xinaju, Zhejiang Province
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	CEP certificate is provided and the firm has stated that the re-test period for the drug substance is 36 months when stored in double PE bags placed in carton drums.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has submitted pharameutical equivalence data against Endometrin Tablet 100mg by M/s QPharma Ab, Sweden by performing all the quality tests (VK292A).
	Analytical method validation/verification of product	The firm has submitted relevant data including analytical method validation for the drug product including the impurities
	Container closure system of the drug product	Blisters of PVC/PVDC 90 g/m^2 pharmaceutical white foil and aluminium lidding foil, primary packaging carton box containing blister nad leaflet as secondary packaging.
	Stability study data of drug product, shelf life and storage conditions	• 12 months data of 3 batches at 30 ± 2^0C, 75±5%RH • 6 months at 40^0C±75%RH of 03 batches.
Evaluation by PEC-I: • Firm Submitted CEP (**Certification** of suitability of European Pharmacopoeia monographs) for Progesterone Micronised, non-micronised API which is verified by EDQM website dated 27-12-2019 link attached:		

https://extranet.edqm.eu/4DLink1/4DCGI/Query_CEP?vSelectName=1&Case_TSE=none&vContains=1&vContainsDate=1&vtsubName=Progesterone&vtsubDateBegin=&vtsubDateBtwBegin=&vtsubDateBtwEnd=&SWTP=1&OK=Search

- Vaginal tablets are solid, single-dose preparations. They generally conform to the definitions of uncoated or film-coated tablets given in the monograph (British Pharmacopoeia).
- Disintegration (2.9.2)
  Unless intended for prolonged local action, they comply with the test (special method for vaginal tablets). Examine the state of the tablets after 30 min, unless otherwise justified and authorised. Disintegration test along with the dissolution test (≥80% in 30mins) is included in the final specifications (release and shelf life) of the drug product.
- Moreover, the pharmaceutical equivalence studies have been performed in Dow University of Health sciences at Bioanalytical Lab-IBBPS, Old TLA building 1st floor, DUHS-OJHA Campus Karachi. The applicant has stated that the pharmaceutical equivalence is not a regulatory requirement in exporting country that is why the studies have not been performed.

Decision of 313th meeting:
Since pharmaceutical equivalence and comparative dissolution are performed by Dow University of Health Sciences at Bioanalytical Lab-IBBPS, Old TLA Building 1st Floor, DUHS-OJHA Campus Karachi. The Board after deliberation deferred the case for clarification from the legal division regarding the status of the submitted data of Pharmaceutical equivalence and comparative dissolution profile.

Submission by the firm:

- The firm has submitted comparative dissolution profile of the applied product against Progesterone Vaginal Tablets 100mg (Lutinus tablet) by Ferring GmbH Wittland 11 D-24109 Kiel Germany (Batch No. YL314A) in all the 03 media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer (document No. RDP-PP-RT/020 dated 25/05/2022). The study is performed by the manufacturer of the applied product.
- Moreover, the firm has submitted the results of Pharmaceutical Equivalence studies performed by the manufacturer of the applied product against Lutinus tablet 100mg (B: YL314A).(Even Document No., attachment 10).

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

38. **Genetics Pharmaceuticals pvt ltd**

a. Vepridone (Risperidone Prolonged Release Powder for Injection) 25mg
Dy. No 14162 Dated 05-08-2019 (Rs. 50,000/- Dated 05-08-2019)

MODULE 1: ADMINISTRATIVE

Section	Sub-Section	Heading
1.1		Covering Letter and Fee Deposit Slip Submitted Dy. No 14162 Dated 05-08-2019 (Rs. 50,000/- Dated 05-08-2019) Dy. No 14163 Dated 05-08-2019 (Rs. 50,000/- Dated 05-08-2019)
1.2		Table of Contents (From Module 1 to Module 5) Submitted
1.3		Applicant Information Submitted
	1.3.1	Name, address and contact details of Applicant / Marketing Authorization Holder: M/s Genetics Pharmaceuticals pvt. Ltd. Ltd 539-A, Sundar Industrial Estate, Raiwind Road Lahore
	1.3.2	Name, address and contact details of Manufacturing site.

		M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India
	1.3.3	Specify whether the Applicant is: Importer
	1.3.4	**Drug Sale License** No: 0011000 0000696 valid upto 12-December-2019
	1.3.8	Manufacturer's Site Master File and Credential (for importer) Submitted
1.4		Type of Application Submitted
	1.4.1	Application is for the registration of: Generic Drug Product
	1.4.1	Pharmaceutical product is intended for: □ **Domestic sale**
	1.4.2	For imported products, please specify one of following: □ **Finished Pharmaceutical Product Import**
1.5		Detailed Information of Drug, Dosage From & Labelling Claims Submitted
	1.5.1	Generic name with chemical name & synonyms of the applied drug. Risperidone Extended-release Microspheres for injection 25mg/vial Risperidone Extended-release Microspheres for injection 37.5mg/vial
	1.5.2	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit Each vial contains: Risperidone ……...25mg 2nd Strength Each vial contains: Risperidone ……...37.5mg
	1.5.3	The proposed proprietary name / brand name under which the drug is intended to be sold with trademark certification / clearance. Vepridone (Risperidone Prolonged Release Powder for Injection)
	1.5.4	Proposed Pack size and Proposed unit price of drug e.g., per tablet / capsule. Maximum Retail Price (MRP) per pack shall also be mentioned. 1's
	1.5.5	Pharmacotherapeutic Group of Active Pharmaceutical Ingredient (API) Antipsychotic
	1.5.6	Pharmacopoeial reference / Status of applied formulation In-house
	1.5.7	Route of administration IM
	1.5.9	The registration status of applied drug in same molecule and salt, strength, dosage form, container closure system, indications and route of administration etc. in other countries. The status in reference regulatory authorities is mandatory to mention. RISPERDAL CONSTA 25 mg powder and solvent for prolonged-release suspension for injection (UK) RISPERDAL CONSTA 37.5 mg powder and solvent for prolonged-release suspension for injection
	1.5.10	Dosage form of applied drug Powder for Injection
	1.5.11	Proposed label (outer (secondary) & inner (primary)) & colour scheme in accordance with Drug (Labelling & Packing) Rules, 1986 along with specimens Submitted
	1.5.12	Description of Batch numbering system
	1.5.14	Summary of Product Characteristics (SmPC) including Prescribing Information (PI) along with Patient information Leaflet (PIL) of the Finished Pharmaceuticals Product (FPP). Submitted

	1.5.15	Commitment / Undertaking that after registration of applied drug, the Pharmacovigilance department of the applicant / manufacture is liable to impose similar restrictions, addition of any clinical information (like in Indications, Contra-indications, Side effects, Precautions, Dosage & A0dverse Drug Reactions etc. in Summary of Product Characteristics (SmPC), Labelling & Promotional material) or withdraw the drug from market in Pakistan within fourteen days after knowing that such information (which was not available or approved by the DRAP at the time of registration) / actions taken (for safety reasons) by any reference / stringent drug regulatory agency / authority & also inform the DRAP (Drug Regulatory Authority of Pakistan) for further action in this regard. **Submitted**
	1.5.16	Commitment / Undertaking that the applicant shall recall the defective Finished Pharmaceutical Products (FPP) and notify the compliance to the authority along with detail of actions taken by him as soon as possible but not more than ten days. The level of recall shall also be defined. **Submitted**
	1.5.17	Commitment / Undertaking that in case of any false claim / concealing of information, the DRAP has the right to reject the application at any time, before and even after approval or registration of the product in case if proved so. **Submitted**
	1.5.18	Commitment / Undertaking that the firm shall follow the official pharmacopoeia specifications for product / substance as published in the latest edition & shall update its specification as per latest editions of the same. In case, the specifications of product / substance not present in any official pharmacopoeia the firm shall establish the specifications. In both cases, the validation of specifications shall be done by the applicant. **Submitted**
	1.5.19	Commitment / Undertaking that in case of any post approval change, the applicant shall ensure that the product with both approvals shall not be available in the market at the same time. And the product with new approvals shall be marketed only after consumption / withdrawal of stock with previous approvals. The company shall be liable to inform the same regarding marketing status of product to the DRAP after getting such post-registration approvals. **Submitted**
	1.5.20	Other commitment e.g., regarding stability studies etc.
	1.5.21	Protocols along with the commitment to follow Good Laboratory Practices (GLP) by the Manufacturer.
	1.5.22	Protocols to implement Good Pharmacovigilance Practice by the Pharmacovigilance department/section of the Manufacturer / Company.
1.6		Miscellaneous Information Submitted
	1.6.1	Information on Prior-related Applications
	1.6.2	Appendix
	1.6.3	Electronic Review Package
	1.6.4	QIS (Quality Information Summary)
	1.6.5	Drug Substance related Document including following: Name and address of API manufacturer. M/s Jubilant Lifesciences Limited Block 133, village samlaya, Taluka Savli, Distt. Vadodara-391520, Gujrat India
	• Copy of Legalized, Notarized CoPP for Risperidone Pronged Release Powder for Injection 25mg (Certificate#. 4892/2019) dated 03-04-2019 issued by Commissionerate, FDA Punjab India declaring the free sale of applied product and GMP compliant status of the manufacturer i.e M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India Certificate valid upto: 11/03/2021	

	• Copy of Legalized, Notarized CoPP for Risperidone Pronged Release Powder for Injection 37.5mg (Certificate#. 4893/2019) dated 03-04-2019 issued by Commissionerate, FDA Punjab India declaring the free sale of applied product and GMP compliant status of the manufacturer i.e M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India Certificate valid upto: 11/03/2021 **(Firm has submitted in reply of photocopy of CoPP legalized and Notarized"The Pakistan Embassy & notary public in India do not attest the original CoPP, they only attest the photocopy")** • Sole agency agreement Between Product License Holder M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India and Importer M/s Genetics Pharmaceuticals pvt. Ltd. Ltd 539-A, Sundar Industrial Estate, Raiwind Road Lahore dated 28-12-2018

MODULE 2: CTD SUMMARIES

2.1 Overall CTD Table of Content Submitted
2.2 CTD Introduction Submitted
2.3 Quality Overall Summary (QOS)* Submitted

QUALITY OVERALL SUMMARY (QOS)

2.3	**Drug substance (API)** General information Submitted Manufacture Submitted Characterization Submitted Control of drug substance Submitted Reference standards Submitted Container closure system Submitted Stability Submitted
	Drug product Description and composition of the drug product Submitted Pharmaceutical development Submitted Components of the drug product 2.3.P.2.1.1 Drug substance (API) Submitted 2.3.P.2.1.2 Excipients Submitted Finished Pharmaceutical Product Submitted Manufacturing process development Submitted Container closure system Submitted Manufacture Submitted Control of excipients Submitted Control of drug product Submitted Reference standards and materials Submitted Container closure system Submitted Stability Submitted
2.4	Non-Clinical Overview Submitted
2.5	Clinical Overview Submitted
2.6	Non-Clinical Written and Tabulated Summaries (Normally not required for generics) Submitted
2.7	Clinical summary Submitted

MODULE 3: QUALITY
3.1 Table of Contents of Module 3 Submitted
3.2 Body of Data Submitted

3.2.S DRUG SUBSTANCE (API)

3.2.S.1	GENERAL INFORMATION (May not refer to DMF)	
	3.2.S.1.1	Nomenclature Submitted
	3.2.S.1.2	Structure Submitted
	3.2.S.1.3	General properties Submitted
3.2.S.2	MANUFACTURER	
	3.2.S.2.1	Manufacturer(s) Submitted
	3.2.S.2.2	Description of Manufacturing Process and Process Controls Submitted
	3.2.S.2.3	Control of Materials Submitted
	3.2.S.2.4	Control of Critical steps and intermediates Not Submitted
	3.2.S.2.5	Process Validation and/or Evaluation Not submitted
	3.2.S.2.6	Manufacturing process development not Submitted
3.2.S.3	CHARACTERIZATION	
	3.2.S.3.1	Elucidation of Structure and other Characteristics Submitted
	3.2.S.3.2	Impurities Submitted
3.2.S.4	CONTROL OF DRUG SUBSTANCE (API)	
	3.2.S.4.1	Specification Submitted
	3.2.S.4.2	Analytical procedures Submitted
	3.2.S.4.3	Validation of analytical procedures Submitted
	3.2.S.4.4	Batch analysis Certificate of analysis (COA) specifications and test results from drug substance (API) manufacturer(s) Drug product manufacturer's certificate of analysis with API lot numbers
	3.2.S.4.5	Justification of specifications Submitted
3.2.S.5		REFERENCE STANDARDS Submitted
3.2.S.6		CONTAINER CLOSURE SYSTEMS Submitted
3.2.S.7	STABILITY	
	3.2.S.7.1	Stability Summary and Conclusions Submitted
	3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment Submitted
	3.2.S.7.3	Stability Data Submitted

3.2.P DRUG PRODUCT

3.2.P.1	DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT Submitted	
3.2.P.2	PHARMACEUTICAL DEVELOPMENT	
	3.2.P.2.1	Components of the Drug Product
		3.2.P.2.1.1 Drug Substance Submitted
		3.2.P.2.1.2 Excipients Submitted
	3.2.P.2.2	Drug Product
		3.2.P.2.2.1 Formulation Development Submitted
		3.2.P.2.2.2 Overages Submitted
		3.2.P.2.2.3 Physicochemical and Biological Properties Submitted
	3.2.P.2.3	Manufacturing Process Development Submitted
	3.2.P.2.4	Container Closure System Submitted
	3.2.P.2.5	Microbiological Attributes Submitted
	3.2.P.2.6	Compatibility Not applicable
3.2.P.3	MANUFACTURE	

	3.2.P.3.1	Manufacturer(s) Submitted Name and full address(es) of the facility(i.e.) Contact name, phone and fax numbers, email address
	3.2.P.3.2	Batch formula Submitted
	3.2.P.3.3	Description of manufacturing process and process controls Submitted
	3.2.P.3.4	Controls of critical steps and intermediates Submitted
	3.2.P.3.5	Process validation and/or evaluation Submitted
3.2.P.4	CONTROL OF EXCIPIENTS	
	3.2.P.4.1	Specifications Submitted
	3.2.P.4.2	Analytical procedures Submitted
	3.2.P.4.3	Validation of analytical procedures Submitted
	3.2.P.4.4	Justification of specifications (as applicable) Submitted
	3.2.P.4.5	Excipients of human or animal origin Submitted
	3.2.P.4.6	Novel excipients Submitted
3.2.P.5	CONTROLS OF DRUG PRODUCT	
	3.2.P.5.1	Specification(s) Submitted
	3.2.P.5.2	Analytical procedures Submitted
	3.2.P.5.3	Validation of analytical procedures Submitted
	3.2.P.5.4	Batch analysis Submitted
	3.2.P.5.5	**Characterization of impurities Not submitted** **Firm submit substance related impurities and claim that "we confirm impurities in finished product will be well within the limit.**
	3.2.P.5.6	Justification of specifications Submitted
3.2.P.6		Reference Standards or Materials Submitted
3.2.P.7		CONTAINER CLOSURE SYSTEM Submitted
3.2.P.8	STABILITY	
	3.2.P.8.1	Stability summary and conclusion (Finished Dosage Form) Submitted Stability protocol submitted
	3.2.P.8.2	Post-approval Stability Protocol and Stability Commitment Submitted
	3.2.P.8.3	Stability Submitted
		Firm has submitted three batches long term stability data 3 batches 36 months at 30 ± 2^0C,75%RH and 6 months at 40^0C±75%RH for three batches for applied strengths separately.

Decision of 292nd meeting:

Deferred due to following:

i. Importable from India as per IPO
ii. Provided photocopy of CoPP legalized not original.
iii. Submissionof relevant informationagainst section 3.2.P.5.5 (Characterization of Impurities.)

Submission by the firm:

- Original legalized CoPP (certificate No. 5375/2019 issued for Vepridone 25mg) valid till 13/11/2021 issued by Food and Drugs Administration Punjab, India.
  The applied product is present for free sale in the market of exporting country.
  The facilities and operations conform to WHO-GMP.
  Product License holder and Manufacturer: M/s Kwality Pharmaeucticals Limited, Village Nag Kalan, Majitha road, Amritsar, Punjab, India.
- Original legalized CoPP (certificate No. 5374/2019 issued for Vepridone 37.5mg) valid till 13/11/2021 issued by Food and Drugs Administration Punjab, India.
  The applied product is present for free sale in the market of exporting country.
  The facilities and operations conform to WHO-GMP.

Product License holder and Manufacturer: M/s Kwality Pharmaeucticals Limited, Village Nag Kalan, Majitha road, Amritsar, Punjab, India.

- The firm has submitted relevant details regarding characterization of impurities.

Decision of 308th meeting:

The Board decided to refer the case to DRAP's Authority in light of its decision regarding importability from India.

Evaluation by PEC:

The case was placed in 136th meeting of the Authority for deciding whether the applied product is importable form India or otherwise. The authority has decided as follows:

"The Authority after due deliberation noted that as Risperidone 25mg & 37.5mg Extended Release Microsphere Injection having HS code 3004.4900, is importable from India under Import Policy Order-2016, so Registration Board may take its decision keeping in view the safety, efficacy and quality of the applied product".

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

b. Vepridone (Risperidone Prolonged Release Powder for Injection) 37.5mg

Dy. No 14163 Dated 05-08-2019 (Rs. 50,000/- Dated 05-08-2019)

MODULE 1: ADMINISTRATIVE

Section	Sub-Section	Heading
1.1		Covering Letter and Fee Deposit Slip Submitted Dy. No 14163 Dated 05-08-2019 (Rs. 50,000/- Dated 05-08-2019)
1.2		Table of Contents (From Module 1 to Module 5) Submitted
1.3		Applicant Information Submitted
	1.3.1	Name, address and contact details of Applicant / Marketing Authorization Holder: M/s Genetics Pharmaceuticals pvt. Ltd. Ltd 539-A, Sundar Industrial Estate, Raiwind Road Lahore
	1.3.2	Name, address and contact details of Manufacturing site. M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India
	1.3.3	Specify whether the Applicant is: Importer
	1.3.4	**Drug Sale License** No: 0011000 0000696 valid upto 12-December-2019
	1.3.8	Manufacturer's Site Master File and Credential (for importer) Submitted
1.4		Type of Application Submitted
	1.4.1	Application is for the registration of: Generic Drug Product
	1.4.1	Pharmaceutical product is intended for: □ **Domestic sale**
	1.4.2	For imported products, please specify one of following: □ **Finished Pharmaceutical Product Import**
1.5		Detailed Information of Drug, Dosage From & Labelling Claims Submitted
	1.5.1	Generic name with chemical name & synonyms of the applied drug. Risperidone Extended-release Microspheres for injection 25mg/vial Risperidone Extended-release Microspheres for injection 37.5mg/vial
	1.5.2	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit Each vial contains:

		Risperidone ……...37.5mg
	1.5.3	The proposed proprietary name / brand name under which the drug is intended to be sold with trademark certification / clearance. Vepridone (Risperidone Prolonged Release Powder for Injection)
	1.5.4	Proposed Pack size and Proposed unit price of drug e.g., per tablet / capsule. Maximum Retail Price (MRP) per pack shall also be mentioned. 1's
	1.5.5	Pharmacotherapeutic Group of Active Pharmaceutical Ingredient (API) Antipsychotic
	1.5.6	Pharmacopoeial reference / Status of applied formulation In-house
	1.5.7	Route of administration IM
	1.5.9	The registration status of applied drug in same molecule and salt, strength, dosage form, container closure system, indications and route of administration etc. in other countries. The status in reference regulatory authorities is mandatory to mention. RISPERDAL CONSTA 25 mg powder and solvent for prolonged-release suspension for injection (UK) RISPERDAL CONSTA 37.5 mg powder and solvent for prolonged-release suspension for injection
	1.5.10	Dosage form of applied drug Powder for Injection
	1.5.11	Proposed label (outer (secondary) & inner (primary)) & colour scheme in accordance with Drug (Labelling & Packing) Rules, 1986 along with specimens Submitted
	1.5.12	Description of Batch numbering system
	1.5.14	Summary of Product Characteristics (SmPC) including Prescribing Information (PI) along with Patient information Leaflet (PIL) of the Finished Pharmaceuticals Product (FPP). Submitted
	1.5.15	Commitment / Undertaking that after registration of applied drug, the Pharmacovigilance department of the applicant / manufacture is liable to impose similar restrictions, addition of any clinical information (like in Indications, Contra-indications, Side effects, Precautions, Dosage & A0dverse Drug Reactions etc. in Summary of Product Characteristics (SmPC), Labelling & Promotional material) or withdraw the drug from market in Pakistan within fourteen days after knowing that such information (which was not available or approved by the DRAP at the time of registration) / actions taken (for safety reasons) by any reference / stringent drug regulatory agency / authority & also inform the DRAP (Drug Regulatory Authority of Pakistan) for further action in this regard. **Submitted**
	1.5.16	Commitment / Undertaking that the applicant shall recall the defective Finished Pharmaceutical Products (FPP) and notify the compliance to the authority along with detail of actions taken by him as soon as possible but not more than ten days. The level of recall shall also be defined. **Submitted**
	1.5.17	Commitment / Undertaking that in case of any false claim / concealing of information, the DRAP has the right to reject the application at any time, before and even after approval or registration of the product in case if proved so. **Submitted**
	1.5.18	Commitment / Undertaking that the firm shall follow the official pharmacopoeia specifications for product / substance as published in the latest edition & shall update its specification as per latest editions of the same. In case, the specifications of product / substance not present in any official pharmacopoeia the firm shall establish

		the specifications. In both cases, the validation of specifications shall be done by the applicant. **Submitted**
	1.5.19	Commitment / Undertaking that in case of any post approval change, the applicant shall ensure that the product with both approvals shall not be available in the market at the same time. And the product with new approvals shall be marketed only after consumption / withdrawal of stock with previous approvals. The company shall be liable to inform the same regarding marketing status of product to the DRAP after getting such post-registration approvals. **Submitted**
	1.5.20	Other commitment e.g., regarding stability studies etc.
	1.5.21	Protocols along with the commitment to follow Good Laboratory Practices (GLP) by the Manufacturer.
	1.5.22	Protocols to implement Good Pharmacovigilance Practice by the Pharmacovigilance department/section of the Manufacturer / Company.
1.6		Miscellaneous Information Submitted
	1.6.1	Information on Prior-related Applications
	1.6.2	Appendix
	1.6.3	Electronic Review Package
	1.6.4	QIS (Quality Information Summary)
	1.6.5	Drug Substance related Document including following: Name and address of API manufacturer. M/s Jubilant Lifesciences Limited Block 133, village samlaya, Taluka Savli, Distt. Vadodara-391520, Gujrat India
	• Copy of Legalized, Notarized CoPP for Risperidone Pronged Release Powder for Injection 25mg (Certificate#. 4892/2019) dated 03-04-2019 issued by Commissionerate, FDA Punjab India declaring the free sale of applied product and GMP compliant status of the manufacturer i.e M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India Certificate valid upto: 11/03/2021 • Copy of Legalized, Notarized CoPP for Risperidone Pronged Release Powder for Injection 37.5mg (Certificate#. 4893/2019) dated 03-04-2019 issued by Commissionerate, FDA Punjab India declaring the free sale of applied product and GMP compliant status of the manufacturer i.e M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India Certificate valid upto: 11/03/2021 **(Firm has submitted in reply of photocopy of CoPP legalized and Notarized"The Pakistan Embassy & notary public in India do not attest the original CoPP, they only attest the photocopy")** • Sole agency agreement Between Product License Holder M/s Kwality Pharmaceuticals Ltd Vill. Nag Kalan, Majitha Road, Amritsar-143601 India and Importer M/s Genetics Pharmaceuticals pvt. Ltd. Ltd 539-A, Sundar Industrial Estate, Raiwind Road Lahore dated 28-12-2018	

MODULE 2: CTD SUMMARIES

2.1 Overall CTD Table of Content Submitted
2.2 CTD Introduction Submitted
2.3 Quality Overall Summary (QOS)* Submitted

QUALITY OVERALL SUMMARY (QOS)

2.3	**Drug substance (API)** General information Submitted Manufacture Submitted Characterization Submitted

	Control of drug substance Submitted Reference standards Submitted Container closure system Submitted Stability Submitted
	Drug product Description and composition of the drug product Submitted Pharmaceutical development Submitted Components of the drug product 2.3.P.2.1.1 Drug substance (API) Submitted 2.3.P.2.1.2 Excipients Submitted Finished Pharmaceutical Product Submitted Manufacturing process development Submitted Container closure system Submitted Manufacture Submitted Control of excipients Submitted Control of drug product Submitted Reference standards and materials Submitted Container closure system Submitted Stability Submitted
2.4	Non-Clinical Overview Submitted
2.5	Clinical Overview Submitted
2.6	Non-Clinical Written and Tabulated Summaries (Normally not required for generics) Submitted
2.7	Clinical summary Submitted

MODULE 3: QUALITY

3.1 Table of Contents of Module 3 Submitted

3.2 Body of Data Submitted

3.2.S DRUG SUBSTANCE (API)

3.2.S.1	GENERAL INFORMATION (May not refer to DMF)	
	3.2.S.1.1	Nomenclature Submitted
	3.2.S.1.2	Structure Submitted
	3.2.S.1.3	General properties Submitted
3.2.S.2	MANUFACTURER	
	3.2.S.2.1	Manufacturer(s) Submitted
	3.2.S.2.2	Description of Manufacturing Process and Process Controls Submitted
	3.2.S.2.3	Control of Materials Submitted
	3.2.S.2.4	Control of Critical steps and intermediates Not Submitted
	3.2.S.2.5	Process Validation and/or Evaluation Not submitted
	3.2.S.2.6	Manufacturing process development not Submitted
3.2.S.3	CHARACTERIZATION	
	3.2.S.3.1	Elucidation of Structure and other Characteristics Submitted
	3.2.S.3.2	Impurities Submitted
3.2.S.4	CONTROL OF DRUG SUBSTANCE (API)	
	3.2.S.4.1	Specification Submitted
	3.2.S.4.2	Analytical procedures Submitted
	3.2.S.4.3	Validation of analytical procedures Submitted

	3.2.S.4.4	Batch analysis Certificate of analysis (COA) specifications and test results from drug substance (API) manufacturer(s) Drug product manufacturer's certificate of analysis with API lot numbers
	3.2.S.4.5	Justification of specifications Submitted
3.2.S.5		REFERENCE STANDARDS Submitted
3.2.S.6		CONTAINER CLOSURE SYSTEMS Submitted
3.2.S.7	STABILITY	
	3.2.S.7.1	Stability Summary and Conclusions Submitted
	3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment Submitted
	3.2.S.7.3	Stability Data Submitted

3.2.P DRUG PRODUCT

3.2.P.1	DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT Submitted	
3.2.P.2	PHARMACEUTICAL DEVELOPMENT	
	3.2.P.2.1	Components of the Drug Product
		3.2.P.2.1.1 Drug Substance Submitted
		3.2.P.2.1.2 Excipients Submitted
	3.2.P.2.2	Drug Product
		3.2.P.2.2.1 Formulation Development Submitted
		3.2.P.2.2.2 Overages Submitted
		3.2.P.2.2.3 Physicochemical and Biological Properties Submitted
	3.2.P.2.3	Manufacturing Process Development Submitted
	3.2.P.2.4	Container Closure System Submitted
	3.2.P.2.5	Microbiological Attributes Submitted
	3.2.P.2.6	Compatibility Not applicable
3.2.P.3	MANUFACTURE	
	3.2.P.3.1	Manufacturer(s) Submitted Name and full address(es) of the facility(i.e.) Contact name, phone and fax numbers, email address
	3.2.P.3.2	Batch formula Submitted
	3.2.P.3.3	Description of manufacturing process and process controls Submitted
	3.2.P.3.4	Controls of critical steps and intermediates Submitted
	3.2.P.3.5	Process validation and/or evaluation Submitted
3.2.P.4	CONTROL OF EXCIPIENTS	
	3.2.P.4.1	Specifications Submitted
	3.2.P.4.2	Analytical procedures Submitted
	3.2.P.4.3	Validation of analytical procedures Submitted
	3.2.P.4.4	Justification of specifications (as applicable) Submitted
	3.2.P.4.5	Excipients of human or animal origin Submitted
	3.2.P.4.6	Novel excipients Submitted
3.2.P.5	CONTROLS OF DRUG PRODUCT	
	3.2.P.5.1	Specification(s) Submitted
	3.2.P.5.2	Analytical procedures Submitted
	3.2.P.5.3	Validation of analytical procedures Submitted
	3.2.P.5.4	Batch analysis Submitted
	3.2.P.5.5	**Characterization of impurities Not submitted** **Firm submit substance related impurities and claim that "we confirm impurities in finished product will be well within the limit.**
	3.2.P.5.6	Justification of specifications Submitted

3.2.P.6		Reference Standards or Materials Submitted
3.2.P.7		CONTAINER CLOSURE SYSTEM Submitted
3.2.P.8	STABILITY	
	3.2.P.8.1	Stability summary and conclusion (Finished Dosage Form) Submitted Stability protocol submitted
	3.2.P.8.2	Post-approval Stability Protocol and Stability Commitment Submitted
	3.2.P.8.3	Stability Submitted
		Firm has submitted three batches long term stability data 3 batches 36 months at 30±2^{0}C,75%RH and 6 months at 40^{0}C±75%RH for three batches for applied strengths separately.

Decision of 292nd meeting:

Deferred due to following:

iv. Importable from India as per IPO
v. Provided photocopy of CoPP legalized not original.
vi. Submissionof relevant informationagainst section 3.2.P.5.5 (Characterization of Impurities.)

Submission by the firm:

- Original legalized CoPP (certificate No. 5375/2019 issued for Vepridone 25mg) valid till 13/11/2021 issued by Food and Drugs Administration Punjab, India.
  The applied product is present for free sale in the market of exporting country.
  The facilities and operations conform to WHO-GMP.
  Product License holder and Manufacturer: M/s Kwality Pharmaeucticals Limited, Village Nag Kalan, Majitha road, Amritsar, Punjab, India.
- Original legalized CoPP (certificate No. 5374/2019 issued for Vepridone 37.5mg) valid till 13/11/2021 issued by Food and Drugs Administration Punjab, India.
  The applied product is present for free sale in the market of exporting country.
  The facilities and operations conform to WHO-GMP.
  Product License holder and Manufacturer: M/s Kwality Pharmaeucticals Limited, Village Nag Kalan, Majitha road, Amritsar, Punjab, India.
- The firm has submitted relevant details regarding characterization of impurities.

Decision of 308th meeting:

The Board decided to refer the case to DRAP's Authority in light of its decision regarding importability from India.

Evaluation by PEC:

The case was placed in 136th meeting of the Authority for deciding whether the applied product is importable form India or otherwise. The authority has decided as follows:

"The Authority after due deliberation noted that as Risperidone 25mg & 37.5mg Extended Release Microsphere Injection having HS code 3004.4900, is importable from India under Import Policy Order-2016, so Registration Board may take its decision keeping in view the safety, efficacy and quality of the applied product".

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,50/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

39.	Name and address of Applicant	M/s The Searle Company Limited, 1st floor, N.I.C.L building Abbasi Shaheed Road, Karachi
	Detail of Drug Sale License	License No.: 016 Address: The Searle company limited, Plot No. F-319, S.I.T.E., Karachi Godown: 1. Plot No. section 1f-2/Q SITE Karachi. 2. Plot No. 54 Dedhu pass tapo gabo pat Baldia town Karachi. Validity: 15/05/2021 Status: Drug sale license by the way of wholesale

	Name and address of manufacturer	M/s Midascare Pharmaceuticals Pvt. Ltd. B-16, MIDC Waluj, Aurangabad 431 136, India
	Name and address of marketing authorization holder	M/s Midascare Pharmaceuticals Pvt. Ltd. B-16, MIDC Waluj, Aurangabad 431 136, India
	Name of exporting country	India
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No.2145 Dated 01/11/2016
	Fee including differential fee	Rs. 100,000/- Dated 28/10/2016
	Brand Name +Dosage Form + Strength	FLUSAL 125 HFA Inhaler 25mcg/125mcg
	Composition	Each actuation delivers: Salmeterol as xinafoate…….. 25mcg Fluticasone propionate….. 125mcg
	Finished Product Specification	In House
	Pharmacological Group	Adrenergics, corticosteroids
	Shelf life	24 motnhs
	Demanded Price	As per DPC
	Pack size	1's
	International availability	Seroflo (25mcg/125mcg and 25mcg/250mcg) Inhaler by M/s Fanin Uk Ltd. (MHRA approved)
	Me-too status	Saltra Inhaler (25mcg/125mcg and 25mcg/250mcg) by M/s Getz Pharma (Reg No. 081557)
	Detail of certificates attached • Original legalized Free sale Certificate (FSC) (certificate No. 6094076) issued by FDA Maharashtra State, India valid till 29/05/2021. Following product are available for free sale in exporting country as per FSC. Flusal 50 HFA 25mcg/50mcg Flusal 250 HFA 25mcg/250mcg Flusal 125 HFA 25mcg/125mcg • Original legalized GMP (No. NEW-WHO-GMP/CERT/AD/88344/2019/11/30633) issued by FDA Maharashtra, India valid till 25/12/2022. • sole agency agreement is submitted whereby M/s Midas Care Pharmaceuticals pvt. Ltd., authorized M/s The Searle Company Limited as an agent for Flusal 50, Flusal 250 and Flusal 125.	
	Stability studies	Long term/ Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Remarks of the Evaluator.	• The firm has claimed In House manufacturing specifications while the product is present in BP and USP. Validity of FSC is 29/05/2021.
	Decision of 308th meeting: Deferred for confirmation for importability from India as per DRAP's Authority decision. **Submission by the firm:** • The firm has stated that as per Import Policy Order 2016, the applied product does not come under Apendix-G (list of non-importable products). • Fluticasone propionate is Corticosteroid. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/076504_original%20approval_package.pdf (REF: USFDA, accessed 22/07/2022) • Salmeterol Xinofoate is Beta-2 Adrenergic Bronchodilator. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020692s047lbl.pdf (Ref: USFDA Accessed on 22/07/2022). • However, as per import policy order serial No. 66 of Appendix G *"Containing Corticosteroid Hormones, Their Derivatives or Structural Analogues".*	

Decision: The Board discussed the case in detail regarding importability from India and decided to defer the case for seeking guidance from DRAP Authority for importability of the applied product from India as import policy order 2016 and DRAP's Authority decision.		
40.	Name and address of Applicant	M/s The Searle Company Limited, 1st floor, N.I.C.L building Abbasi Shaheed Road, Karachi
	Detail of Drug Sale License	License No.: 016 Address: The Searle company limited, Plot No. F-319, S.I.T.E., Karachi Godown: 1. Plot No. section 1f-2/Q SITE Karachi. 2. Plot No. 54 Dedhu pass tapo gabo pat Baldia town Karachi. Validity: 15/05/2021 Status: Drug sale license by the way of wholesale
	Name and address of manufacturer	M/s Midascare Pharmaceuticals Pvt. Ltd. B-16, MIDC Waluj, Aurangabad 431 136, India
	Name and address of marketing authorization holder	M/s Midascare Pharmaceuticals Pvt. Ltd. B-16, MIDC Waluj, Aurangabad 431 136, India
	Name of exporting country	India
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No.2144 Dated 01/11/2016
	Fee including differential fee	Rs. 100,000/- Dated 28/10/2016
	Brand Name +Dosage Form + Strength	FLUSAL 50 HFA Inhaler 25mcg/50mcg
	Composition	Each actuation delivers: Salmeterol as xinafoate…….. 25mcg Fluticasone propionate….. 50mcg
	Finished Product Specification	In House
	Pharmacological Group	Adrenergics, corticosteroids
	Shelf life	24 motnhs
	Demanded Price	As per DPC
	Pack size	1's
	International availability	Seretide Evohaler 25 microgram /50 microgram by M/s Glaxo Wellcome UK Ltd (MHRA Approved)
	Me-too status	Salmicort inhaler 25mcg/50mcg by M/s Macter Int. (Reg # 045209)
	Detail of certificates attached • Original legalized Free sale Certificate (FSC) (certificate No. 6094076) issued by FDA Maharashtra State, India valid till 29/05/2021. Following product are available for free sale in exporting country as per FSC. Flusal 50 HFA 25mcg/50mcg Flusal 250 HFA 25mcg/250mcg Flusal 125 HFA 25mcg/125mcg • Original legalized GMP (No. NEW-WHO-GMP/CERT/AD/88344/2019/11/30633) issued by FDA Maharashtra, India valid till 25/12/2022. • sole agency agreement is submitted whereby M/s Midas Care Pharmaceuticals pvt. Ltd., authorized M/s The Searle Company Limited as an agent for Flusal 50, Flusal 250 and Flusal 125.	
	Stability studies	Long term/ Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

	Remarks of the Evaluator.	• The firm has claimed In House manufacturing specifications while the product is present in BP and USP. Validity of FSC is 29/05/2021.
	Decision of 308th meeting: Deferred for confirmation for importability from India as per DRAP's Authority decision. **Submission by the firm:** • The firm has stated that as per Import Policy Order 2016, the applied product does not come under Apendix-G (list of non-importable products). • Fluticasone propionate is Corticosteroid. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/076504_original%20approval_package.pdf (REF: USFDA, accessed 22/07/2022) • Salmeterol Xinofoate is Beta-2 Adrenergic Bronchodilator. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020692s047lbl.pdf (Ref: USFDA Accessed on 22/07/2022). • However, as per import policy order serial No. 66 of Appendix G *"Containing Corticosteroid Hormones, Their Derivatives or Structural Analogues".*	
Decision: The Board discussed the case in detail regarding importability from India and decided to defer the case for seeking guidance from DRAP Authority for importability of the applied product from India as import policy order 2016 and DRAP's Authority decision.		
41.	Name and address of Applicant	M/s The Searle Company Limited, 1st floor, N.I.C.L building Abbasi Shaheed Road, Karachi
	Detail of Drug Sale License	License No.: 016 Address: The Searle company limited, Plot No. F-319, S.I.T.E., Karachi Godown: 1. Plot No. section 1f-2/Q SITE Karachi. 2. Plot No. 54 Dedhu pass tapo gabo pat Baldia town Karachi. Validity: 15/05/2021 Status: Drug sale license by the way of wholesale
	Name and address of manufacturer	M/s Midas care Pharmaceuticals Pvt. Ltd. B-16, MIDC Waluj, Aurangabad 431 136, India
	Name and address of marketing authorization holder	M/s Midascare Pharmaceuticals Pvt. Ltd. B-16, MIDC Waluj, Aurangabad 431 136, India
	Name of exporting country	India
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No.2146 Dated 01/11/2016
	Fee including differential fee	Rs. 100,000/- Dated 28/10/2016
	Brand Name +Dosage Form + Strength	FLUSAL 250 HFA Inhaler 25mcg/250mcg
	Composition	Each actuation delivers: Salmeterol as xinafoate…….. 25mcg Fluticonasone propionate…... 250mcg
	Finished Product Specification	In House
	Pharmacological Group	Adrenergics, corticosteroids
	Shelf life	24 motnhs
	Demanded Price	As per DPC
	Pack size	1's
	International availability	Seroflo (25mcg/125mcg and 25mcg/250mcg) Inhaler by M/s Fanin Uk Ltd. (MHRA approved)

	Me-too status	Saltra Inhaler (25mcg/125mcg and 25mcg/250mcg) by M/s Getz Pharma (Reg No. 081558)
	Detail of certificates attached • Original legalized Free sale Certificate (FSC) (certificate No. 6094076) issued by FDA Maharashtra State, India valid till 29/05/2021. Following product are available for free sale in exporting country as per FSC. Flusal 50 HFA 25mcg/50mcg Flusal 250 HFA 25mcg/250mcg Flusal 125 HFA 25mcg/125mcg • Original legalized GMP (No. NEW-WHO-GMP/CERT/AD/88344/2019/11/30633) issued by FDA Maharashtra, India valid till 25/12/2022. • Copy of sole agency agreement is submitted whereby M/s Midas Care Pharmaceuticals pvt. Ltd., authorized M/s The Searle Company Limited as an agent for Flusal 50, Flusal 250 and Flusal 125.	
	Stability studies	Long term/ Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Remarks of the Evaluator-I	• The firm has claimed In House manufacturing specifications while the product is present in BP and USP. Validity of FSC is 29/05/2021.
	Decision of 308th meeting: Deferred for confirmation for importability from India as per DRAP's Authority decision. **Submission by the firm:** • The firm has stated that as per Import Policy Order 2016, the applied product does not come under Apendix-G (list of non-importable products). • Fluticasone propionate is Corticosteroid. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/076504_original%20approval_package.pdf (REF: USFDA, accessed 22/07/2022) • Salmeterol Xinofoate is Beta-2 Adrenergic Bronchodilator. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020692s047lbl.pdf (Ref: USFDA Accessed on 22/07/2022). • However, as per import policy order serial No. 66 of Appendix G *"Containing Corticosteroid Hormones, Their Derivatives or Structural Analogues".*	
Decision: The Board discussed the case in detail regarding importability from India and decided to defer the case for seeking guidance from DRAP Authority for importability of the applied product from India as import policy order 2016 and DRAP's Authority decision.		

Case No. III: Import (Veterinary)
New Cases:

42.	**Name and address of Applicant**	M/s Atzan Pharmaceuticals, commercial area aziz Bhatti town Sargodha
	Detail of Drug Sale License	DSL No. 0011000 0001644 valid up 14-Apr-2020
	Name and address of manufacturer	M/s Vietnam Sakan Technology Development & Investment Joint Stock Company, Lot D1-D4 Dong Tho Industrial Complex, Yen Phong District, BAC Ninh Province, Vietnam.
	Marketing authorization holder	M/s Vietnam Sakan Technology Development & Investment Joint Stock Company, Lot D1-D4 Dong Tho Industrial Complex, Yen Phong District, BAC Ninh Province, Vietnam.
	Name of exporting country	Vietnam
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No 23395 Dated 07-12-2017
	Fee including differential fee	Rs. 100,000/- Dated 07-12-2017

	Brand Name +Dosage Form + Strength	Cefquin 2.5 LA suspension for injection
	Composition	Each ml of suspension contains; Cefquinome as sulfate……..25mg
	Finished Product Specification	In-House
	Pharmacological Group	Antiobiotic
	Shelf life	24 months
	Demanded Price	Decontrolled.
	Pack size	1's (type I glass vial)
	Me-too status	COBACTAN 2.5% SUSPENSION FOR INJECTION (50mL), Reg. No. 078219
	Stability studies	Firm has submitted long term (24 months) at 30°C 65±5%RH & accelerated (06 months) stability data at 40°C, 75±5% RH for three batches.
	Detail of certificates attached	➢ Original Legalized Free Sale Certificate issued by Ministry of Agriculture and Rural Development, Department of Animal Health Vietnam (certificate no. 494/2017/QLT-CFS) dated 26/06/2017 is submitted. ➢ Copy of GMP certificate (No.23/22/GCN-GMP) dated 25/07/2022 issued by Ministry of Agriculture and Rural Development. The certificate is valid for 05 years. **As per copy of GMP certificate the manufacturer has production lines of Beta-Lactam in the form suspension for Injection.** ➢ Copy of authorization letter is submitted through which M/s Atzan Pharmaceuticals is appointed as agent for different products including the applied product.

Remarks of the Evaluator:

Observations	Response
Since registration of injections is granted with 01filled volume but you have applied for 03, therefore, select 01 filled volume of the applied product along with the stability study data conducted under the conditions of zone IV-A of 03 batches of relevant filled volume, please. Moreover, provide me-too status of the applied product in same filled volume as selected.	The firm has requested for 50mL filled volume. Me too: COBACTAN 2.5% SUSPENSION FOR INJECTION (50mL), Reg. No. 078219
Submit valid copy of drug sale license.	The firm has submitted receipt for renewal of DSL. Ref No. 384-11940097-2022 Add: 13-E, Commercial area, Aziz Bhatti Town, District Sargodha.
Detail of primary packaging material is required.	Type I glass vial, 50mL.

Decision: The Board discussed that B-Lactam preparations include Penecillins as well as Cephalosporins and submitted copy of GMP certificate does not clarify that the production lines of manufacturer are for Penecillins or Cephalosporins. Keeing in view, the Board decided to defer the case for further clarification of availability of manufacturing failcity for the applied product.

Deferred cases:

43.	Name and address of Applicant	M/s HPI Pharma, Bao wala Opposite truck stand gate no. 2 Rasheed Abad, Jhang Road Faisalabad.
	Detail of Drug Sale License	Drug License by way of wholesale

		Address: HPI Pharma, Ground floor P-171 Medol Town-B, District Faisalabad. Karachi. Validity: 08/08/2020
	Manufacturer & Product License Holder	**Manufacturer & MAH:** M/s Industrial Veterinaria, S.A Esmeralda 19, 08950 Espulgues de Llobregat Barcelona, Spain.
	Name of exporting country	spain
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No 5170-B Dated 06/02/2019
	Fee including differential fee	Rs. 100,000/- Dated 06/02/2019
	Brand Name +Dosage Form + Strength	Pluscolan concentrate for oral solution
	Composition	Each ml contaions: Colistin sulfate……..5,000,000 IU
	Finished Product Specification	In house
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Pack size & Demanded Price	100ml, 1litre, 5litre, price decontrolled
	Me-too status	
	Stability studies	24 moths real time and 06 months accelerated of 3 batches as per ZONE IV-A.
	Detail of certificates attached	Original legalized free sale certificate issued on 06/07/2018, the product is freely sold in exporting country and the manufacturer conforms to WHO-GMP as per the certificate.
	Remarks of the Evaluator.	Clarification is required since the submitted documents (free sale certificate and stability study data) along with the dossier show that the applied product contains Colistin Sulfate (in terms of international units IUs) while the calculation of IU's is based upon the activity of base only. Submit drug product specification data in the light of decision of Registration Board in its 267th meeting. Provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Decision: Deferred for the following: • Clarification is required since the submitted documents (free sale certificate and stability study data) along with the dossier show that the applied product contains Colistin Sulfate (in terms of international units IUs) while the calculation of IU's is based upon the activity of base only. • Submit drug product specification data in the light of decision of Registration Board in its 267th meeting. • Provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. **Submission by the firm:** • The firm has stated that the applied product will be imported from Spain and is approved by the Spanish authority (CimaVet). The approval status of the applied product is verified from available online data base of Spanish Authority. The composition of the applied product is:	

	2. QUALITATIVE AND QUANTITATIVE COMPOSITION Each ml contains: **Active substance:** colistin sulfate 5,000,000 IU file:///C:/Users/farooq.aslam/Downloads/FT_3204%20ESP%20(2).pdf (Accessed on 22/07/2022 at 12:40pm). • As per the document No. EMEA/MRL/016/95-Final (Summary Report for colistin) issued by Committee for Veterinary Medical Products, Colistin Base has been assigned a potency of 1000ug base activity per mg (30,000 IU/mg) and theoretical potency of Colistin Sulphate is 800ug per mg (24,000IU/mg). https://www.ema.europa.eu/en/documents/mrl-report/colistin-summary-report-1-committee-veterinary-medicinal-products_en.pdf (accessed on 22/07/2022 at 1:10pm). • The firm has stated that the formulation is not present in any pharmacopoeia therefore Innovator's specifications may be granted. Initially the firm had applied for In-House specifications. • Me-too status: COLISTIN WATER SOLUBLE POWDER Reg. No. 071022 by M/s Biogen Pharma.
Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Registration Board further decided that registration letter will be issued after submission of applicable fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

Case No IV: Registration application submitted on form 5
Deferred Cases of Form 5 Local Manufacturing:
Covid cases:

Sr. No.	Name of applicant/manufacturer	Brand name	Composition	Dy.No. / Date / Fee	Last Inspection report	Remarks
44.	M/s Biorex Pharmaceuticasl plot No. 251-A, Industrial Triangle Kahuta Road, Islamabad.	Bioquine 200mg tablet	Each Film Coated Tablet contains: Hydroxychloroquine sulfate ……200mg Pack size and price: As per SRO	Dy. No.7617 dated 15/04/2020 Rs. 20,000/- Form 5		Last inspection report is older than 3 years. The firm has applied for uncoated tablet in contrast to innovator's product.

Decision of 295th meeting:
Deferred for the following:
 Submission of evidence of approval of applied formulation as "uncoated tablets" in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting or else the formulation may be revised in accordance with reference product along with submission of requisite fee.
 Referred the case to QA & LT Division to conduct GMP inspection of the firm on priority.
Submission by the firm:
The firm has:
- Revised the formulation from uncoated tablet to film coated tablet and submitted fee of Rs. 7500/- vide challan number 6594010172 dated 24/05/2022.

• Last inspection report dated 28/09/2021, 21/10/2021, 09/12/2021 is submitted. The panel recommended for the renewal of DML for Tablet (General) section, Capsule (General), Capsule (Ceph), Dry Suspension (Ceph), Dry Powder Injection (Ceph) and for additional sections Syrup (General), Dry Suspension (General), Liquid Injectable (Ampoule), Liquid Injectable (Vial), Creams/Ointments (Topical General), Lotions/Gels (Topical General).
Decision: Registration Board approved the registration of the applied product. Conditions regarding validity of registration and data requirement will be same as decided by the Board in its general decision recorded in its 295th meeting.

Routine Cases (Deferred Form 5):

45.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Doxetal 80mg/2ml Injection
	Diary No. Date of R& I & fee	Dy. No 5589 dated 07-02-2019 Rs.20,000/-
	Composition	Each injection vial contains: Docetaxel……80mg
	Pharmacological Group	plant alkaloids and other natural products
	Type of Form	Form-5
	Finished Product Specification	USP
	Pack Size & Demanded Price	Asper SRO
	Approval Status of Product in Reference Regulatory Authorities	Approved in TGA Australia (DOCETAXEL AN docetaxel 80mg/2mL concentrated solution for injection vial with diluent vial)
	Me-too Status	Plustaxano Anhidro 80mg/2ml Concentrate Solution for Infusion of M/s. Ghani brothers Reg. no. 044885 (registered in import)
	GMP Status	GMP inspection conducted on 19.09.2018 concluded satisfactory level of GMP compliance.
	Remarks of the Evaluator.	Terminal sterilization not mentioned • Packaging material not mentioned submit separate application for diluent
	Previous Decision of Registration Board (M-296)	Deferred for the following: • Submit justification on scientific grounds for not performing terminal sterilization of applied formulation. • Mention type of primary packaging material of applied formulation whether it is type I, II, or III glass container. • Status of Diluent whether it is combo pack or otherwise.
	Response of the Firm	• Firm informed that revised method of manufacturing has been submitted with terminal sterilization process. • Primary packaging material is Glass vial Type-I • Firm stated that they have already given registration of higher strength of same formulation in 275th meeting of Registration Board in which the approval has been granted with 9ml diluent. So, firm has demanded for combo pack with diluent.
	Decision of 316th meeting:	

	Deferred for clarification regarding availability of diluent whether, it will be procured or it will be self-manufactured. In case of self-manufacturing of diluent by M/s Rotex Pharma Pvt Ltd., firm shall submit manufacturing process along with detail of manufacturing area in which the diluent will be manufactured. **Submission by the firm:** • The firm has stated that the diluent will be self-manufactured in Liquid vial (SVP) Oncology section. The approval of the section was granted vide letter No. F.1-53/2003-Lic(Vol-I) dated 13/06/2017. • Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued n the basis of inspection conducted on 12/08/2020. • The firm has submitted complete method of manufacturing for manufacturing of the diluent. • The firm has the registration of another strength of Docetaxel Injection 120mg/6mL along with the diluent 9mL (Reg. No. 092154) approved in 275th meeting. • The composition of diluent is as per the product approved by TGA Australia. **Label claim:** Each vial (2mL) contains: Docetaxel……..80mg **Composition of diluent:** Each vial (6.5mL) contains: Ethanol absolute……0.845mL Water for injection….6.5mL (q.s)	
	Decision: The Board deliberated that the applied product is in combo pack and the diluent will be manufactured by the manufacturer, therefore the Board approved the case and decided that the applicant will submit full fee that is Rs. 30,000/- for revision of composition of diluent as per reference product before issuance of registration letter.	
46.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Doxetal 20mg/0.5ml Injection
	Diary No. Date of R& I & fee	Dy. No 5595 dated 07-02-2019 Rs.20,000/-
	Composition	Each injection vial contains: Docetaxel……20mg
	Pharmacological Group	plant alkaloids and other natural products
	Type of Form	Form-5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1's(0.5ml) vial: As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Approved in TGA Australia (DOCETAXEL AN docetaxel 80mg/2mL concentrated solution for injection vial with diluent vial)
	Me-too Status	Plustaxano Anhidro 80mg/2ml Concentrate Solution for Infusion of M/s. Ghani brothers Reg. no. 044885 (registered in import)
	GMP Status	GMP inspection conducted on 19.09.2018 concluded satisfactory level of GMP compliance.
	Remarks of the Evaluator.	Terminal sterilization not mentioned • Packaging material not mentioned submit separate application for diluent
	Previous Decision of Registration Board (M-296)	Deferred for the following: • Submit justification on scientific grounds for not performing terminal sterilization of applied formulation.

		• Mention type of primary packaging material of applied formulation whether it is type I, II, or III glass container. • Status of Diluent whether it is combo pack or otherwise.
	Response of the Firm	• Firm informed that revised method of manufacturing has been submitted with terminal sterilization process. • Primary packaging material is Glass vial Type-I • Firm stated that they have already given registration of higher strength of same formulation in 275th meeting of Registration Board in which the approval has been granted with 9ml diluent. So, firm has demanded for combo pack with diluent.
	Decision of 316th meeting: Deferred for clarification regarding availability of diluent whether, it will be procured or it will be self-manufactured. In case of self-manufacturing of diluent by M/s Rotex Pharma Pvt Ltd., firm shall submit manufacturing process along with detail of manufacturing area in which the diluent will be manufactured. **Submission by the firm:** • The firm has stated that the diluent will be self-manufactured in Liquid vial (SVP) Oncology section. The approval of the section was granted vide letter No. F.1-53/2003-Lic(Vol-I) dated 13/06/2017. • Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued n the basis of inspection conducted on12/08/2020. • The firm has submitted complete method of manufacturing for manufacturing of the diluent. • The firm has the registration of another strength of Docetaxel Injection 120mg/6mL along with the diluent 9mL (Reg. No. 092154) approved in 275th meeting. • The composition of diluent is as per the product approved by TGA Australia. **Label claim:** Each vial (0.5mL) contains: Docetaxel……..20mg **Composition of diluent:** Each vial (1.83mL) contains: Ethanol absolute……0.2379mL Water for injection….1.83mL (q.s)	
	Decision: The Board deliberated that the applied product is in combo pack and the diluent will be manufactured by the manufacturer, therefore the Board approved the case and decided that the applicant will submit full fee that is Rs. 30,000/- for revision of composition of diluent as per reference product before issuance of registration letter.	
47.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd., Plot No. 206 & 207. industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Gemnil 1g Injection Lyophilized Powder for Injection
	Diary No. Date of R& I & fee	Dy.No. 5588 dated: 07/02/2019 Rs.20,000/-
	Composition	Each Vial Contains: Gemcitabine as HCL…..…1gm
	Pharmacological Group	Antineoplastic
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1's (26.3mL), Price as per SRO

	Approval Status of Product in Reference Regulatory Authorities	GEMZAR (gemcitabine) for injection, Lyophilized powder (200mg/via & 1gm/vial) by M/s Lilly USA, LLC, USFDA Approved.
	Me-too Status	ONCOGEM 1gm injection by M/s AJ MIRZA PHARMA (PVT) LTD., (Imported) Reg. No. 45672
	GMP Status	Following additional sections were approved vide letter No.F.1-53/2003-Lic.(Vol-I) dated 13th June, 2017. • Tablet (oncology) • Capsule (oncology) • Liquid vial SVP (oncology) • Liquid Ampoule SVP (Onclology) • Dry powder vial (oncology) • Capsule (Ceph) • Dry [powder for oral suspension (ceph) • Dry Powder vial (ceph) • Dry Powder vial (Ceph)
	Remarks of the Evaluator.	Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm with same strength and filled volume could not be confirmed.
	Decision: Decision of 293rd meeting: Deferred for confirmation of manufacturing method (powder filling or lyophilization) and requisite facility. **Submission by the firm:** • The applicant has stated that they had applied for Gemnil 1g & 200mg liquid injection but these products were deferred in 293rd meeting for confirmation of manufacturing facility. • Furthermore, as per the response of the firm, the product will be manufactured in approved Liquid vial SVP Oncology section. • The firm has submitted full fee Rs. 30,000/- vide challan number 17153518278 dated 03/08/2022 along with the duplicate dossiers.. • Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued on the basis of inspection conducted on12/08/2020. **Label Claim:** Each vial (26.3mL) contains: Gemcitabine as HCl…….1g **Reference:** **1.** Gemcitabine IV Infusion 1 g/ 26.3 mL (solution for infusion) Hospira, TGA Australia approved **2.** Gemcitabine Ebewe 80mg Injection By M/s Novartis Reg. no. 66183	
	Decision: The Board discussed that the applied formualtion is approved in reference regualtory authorities as Lyophilised Powder for Injeciton as well as Solution for Injection and the firm has requested the change of dosage form of the applied formualtuion from Lyophilised Powder for Injeciton to Solution for Injection. Keeping in view, the Board deferred the case for furhter clarification of the applied dosage form from the firm.	
48.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd., Plot No. 206 & 207. industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Gemnil 200mg Injection Powder for Injection
	Diary No. Date of R& I & fee	Dy.No. 5600 dated: 07/02/2019 Rs.20,000/-

	Composition	Each Vial Contains: Gemcitabine as HCL…..…200mg
	Pharmacological Group	Antineoplastic
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1's, Price as per SRO
	Approval Status of Product in Reference Regulatory Authorities	GEMZAR (gemcitabine) for injection, Lyophilized powder (200mg/via & 1gm/vial) by M/s Lilly USA, LLC, USFDA Approved.
	Me-too Status	ONCOGEM 200mg injection by M/s AJ MIRZA PHARMA (PVT) LTD., (Imported) Reg. No. 45671
	GMP Status	Following additional sections were approved vide letter No.F.1-53/2003-Lic.(Vol-I) dated 13th June, 2017. • Tablet (oncology) • Capsule (oncology) • Liquid vial SVP (oncology) • Liquid Ampoule SVP (Onclology) • Dry powder vial (oncology) • Capsule (Ceph) • Dry [powder for oral suspension (ceph) • Dry Powder vial (ceph) • Dry Powder vial (Ceph)
	Remarks of the Evaluator.	
	Decision: Decision of 293rd meeting: Deferred for confirmation of manufacturing method (powder filling or lyophilization) and requisite facility. **Submission by the firm:** • The applicant has stated that they had applied for Gemnil 1g & 200mg liquid injection but these products were deferred in 293rd meeting for confirmation of manufacturing facility. • Furthermore, as per the response of the firm, the product will be manufactured in approved Liquid vial SVP Oncology section. • The firm has submitted full fee Rs. 30,000/- vide challan number 17153518278 dated 03/08/2022 along with the duplicate dossiers. • Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued n the basis of inspection conducted on12/08/2020. **Label Claim:** Each vial (5.3mL) contains: Gemcitabine as HCl…….200mg **Reference:** **1.** Gemcitabine IV Infusion 200 mg/ 5.3 mL Hospira, TGA Australia approved. 2. Gemcitabine Ebewe 200mg Injection By M/s Novartis Reg. no. 66182	
	Decision: The Board discussed that the applied formualtion is approved in reference regualtory authorities as Lyophilised Powder for Injeciton as well as Solution for Injection and the firm has requested the change of dosage form of the applied formualtuion from Lyophilised Powder for Injeciton to Solution for Injection. Keeping in view, the Board deferred the case for furhter clarification of the applied dosage form from the firm.	
49.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Rubidox P 50mg/25ml Injection
	Diary No. Date of R& I & fee	Dy. No 5607 dated 07-02-2019 Rs.20,000/-

	Composition	Each ml contains: Doxorubicin hydrochloride…2mg (as liposomal pegylated)
	Pharmacological Group	Anthracyclines and related substances
	Type of Form	Form-5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1's(25ml): As per SRO
	Approval Status of Product in Reference Regulatory Authorities	USFDA (Doxil Liposomal)
	Me-too Status	Nagun 50 Injection of M/s. Ghani Brothers registered in import (Reg. no. 072574)
	GMP Status	GMP inspection conducted on 19.09.2018 concluded satisfactory level of GMP compliance.
	Remarks of the Evaluator.	Terminal sterilization not mentioned • Packaging material not mentioned submit separate application for diluent
	Previous Decision of Registration Board (M-296)	Deferred for the following: • Submit justification on scientific grounds for not performing terminal sterilization of applied formulation. • Mention type of primary packaging material of applied formulation whether it is type I, II, or III glass container..
	Response of the Firm	• Firm informed that they import ready to fill sterile bulk solution for infusion. • Firm submitted that filling of product done under aseptic condition and prior to filling solution has been filtered for sterilization. • Primary packaging material is Glass vial Type-I.
	Decision of 316th meeting: Deferred for clarification regarding availability of diluent whether, it will be procured or it will be self manufactured. In case of self manufacturing of diluent by M/s Rotex Pharma Pvt Ltd., firm shall submit manufacturing process along with detail of manufacturing area in which the diluent will be manufactured. **Submission by the firm:** • The firm has stated that no diluent is applied and there is no requirement for any diluent as well. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/050718Orig1s060lbl.pdf (Accessed on 21/07/2022 at 1:50pm).	
	Decision: The Board was apprised that the applied product is in liposomal dispersion and the liposomal carriers used in the applied formulation have a complex composition and also product is pegylated. The Board after deliberation regarding complexity of manufacturing method decided to defer the case for detail of manufacturing technique and facility including the detail of equipments used in the manufacturing of the applied product.	
50.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Neoplaxol 100mg/5ml Injection
	Diary No. Date of R& I & fee	Dy.No 5592 dated 07-02-2019 Rs.20,000/-
	Composition	Each 5ml ampoule contains: Etoposide as phospate…100mg
	Pharmacological Group	PLANT ALKALOIDS AND OTHER NATURAL

		PRODUCTS
	Type of Form	Form-5
	Finished Product Specification	USP Specifications
	Pack Size & Demanded Price	1's (5ml):As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Approved in TGA
	Me-too Status	SEDOL 100MG/5ML INJECTION of Helix
	GMP Status	GMP inspection conducted on 19.09.2018 concluded satisfactory level of GMP compliance.
	Remarks of the Evaluator.	Terminal sterilization not mentioned Packaging material not mentioned
	Previous Decision of Registration Board (M-296)	□ Submit justification on scientific grounds for not performing terminal sterilization of applied formulation. □ Mention type of primary packaging material of applied formulation whether it is type I, II, or III glass container.
	Submission by the firm: • The firm has stated that Etoposide API is found to undergo a dehydration reaction in the temperature range of 85^0C to 115^0C which forms new polyform, hence sterilization process performed by filtration under aseptic manufacturing conditions. • Primary packaging material is Glass Ampoule (Type I). • Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued on the basis of inspection conducted on12/08/2020.	
	Decision: Approved.	
51.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Irotec 300mg Injection
	Diary No. Date of R& I & fee	Dy.No 5587 dated 07-02-2019 Rs.20,000/-
	Composition	Each ml contains: Irinotecan Hcl Trihydrate…20mg
	Pharmacological Group	Other antineoplastic agents
	Type of Form	Form-5
	Finished Product Specification	USP Specifications
	Pack Size & Demanded Price	1's (15ml):As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Approved in USFDA
	Me-too Status	IRINOTECAN EBEWE 100MG/5ML of Novartis
	GMP Status	GMP inspection conducted on 19.09.2018 concluded satisfactory level of GMP compliance.
	Remarks of the Evaluator.	Terminal sterilization not mentioned Packaging material not mentioned
	Previous Decision of Registration Board (M-296) □ Submit justification on scientific grounds for not performing terminal sterilization of applied formulation. □ Mention type of primary packaging material of applied formulation whether it is type I, II, or III glass container.	
	Response of the Firm	

	• Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued n the basis of inspection conducted on12/08/2020. • The firm has submitted revised method of manufacturing with the details of terminal sterilization. • Primary packaging material is Type I glass vial.	
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of pre-registration variation fee that is Rs. 30,000/- for revision of manufacturing method as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
52.	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals**,** Plot No. 224, Sector-23, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	Ezesel 10mg+10mg Tablet
	Diary No. Date of R& I & fee	Diary No:15805, 21/09/2017, Rs: 20,000/-
	Composition	Each film coated tablet contains: Atorvastatin …10mg Ezetimibe …10mg
	Pharmacological Group	HMG CoA reductase inhibitors in combination with other lipid modifying agents
	Type of Form	Form-5
	Finished Product Specification	Innovator's specifications
	Pack Size & Demanded Price	10's, 14's, 28's / As per SRO
	Approval Status of Product in Reference Regulatory Authorities	ATOZET 10 mg/10 mg, film-coated tablets by M/s TEVA UK Limited (MHRA approved)
	Me-too Status	Zetab Plus Tablet by M/s Schazoo Laboratories (Reg#046244)
	GMP Status	Last GMP inspection conducted on 19-07-2017 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator.	Firm has applied as Atorvastatin base while approved formulation in MHRA has Atorvastatin (as calcium trihydrate).
	Decision of 313th meeting: Deferred for submission of fee for revision of formulation **Submission by the firm:** • The firm has revised the formulation (Salt form Correction: Atorvastatin as Calcium Trihydrate). The firm has submitted Rs. 7500/- vide challan No. 139609523267 dated 13/04/2022 while full fee is required for revision of formulation. • The revised label claim is: Each film coated tablet contains: Atorvastatin as Calcium Trihydtrate …10mg Ezetimibe …10mg • Initially the firm has applied for Atorvastatin base. • The Gmp inspection is conducted on 12December, 2021 is based on evaluation conducted on 30th June, 2021.	
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of differential fee that is Rs. 22,500/- for revision of formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
53.	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals**,** Plot No. 224, Sector-23, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	Spadix 80mg+80mg Tablet
	Diary No. Date of R& I & fee	Diary No:15805, 21/09/2017, Rs: 20,000/-
	Composition	Each tablet contains:

		Phloroglucinol hydrate …80mg Trimethylphloroglucinol …80mg
	Pharmacological Group	Other drugs for functional gastrointestinal disorders
	Type of Form	Form-5
	Finished Product Specification	Innovator's specifications
	Pack Size & Demanded Price	10's, 14's, 30's / As per SRO
	Approval Status of Product in Reference Regulatory Authorities	SPASFON, coated tablet by M/s Teva Health (ANSM approved.)
	Me-too Status	Anafortan Plus Tablet by M/s AGP Pharma (Reg#024504)
	GMP Status	Last GMP inspection conducted on 19-07-2017 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator.	Firm has applied as plain tablet whereas reference product is approved as sugar coated tablet.
	Decision of 313th meeting: Deferred for submission of fee for revision of formulation **Submission by the firm:** The firm has revised the formulation from plain tablet to Sugar coated Tablet and submitted Rs. 7500/- vide challan No. 3443003125 dated 09/05/2022 for revision of formulation. The revised label claim is: **Each sugar coated tablet contains:** Phloroglucinol hydrate …80mg Trimethylphloroglucinol …80mg The Gmp inspection is conducted on 12th December, 2021 is based on evaluation conducted on 30th june, 2021.	
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of differential fee that is Rs. 22,500/- for revision of formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
54.	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals**,** Plot No. 224, Sector-23, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	Co-Mesart 20mg+10mg Tablet
	Diary No. Date of R& I & fee	Diary No:15805, 21/09/2017, Rs: 20,000/-
	Composition	Each film-coated tablet contains: Olmesartan medoxomil …20mg Amlodipine as besilate …10mg
	Pharmacological Group	Angiotensin II antagonists and calcium channel blockers
	Type of Form	Form-5
	Finished Product Specification	Innovator's specifications
	Pack Size & Demanded Price	10's, 14's, 20's, 28's, 30's / As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Not confirmed
	Me-too Status	Comcarb 10/20mg tablet by M/s Maple Pharmaceuticals (Pvt) Ltd (Reg#061883)
	GMP Status	Last GMP inspection conducted on 19-07-2017 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator.	Firm has applied as Atorvastatin base while approved formulation in MHRA has Atorvastatin (as calcium trihydrate).
	Decision of 313th meeting:	

	Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. **Submission by the firm:** The firm has submitted following reference which has been verified through online data base. • Olmesart amlodipine by Arrotex Pharamceuticals. Each film coated tablet contains: (Olmesartan medoxomil……20mg Amlodipine as besilate…….. 10mg) • TGA Australia Approved https://www.ebs.tga.gov.au/servlet/xmlmillr6?dbid=ebs/PublicHTML/pdfStore.nsf&docid=290091&agid=(PrintDetailsPublic)&actionid=1 (Accessed on 21/07/2022 at 2:44pm) The Gmp inspection is conducted on 12December, 2021 is based on evaluation conducted on 30th june, 2021.	
	Decision: Approved.	
55.	Name and address of manufacturer / Applicant	M/s ZAFA Pharmaceutical Laboratories (Private) Limited L1/B Block-22 Federal B Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Trimezat Tablet 100mg
	Diary No. Date of R& I & fee	Dy No. : 21.05.2011 PKR 8,000/-: 21.05.2011 (Duplicate Dossier) Dy.No. 1209 PKR 12,000/- (slip No. 0730281) 09.01.2019
	Composition	Each tablet contains: Trimebutine maleate…….100mg
	Pharmacological Group	Synthetic anticholinergics, esters with tertiary amino group
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed manufacturer's specifications
	Pack Size & Demanded Price	2 x10's; Rs. 131.45 10 x 10's; Rs. 657.25
	Approval Status of Product in Reference Regulatory Authorities	Debricalm 100mg film-coated tablets. ANSM approved
	Me-too Status	Tribate Tablets. Reg. No. 20257
	GMP Status	GMP certificate dated 25/08/2022 issued on the basis of inspection conducted on 12/08/2022. Tablet general section approved vide letter no. F.2-11/2002-Lic(Vol-I) dated 26/05/2022.
	Remarks of the Evaluator.	The firm was asked for complete finished product specifications; however, the firm submitted incomplete specifications.
	Decision of 288th meeting: Consideration on its turn. **Submission by the firm:** The firm has submitted complete specifications for the applied product along with the testing method. Inspection report is older than 3 years (GMP certificate issue don 23/05/2018)	
	Decision: Approved with innovator's specifications. • **Registration Board further decided that registration letter will be issued after submission of fee that is Rs. 7,500/- for revision of for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021**	

56.	Name and address of manufacturer / Applicant	M/s Welwrd Pharmaceuticals, Plot # 3, Block_A, Phase I-II, Hattar Industrial Estate, Hattar
	Brand Name +Dosage Form + Strength	Thiowalt Capsule 4mg
	Diary No. Date of R& I & fee	Dy No. 22958: 04.12.2017 PKR 20,000/-: 28.11.2017
	Composition	Each capsule contains: Thiocolchicoside…….4mg
	Pharmacological Group	Other centrally acting agents
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed manufacturer's specifications
	Pack Size & Demanded Price	1x10's; as per policy
	Approval Status of Product in Reference Regulatory Authorities	MIOREL 4 mg capsule. ANSM approved
	Me-too Status	Muscucoside capsule 4mg. Reg. No. 81656
	GMP Status	Inspection was conducted on 12.11.2018, wherein the following sections of the firm were considered to be operating at satisfactory level of GMP. i) Tablet Section (General/antibiotics) ii) Liquid injectable section (General/antibiotics) iii) Dry injectable section (General/antibiotics) iv) Dry powder injectable (cephalosporins) While the remaining sections viz Capsule general, dry powder suspension general and Sachet sections were observed with certain shortcomings that need to be rectified.
	Remarks of the Evaluator.	
	Decision of 288th meeting: Deferred for updated status of GMP of the firm form QA & LT division as inspection report submitted by firm does not recommend GMP compliant status for capsule general section**.** **Submission by the firm:** The firm has submitted copy of GMP Certificate No. F.11-76/2022-DRAP-69 issued on 10/06/2022 valid till 30/03/2022.	
	Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
57.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Lab Pvt Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Fexofed 180mg Tablets
	Diary No. Date of R& I & fee	Dy.No 26057 dated 27-12-2017 Rs. 20,000 Dated 27-12-2017
	Composition	Each Tablet Contains: Fexofenadine HCL…180mg
	Pharmacological Group	NSADI
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1x 10's, 20's As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Fexofenadine hydrochloride tablets by Mylan (USFDA Approved) Approved as Film coated tablet
	Me-too Status	Fenadex 180mg tablet of M/s Global Pharmaceuticals (Reg. #031139)

	GMP Status	3-3-2017 Panel recommends the renewal of DML.
	Remarks of the Evaluator.	Internationally approved product is film coated tablet.
	Decision of 287th meeting: Deferred for revision of formulation as per reference product along with submission of requisite fee for change of formulation. Submission by the firm: • The firm has revised the formulation from uncoated to film coated tablet and submitted Rs. 7500/- vide challan number 37219921503 dated 21/07/2022. • Copy of GMP certificate No.F.11-12/2022-DRAP-39 issued on the basis of inspection conducted on 03/02/2022.	
	Decision: Approved.	
58.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Lab Pvt Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Fexofed 180mg Tablets
	Diary No. Date of R& I & fee	Dy.No 26060 dated 27-12-2017 Rs. 20,000 Dated 27-12-2017
	Composition	Each Tablet Contains: Fexofenadine HCL…120mg
	Pharmacological Group	NSADI
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1x 10's, 20's As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Fexofenadine hydrochloride tablets by (MHRA Approved)
	Me-too Status	Epodin 120mg Tablet M/s Epoch Pharmaceutical,
	GMP Status	3-3-2017 Panel recommends the renewal of DML.
	Remarks of the Evaluator.	Internationally approved product is film coated tablet.
	Decision of 287th meeting: Deferred for revision of formulation as per reference product along with submission of requisite fee for change of formulation. Submission by the firm: • The firm has revised the formulation from uncoated to film coated tablet and submitted Rs. 7500/- vide challan number 52136851387 dated 21/07/2022. • Copy of GMP certificate No.F.11-12/2022-DRAP-39 issued on the basis of inspection conducted on 03/02/2022.	
	Decision: Approved.	
59.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceutical labs. (Pvt) Ltd., 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	FE-ZOLE 2.5mg Tablet
	Diary No. Date of R& I & fee	17901, 15-05-2018, 20,000/-, 11-05-2018
	Composition	Each film coated tablet contains: Letrozole…….2.5mg
	Pharmacological Group	Aromatase inhibitor
	Type of Form	Form 5
	Finished Product Specification	In-House
	Pack Size & Demanded Price	10's; As per SRO
	Approval Status of Product in Reference Regulatory Authorities	FEMARA 2.5 mg Tablet by M/s Novartis Pharma **(**USFDA approved)

	Me-too Status	Aromek 2.5mg Tablet by M/s Glaxy Pharmaceuticals (Reg#052258)
	GMP Status	Panel inspection dated 03-03-2017 recommends for renewal of DML.
	Remarks of the Evaluator.	
	Decision of 285th meeting: Registration Board referred the case to QA & LT Division to conduct GMP inspection of Firm on priority. Submission by the firm: The firm has submitted copy of GMP Certificate No. F.11-12/2022-DRAP-39 issued on 28/04/2022 valid till 03/02/2022.	
	Decision: Registration Board approved registration of product with USP specifications in general manufacturing areas with condition that manufacturer shall provide safety and protective measures for workers and personnel which remain in direct contact or are involved in close handling of these drugs. Furthermore, the registration letter will be issued after submission of fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
60.	Name and address of manufacturer / Applicant	M/s Akson Pharmaceuticals Private limited, Plot # 9-B/1&2, old Industrial Estate, Sector D1,Mirpur, Azad Kashmir.
	Brand Name +Dosage Form + Strength	Sulosin 0.2mg capsule
	Diary No. Date of R& I & fee	Dy. No. 41634 dated 07/12/2018 Fee Rs. 20,000/-
	Composition	Each capsule contains: Tamsulosin HCl (pellets SR 0.2%)……..0.2mg Pellets Source of pellets: M/s Vision Pharma
	Pharmacological Group	Alph adrenergic antagonist
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	10's, 30's, 50's, price as per SRO
	Approval Status of Product in Reference Regulatory Authorities	Could not be confirmed
	Me-too Status	Harnal 0.2mg Capsules by M/s Hilton Pharma, Reg No. 45084
	GMP Status	Last inspection report dated 16/06/2017 and 25/07/2017, the panel recommended the renewal of license by the way of formulation.
	Remarks of the Evaluator.	The firm has revised the formulation from Enteric Coated pellets to Sustained Released pellets as per the reference product with submission of fee Rs. 5000/- vide challan number 1983152 dated 30/03/2020.
	Decision of 295th meeting: Deferred for submission of remaining fee. Submission by the firm: The firm has submitted Rs. 15,000/- fee for revision of formulation vide challan No. 94421040 dated 23/12/2021. Last inspection report dated 22/02/2019 concludes "Keeping in view the above stated facts based upon the areas visited, records reviewed and people met, it may be concluded that the management has rectified almost all the observations from previous inspection and as of today the firm's facility is suitable to carry out manufacturing and testing of pharmaceuticals. As , the GMP is a continual process of improvement, hence updating the procedures shall always	

	remain a task, the management is advised to develop a forward thinking progressive environment, adapting the recent trends".	
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of differential fee that is Rs. 15,000/- for revision of formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

Routine Cases (Veterinary):

61.	Name and address of manufacturer / Applicant	M/s Bio-Labs (Pvt) Ltd. Plot No. 145, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Super Dox 80 Powder
	Diary No. Date of R& I & fee	Dy.No 1161: 09-01-2019 Rs. 20,000/-: 04-01-2019
	Composition	Each 1000gram contains: Doxycycline as hyclate…800g
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished Product Specification	Innovator's
	Pack Size & Demanded Price	As per SRO
	Me-too Status	Could not be confirmed
	GMP Status	Inspection report: 18 & 23.04.2019 concludes that: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Bio Labs Pvt Ltd was considered to be operating at a reasonably acceptable compliance with GMP as of today as per the Drugs Act, 1976 and Drap, Act, 2012 and rules framed there under.
	Remarks of the Evaluator[ix]	□ Form 5 has been signed by the quality control manager. □ Provide proof of me-too product (name and registration number) having same strength and salt form already approved by DRAP.
	Previous decision	The board in its 295th meeting deferred the case for confirmation of me-too product.
	Evaluation by PEC	□ Reply dated 02.08.2021: □ The firm submitted signed Form 5. □ The firm provided the following me too: Doxyral 80% water soluble powder Reg. No. 082504 □ The firm has not adjusted the weight of API in master formula as per salt factor.
	Decision of 312th meeting: Deferred for adjustment of the weight of API in master formula as per salt factor along with submission of applicable fee. **Submission by the firm:** The firm has adjusted the weight of API in accordance with the salt factor and has submitted the revised master formula along with the fee of Rs. 30,000/- vide challan number 3243123802 dated 14/06/2022.	
	Decision: Approved.	
62.	Name and address of manufacturer / Applicant	M/s Bio-Labs (Pvt) Ltd. Plot No. 145, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Bio-Cosul 50 WSP
	Diary No. Date of R& I & fee	Dy. No 5561: 08-05-2019 Rs. 20,000/-: 08-05-2019

	Composition	Each Gram Powder Contains: Colistin sulphate…50 MIU
	Pharmacological Group	cationic polypeptide antibiotic
	Type of Form	Form 5
	Finished Product Specification	Innovator's
	Pack Size & Demanded Price	As per SRO
	Me-too Status	Could not be confirmed
	GMP Status	Inspection report: 18 & 23.04.2019 concludes that: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Bio Labs Pvt Ltd was considered to be operating at a reasonably acceptable compliance with GMP as of today as per the Drugs Act, 1976 and Drap, Act, 2012 and rules framed there under.
	Remarks of the Evaluator[ix]	□ Form 5 has been signed by the quality control manager. □ Provide proof of me-too product (name and registration number) having same strength and salt form already approved by DRAP.
	Previous decision	The board in its 295th meeting deferred the case for confirmation of me-too product.
	Evaluation by PEC	□ Reply dated 04.08.2021: □ The firm submitted signed Form 5. □ Now, the firm has claimed in-house specifications without submission of details. □ The firm provided the following me too: COLISTIN WATER SOLUBLE POWDER Reg. No. 071022 with the label claim: EACH 100GM CONTAINS:- COLISTIN SULPHATE..5,000,000 IU, which is not in line with the applied product.
	Decision of 312th meeting: Deferred for confirmation of generic status. Submission by the firm: The firm has revised the label claim in-lined with the me-too product. Each 100gm Contains: Colistin Sulphate…….5,000,000 IU.	
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of full fee that is Rs. 30,000/- for revision of formulation according to me-too product as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

Agenda of Evaluator PEC-II

Case no. 01 New Registration applications on Form 5F (Human)

New Cases (Human)

63.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore**

	Name, address of Manufacturing site.	M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 26927 dated 29-09-2021
	Details of fee submitted	Rs.30,000/- dated 17-09-2021
	The proposed proprietary name / brand name	**Coliate 4.5MIU Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Colistimethate sodium …….. 4.5MIU
	Pharmaceutical form of applied drug	Dry powder injection
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by MHRA of UK
	For generic drugs (me-too status)	Colicraft 2MIU Lypholized powder for solution for injection Reg.# 094751
	GMP status of the Finished product manufacturer	GMP certificate issued on the basis of inspection conducted on 17& 18-01-2019
	Evidence of manufacturing facility.	GMP certificate issued on the basis of inspection conducted on 17& 18-01-2019, declares availability of Dry powder injectable section.
	Name and address of API manufacturer.	M/s Hebei Shengxue Dacheng Pharmaceutical Co., Ltd., China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of

		manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Colixiin Injection of Pharmis Biofarmaceutica, Lda.
	Analytical method validation/verification of product	--

STABILITY STUDY DATA

Manufacturer of API	M/s Hebei Shengxue Dacheng Pharmaceutical Co., Ltd., No. 50 Shengxue Road, Luancheng, Shijiazhuang, China	
API Lot No.	HN180401	
Description of Pack (Container closure system)	Amber glass vial	
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH	
Time Period	Real time: 6 months Accelerated: 6 months	
Frequency	Accelerated: 0,3,6 (Months) Real Time: 0,3,6 (Months)	
Batch No.	Trial-005	Trial-006
Batch Size	2700 packs	2700 packs
Manufacturing Date	06-2020	06-2020
No. of Batches	03	

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No.HE20190058 issued by NMPA China valid till 14/08/2024.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of commercial invoice no. TM20181106 attested by AD DRAP I&E Lahore dated 19-11-2018 for the import of 8Kg Colistimethate sodium.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.1	Submitted covering letter & fee slip mentins the strength as 4MIU whereas the dossier reflects 4.5MIU strength. Clarifcation shall be submittein this regard.	Firm has submitted an "Afffidavit" stating that "Ms English Pharmaceutical do hereby undertake that we have submitted fee challan# 6195143544 dated 17th Spetember 2021, for Coliate 4.5MIU injection bu due to typographical mistake we have written 4MIu instead of 4.5MIU in fee challan & covering letter of said product, we undertake that we will not use dthis fee challan in any other product further.
3.2.S.4.4	Submitted COA of drug substance from M/s English Pharma declares Assay limit in terms of %age instead of mcg/mg or IU/mg. Clarification shall be submitted in this regard	Firm has submitted revise COA of drug substance declaring Assay results both in terms of mcg/mg & %age.
3.2.S.4.5	Clarification shall be submitted whether drug specifications are as per BP or USP monograph.	Specifications by drug substance manufacturer & drug product manufacturer are as per USP monograph as confirmed by the COA and test methods.
3.2.P.1	Provide information including type of diluent, its composition, quantity or volume, which is to be provided along with the applied drug.	2 ml sterile water for injection filled in glass ampoule is accompanying reconstitution diluent.
3.2.P.2.6	Compatibility studies for the dry powder for injections shall be submitted as per the instructions provided in individual label of the drug product.	Firm has submitted results of compatibility study with 2ml sterile water for uinjection with performance of tests of Clarity of solution, pH & Assay.
3.2.P.5.2	• Analytical method has been submitted for Coliate 1MIU injection instead of the applied strength of 4.5 MIU injection. • Clarification shall be submitted regarding incubation time for the performance of Assay test.	• As idenitifed by your good office,there was a typo error in the method drafting , and test method of 4.5MIU injection is now submitted. Incubation time for assay performance is 24 hours or until

		growth is apparent at 32°C to 35 °C.
3.2.P.8	Submitted raw data sheets are not readable. Submit readable copies of the raw data sheets of the stability studies.	Firm has submitted new set of prints for the raw data sheets.

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

64.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore**
	Name, address of Manufacturing site.	M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 26926 dated 29-09-2021
	Details of fee submitted	Rs.30,000/- dated 17-09-2021
	The proposed proprietary name / brand name	**Coliate 2MIU Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Colistimethate sodium …….. 2MIU
	Pharmaceutical form of applied drug	Dry powder injection
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by MHRA of UK
	For generic drugs (me-too status)	Colicraft 2miu Lypholized powder for solution for injection Reg.# 094751
	GMP status of the Finished product manufacturer	GMP certificate issued on the basis of inspection conducted on 17& 18-01-2019
	Evidence of manufacturing facility.	GMP certificate issued on the basis of inspection conducted on 17& 18-01-2019, declares availability of Dry powder injectable section.

	Name and address of API manufacturer.	M/s Hebei Shengxue Dacheng Pharmaceutical Co., Ltd., China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Colixiin Injection of Pharmis Biofarmaceutica, Lda.
	Analytical method validation/verification of product	--

STABILITY STUDY DATA

Manufacturer of API	M/s Hebei Shengxue Dacheng Pharmaceutical Co., Ltd., No. 50 Shengxue Road, Luancheng, Shijiazhuang, China
API Lot No.	HN180401
Description of Pack (Container closure system)	Amber glass vial
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency		Accelerated: 0,1,3,6 (Months) Real Time: 0,1,3,6 (Months)	
Batch No.		T-001	T-002
Batch Size		2700 packs	2700 packs
Manufacturing Date		06-2020	06-2020
No. of Batches		03	
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)		N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.		Copy of GMP certificate No.HE20190058 issued by NMPA China valid till 14/08/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).		• Firm has submitted copy of commercial invoice no. TM20181106 attested by AD DRAP I&E Lahore dated 19-11-2018 for the import of 8Kg Colistimethate sodium.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.		Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing		N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)		Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
3.2.S.4.4	Submitted COA of drug substance from M/s English Pharma declares Assay limit in terms of %age instead of mcg/mg or IU/mg. Clarification shall be submitted in this regard	Firm has submitted revise COA of drug substance declaring Assay results both in terms of mcg/mg & %age.
3.2.S.4.5	Clarification shall be submitted whether drug specifications are as per BP or USP monograph.	Specifications by drug substance manufacturer & drug product manufacturer are as per USP monograph as confirmed by the COA and test methods.
3.2.P.1	Provide information including type of diluent, its composition, quantity or volume, which is to be provided along with the applied drug.	2 ml sterile water for injection filled in glass ampoule is accompanying reconstitution diluent.
3.2.P.2.6	Compatibility studies for the dry powder for injections shall be submitted as per the instructions provided in individual label of the drug product.	Fir mhas submitted results of compatibility study with 2ml sterile water for uinjection with performance of tests of Clarity of solution, pH & Assay.
3.2.P.5.2	• Analytical method has been submitted for Coliate 1MIU injection instead of the applied strength of 2 MIU injection.	• As idenitifed by your good office,there was a typo error in

		• Clarification shall be submitted regarding incubation time for the performance of Assay test.	the method drafting , and test method of 2MIU injection is now submitted. • Incubation time for assay performance is 24 hours or until growth is apparent at 32°C to 35 °C.

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

65.	Name, address of Applicant / Marketing Authorization Holder	**M/s SAMI Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.**
	Name, address of Manufacturing site.	M/s SAMI Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 25927 dated 17-09-2021
	Details of fee submitted	PKR 30,000/-: dated 07/09/2021 PKR 45,000/-: dated 25/10/2021
	The proposed proprietary name / brand name	**Provas Advance 500mg Tablet** **Alternate brand name: PROVAS NOVO 500mg Tablets**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Paracetamol ……. 500mg
	Pharmaceutical form of applied drug	White to off-white colored capsular shaped film coated tablet, break line on one side and other side is plain
	Pharmacotherapeutic Group of (API)	NSAID ATC Code: N02BE01
	Reference to Finished product specifications	USP
	Proposed Pack size	10’s, 20’s, 30’s, 50’s & 100’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Panadol Advance 500mg Tablet, M/s. GSK, approved by MHRA of UK

	For generic drugs (me-too status)	Not applicable
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	**Name:** HEBEI JIHENG (GROUP) PHARMACEUTICAL CO., LTD SHENZHOU PLANT (shortened as Jiheng Shenzhou) **Address:** Southeast Xijingming Village Donganzhuang Township, Shenzhou County Henshui City, Hebei Province, CHINA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, characterization, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted details of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurity J, K, F, individual impurity and total impurity, specifications, analytical procedures and its verification, batch analysis and justification of specification, working standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 Months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is PANADOL ADVANCE 500mg tablet by M/s. GSK. CDP has been performed against the same brand that is PANADOL ADVANCE 500mg tablet by M/s. GSK in Acid media (pH 1.2-4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have been submitted including Linearity, Accuracy & Precision including Repeatability & Specificity.

STABILITY STUDY DATA	
Manufacturer of API	HEBEI JIHENG (GROUP) PHARMACEUTICAL CO., LTD SHENZHOU PLANT, CHINA

API Lot No.	31709016		
Description of Pack (Container closure system)	Alu/PVC Blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-07	Lab-08	Lab-09
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	14-4-2021	14-4-2021	14-4-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted reference of last onsite panel inspection for instant dosage form conducted during last two years i.e. EMPOLI (Empagliflozin) 10mg & 25mg Tablets which was presented in 290th meeting of the registration board & hence approved & registered by registration board Date of inspection: 13th June 2019. The inspection report confirms following points • The HPLC software is 21CFR Compliant. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. HE20180054 issued by Hebei CHINA FOOD AND DRUG ADMINISTRATION valid till 08/07/2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice (Invoice# 1708ZP03 dated 19th October 2017 with received quantity i.e. 5000 kgs) for the purchase of Paracetamol from M/s Hebei Jiheng Shenzhou Pharmaceutical Co., Ltd. China with attestation of DRAP dated 01-11-2017
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator[II]:

- Regarding justification of specifications of drug product, firm has submitted as under:
  "The dissolution parameters and testing procedure is as per USP Pharmacopeia but as the Paracetamol is rapidly dissolving drug and falls in BCS Class I, we stringent the dissolution specifications from 30 minutes to 10 minutes
  The selection of specified time for Dissolution is based on the BCS classification of API, as the drug is independent over physiological pH range (i-e from 1.2 to 6.8) and ·as per USP General chapter <1092>, the dissolution of rapidly dissolving product is achieved within 15 minutes therefore we established our dissolution time within 10minutes."

- Firm has submitted following comparison between the applied formulation and conventional paracetamol tablet already available in market:

Parameters	**PROVAS Novo 500mg Tablet**	**Paracetamol 500mg Tablet**
Dosage Form	Tablet	Tablet
Dosage Design	Immediate release film coated tablet	Immediate release uncoated tablet
Route of Administration	Oral	Oral
Dosage Strength	500mg	500mg
Pharmacokinetics	The special technology allows **PROVAS Novo 500mg Tablet** to begin dissolving in 5 minutes and start to relieve pain within 15 minutes	Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion
Patient's Acceptance & Compliance	• Capsular shape makes it easy to swallow • Bitter taste of Paracetamol is masked through film coating • Quick & Effective Pain Relief Stomach Friendly	• Round shape makes it difficult to swallow • Bitter Taste Delayed Pain Relief
Technology Used	**PROVAS Novo 500mg Tablet** is a Paracetamol formulation that contains an advance technology to rapid the onset of action	**Paracetamol 500mg Tablet** formulated using a conventional wet granulation process
Key Features	• It has unique delivery system as **PROVAS Novo 500mg Tablet** is a Paracetamol formulation that contains a rapid dispersion and dissolution technology which breakdown Paracetamol tablets in the stomach so that the drug is absorbed fast and pain relief can start within 15 minutes after ingestion • The technology contains three main ingredients viz.: ○ **Alginic Acid** draws fluid from the stomach into the tablet causing it to swell and break apart ○ **Calcium Carbonate** works together with Alginic Acid to boost disintegration of the tablet	Onset of action is slow, as peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion

	○ **Crospovidone** acts as a super-disintegrant due to its ability to dissolve well in water • The absorption of Paracetamol occurs in the small intestine and as such is dependent on the rate of emptying of stomach contents into the small intestine and is therefore not associated with gastric irritation. The technology used in **PROVAS Novo 500 mg** Tablet increases gastric emptying time of the drug. • **PROVAS Novo 500mg Tablet** with this advance technology disperses up to five times faster than standard paracetamol tablets Suitable for all such patients requiring low sodium content in their diet	

Section#	Observations	Firm's response
3.2.P.5.1	• Limits for disintegration test i.e., NMT 30 minutes are inconsistent with the limits of dissolution test i.e., NLT 80% (Q) in 10 minutes.	We set disintegration specification according to USP general monograph for Disintegration <701> which specifies NMT 30minutes for film coated tablets. Our product is fast dissoving with a dissolution specs of NLT 80% (Q) in 10 minutes and disintegration time of our product is also found within 01 minute which co relates with dissolution. We have revised the specification of DT from NMT 30 minmutes to NMT 10 minutes.
3.2.P.6	• Submitted COA of working standard declares the "Valid till" date as January 2021, whereas trial batches have been manufactured and analyzed subsequent to this date. • Submitted COA of working standard is of BP grade, whereas drug product specifications have been claimed as per USP monograph.	Firm has submitted new COA of working standard, which had been standardized in January 2021 having validity date as of Jan, 2022. Firm has submitted that the working standard complies with both & USP monograph of Paracetamol, since both the monographs are harmonized.

Decision: The Board was apprised that the firm has applied for two products with the similar formulation that is Paracetamol, film coated tablet with slight difference in method of manufacturing and qualitative composition. The Board after due deliberation decided to defer the case for clarification whether an applicant can apply for registration of more than two products having same composition or otherwise.

66.	Name, address of Applicant / Marketing Authorization Holder	**M/s SAMI Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.**
	Name, address of Manufacturing site.	M/s SAMI Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 25212 dated 10-09-2021
	Details of fee submitted	PKR 75,000/-: dated 27/08/2021
	The proposed proprietary name / brand name	**PROVAS SINU Capsules**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Paracetamol ……. 500mg Caffeine ……. 25mg Phenylephrine HCl ……. 6.1mg
	Pharmaceutical form of applied drug	Unprinted Hard Gelatin Capsule size '0' with orange cap and orange body
	Pharmacotherapeutic Group of (API)	Paracetamol: NSAID ATC Code: N02BE01
		Caffeine: CNS Stimulant ATC Code: N06BC01
		Phenylephrine HCl: Sympathomimetic drug ATC Code: R01BA53
	Reference to Finished product specifications	Innovator's Specs
	Proposed Pack size	10's, 20's, 30's, 50's & 100's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Sudafed Sinus Max Strength 500mg/25mg/6.1mg Capsule. Registered in EMA.
	For generic drugs (me-too status)	Not applicable
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	**<u>Paracetamol</u>** **Name:** HEBIE JIHENG (GROUP) PHARMACEUTICAL CO., LTD., (Shortened as Jiheng Shenzhou) **Address:** Southeast Xijingming Village, Donganzhuang Township, Shenzou County Hengshui City, Hebie Province, CHINA
		<u>Caffeine</u> **Name:** Shandong Xinhua Pharmaceutical Co.,Ltd **Address:** East Chemical Zone of Zibo High & new technology development zone

		<u>Phenylephrine HCl</u> **Name:** Shenzhen Oriental Pharmaceutical Co., Ltd **Address:** 43 Dakeng Road Tongle Village, Longgang District Shenzhen, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**<u>Paracetamol</u>** Stability study conditions: **Real time**: 30°C ± 2°C / 75% ± 5%RH for 60 Months Batches: (31404023, 31404024, 31404025) **Accelerated**: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (31106030, 31106031, 31106032) Declaration for different batch numbers is provided in the dossier **<u>Caffeine</u>** Stability study conditions: **Real time**: 30°C ± 2°C / 75% ± 5%RH for 60 Months Batches: (1307884, 1307890, 1307893) **Accelerated**: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (0904689, 0904690, 0904691) Declaration for different batch numbers is provided in the dossier **<u>Phenylephrine HCl</u>** Stability study conditions: **Real time**: 30°C ± 2°C / 75% ± 5%RH for 48 months Batches: (PEH-170923, PEH-170924, PEH-170925) **Accelerated**: 40°C ± 2°C / 75% ± 5%RH for 6 months

		Batches: (PEH-160404, PEH-160405, PEH-160406) *Declaration for different batch numbers is provided in the dossier*
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, pharmaceutical development, impurities, individual impurity and total impurity, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product i.e. **SUDAFED Sinus Max Strength Capsule** by **M/s. McNeil Products Ltd.** by performing quality tests (Appearance, Average weight, Disintegration, Assay, Dissolution, Microbial Limit Test) CDP has been performed against the same brand i.e. **SUDAFED Sinus Max Strength Capsule** by **M/s. McNeil Products Ltd.** in Acidic media (pH 1.2-4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have been submitted including Linearity, Accuracy, and Precision including Repeatability & Intermediate Precision, Robustness and Specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Paracetamol:** HEBEI JIHENG (Group) Pharmaceutical Co. Ltd. China **Caffeine:** Shandong Xinhua Pharmaceutical Co.,Ltd **Phenylephrine HCl:** Shenzhen Oriental Pharmaceutical Co. Ltd. China		
API Lot No.	**Paracetamol:** 31709016 **Caffeine:** 19101463 **Phenylephrine HCl:** PEH-200303		
Description of Pack (Container closure system)	Alu/PVC (Opaque) blisters		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1,2,3,4 & 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	1000 Capsules	1000 Capsules	1000 Capsules
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	23-11-2020	23-11-2020	23-11-2020
No. of Batches	03		
Administrative Portion			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted reference of last onsite panel inspection for instant dosage form conducted during last two years i.e. EMPOLI (Empagliflozin) 10mg & 25mg Tablets which was presented in 290th meeting of the registration board & hence approved & registered by registration board Date of inspection: 13th June 2019. The inspection report confirms following points • The HPLC software is 21CFR Compliant. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Paracetamol** Copy of GMP certificate (HE20180054) issued to M/s HEBEI JIHENG (Group) Pharmaceutical Co. Ltd. China issued by China Food & Drug Control Administration, valid till 08-07-2023 is submitted **Caffeine** Copy of GMP certificate (SD20190851) issued to M/s. Shandong Xinhua Pharmaceutical Co. Ltd. China issued by China Food & Drug Control Administration, valid till 23-01-2024 is submitted **Phenylephrine HCl** Written confirmation for active substances exported to EU, (Confirmation no. GD190014) issued to M/s. Shenzhen Oriental Pharmaceutical Co. Ltd. China, valid till 11-09-2022 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of following invoices specifying: **Paracetamol** 5000kgs of Paracetamol (invoice # 1708ZP03) attested by AD (I&E), Karachi dated 1-11-2017 is submitted **Caffeine** Detail of loan material (250g of Caffeine Anhydrous, Batch # 191101463) from M/s Semos Pharmaceuticals (Pvt.) Ltd. along with copy of Form-7 of the lot supplied by M/s Shandong Xinhua Pharmaceutical Co. Ltd. under their invoice no. XH191409 dated 07-11-2019 Copy of commercial invoice no. XH19140,9 in the name of M/s Semos, for caffeine anhydrous (batch# 191101463), has also been submitted, attested b AD DRAP I&E Karachi dated 01-01-2020.

		<u>Phenylephrine HCl</u> 1kg of Phenylephrine HCl (Batch # PEH-200303) (invoice # SZ-2003021) attested by AD (I&E), Karachi dated 16-04-2020 is submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator[II]:

- Regarding difference in the stability batches of Caffeine for accelerated and long-term conditions, firm has submitted following declaration from M/s Shandong Xinhua:
  "We did 3 batch stability at 30/75 conditions in 2013; since accelerated was already done in 2009 there was no need to repeat accelerated stability in 2013."

- Regarding difference in the stability batches of Phenylephrine HCl, for accelerated and long-term conditions, firm has submitted following declaration from M/s Shenzhen Oriental:
  "While the batch of long-term stability data for Zone-Iva is not consistent with the accelerated batch, it is because the Zone IV test started from 2017, which is also the first time 3 batches, not involving the process and other any changes, no need to do accelerated tests again."

Section#	Observations	Firm's response
3.2.S.5	COA of primary/working standard, used by M/s Sami Pharma, for the analysis of Caffeine, shall be submitted.	Submitted
1.6.5	Valid GMP certificate for the manufacturer of Phenylephrine HCl shall be submitted instead of written confirmation for active substances exported to EU.	Firm has submitted copy of Drug Manufacturing License (GD20160118) valid upto 23-12-2025, issued by NMPA China,
3.2.P.5.1	MHRA Public assessment report of the refence product recommends dissolution specifications as "Not less than 85% released in 15 minutes", whereas firm has submitted dissolution specifications as "Not less than 85% in 30 minutes". Justification shall be submitted in this regard.	We have developed our product against the reference product Sudafed Sinus Max Strength Capsules. Comparative Dissolution profile (CDP) of PROVAS Sinus Capsule 500mg/25mg/6.1mg Capsule with reference product Sudafed Sinus Max Strength Capsules, shows satisfactory comparable dissolution profile, and product releases more than 85% within 15 minutes

		in all 3 physiological mediums, data already submitted. Initially we have found the MHRA Public Assessment Report of Grippostad day cold and flu relief capsules (Paracetamol 300mg, Phenylephrine hydrochloride 5mg and caffeine 25mg) which does not mentioned the specifications of dissolution test but not found MHRA Public Assessment Report on Max Strength Sinus Relief Capsules (Paracetamol 500mg, Phenylephrine hydrochloride 6.1mg and caffeine 25mg). On query we searched again and found the MHRA Public Assessment Report on Max Strength Sinus Relief Capsules, and that is archived, mentioning the dissolution test 'Not less than 85% released in 15 minutes". But not mentioned the dissolution medium and other dissolution test parameters. We have performed the dissolution test of our product PROVAS Sinu Capsule 500mg/25mg/6.1mg Capsule at 15 minutes and 30 minutes on same lab scale batches (which 6month data was submitted) after 18months at long term stability conditions i.e. 30°C/75% RH and results are attached (*Annex 3)* Based on attached data, our product complies the criteria of NLT 85 % in 15 minutes, therefore we revised the specification of dissolution test 'Not less than 85% released in 15 minutes". Revised Specification and testing method are attached for ready reference, and same specifications will be use for the commercial batches. Hope this will clarify and justify the query
3.2.P.5.6	Justification shall be provided for the selection of dissolution parameters, i.e., medium, apparatus & time.	The development of specification and test method of Paracetamol 500mg + Caffeine 25mg + Phenylephrine HCl 6.1mg capsule is based on general chapters of USP & BP and FDA guideline. Dissolution: Paracetamol, Caffeine & Phenylephrine HCl have solubility over the range in aqueous conditions. Since it is non – pharmacopeia product and no data is published regarding dissolution medium, and other parameters in various sites including FDA dissolution data base till now, therefore, in-house method has been developed having following parameters Apparatus: USP Type I (Basket)

		<table><tr><td>Volume</td><td>900ml</td></tr><tr><td>Dissolution Medium</td><td>Water</td></tr><tr><td>Speed (RPM)</td><td>100</td></tr><tr><td>Time</td><td>30 minutes</td></tr></table> **Basis of Selection of Dissolution Parameters:** Paracetamol, Caffeine & Phenylephrine HCl have solubility over a broad pH range in aqueous conditions as evident from the submitted CDP record (results above 85% within 15 minutes) hence it was inferred that solubility of all 3 APIs were not affected by change in pH and therefore water was selected as dissolution medium Whereas, the speed, time and volume is concerned, we follow the USP general chapter<1092> Dissolution procedure: Development and Validation which states that: **<u>For Speed:</u>** ***For immediate-release capsule or tablet formulations, Apparatus 1 (baskets) at 50–100 rpm or Apparatus 2 (paddles) at 50 or 75 rpm are commonly used***. **<u>For Volume:</u>** ***For compendial Apparatus 1 (basket) and Apparatus 2 (paddle), the volume of the dissolution medium can vary from 500 to 1000 mL.*** **<u>For Time:</u>** ***For immediate-release dosage forms, the duration of the dissolution procedure is typically 15 –60 mins*** On the above basis, we have selected the dissolution parameters viz Speed, time, Medium and apparatus for release and stability of finished product
3.2.P.6	• Submitted COA of working standard declares the "Valid till" date as January 2021, whereas trial batches have been and analysed subsequent to this date. • Submitted COA of working standard is of BP grade, whereas drug product specifications have been claimed as per USP monograph.	• Firm has submitted new COA of working standard, which had been standardized in January 2021 having validity date as of Jan, 2022. • Firm has submitted that the working standard complies with both & USP monograph of Paracetamol, since both the monographs are harmonized.

Decision of 320th meeting: Registration Board while considering the decision of 140th meeting of Authority regarding Borrowing of APIs for performing Product Development, R&D & stability Testing, decided to approved the product with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Furthermore, the Board decided that the firm shall perform dissolution testing as per USFDA method for all commercial batches.**		
67.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. dated 29/09/2021
	Details of fee submitted	PKR 20,000/-: dated 29/09/2021 PKR 10,000/-: dated 29/09/2021
	The proposed proprietary name / brand name	**Rivaxo 2.5mg Tablets**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Rivaroxaban…..2.5mg
	Pharmaceutical form of applied drug	Pink colored, round shaped, biconvex film coated tablet, engraved "GP" on one side and plain on other side.
	Pharmacotherapeutic Group of (API)	Antithrombotic agent
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	1x10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xarelto 2.5mg tablet by M/s Janssen Pharma, USA, USFDA Approved.
	For generic drugs (me-too status)	Revoban 2.5mg Tablet by M/s ATCO laboratories Ltd., Karachi. (Reg. No. 089381)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.

	Name and address of API manufacturer.	**M/s Jiangsu Yongan Pharmaceutical Co., Ltd.** No. 18, 237 provincial highway, Jiangsu Huai'an Economic Development Zone, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (121201, 121202, 130101)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Xcept 2.5mg Tablet by M/s PharmEvo (Pvt.) Ltd., by performing quality tests (Appearance, Average weight, Disintegration time, Assay and Dissolution). CDP has been performed against the same brand that is Xcept 2.5mg Tablet by M/s PharmEvo (Pvt.) Ltd., in Purified Water, Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The f2 values are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including, system suitability, specificity, linearity, accuracy, precision repeatability, Intermediate precision and robustness.

STABILITY STUDY DATA	
Manufacturer of API	M/s Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18, 237 provincial highway, Jiangsu Huai'an Economic Development Zone, China.
API Lot No.	0000174102
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	534DS06	534DS07	534DS08
Batch Size	9000 Tablets	9000 Tablets	9000 Tablets
Manufacturing Date	17-06-2020	26-06-2020	26-06-2020
Date of Initiation	10-07-2020	10-07-2020	10-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine (Ebastine) Tablets 10mg & 20mg on 6th May, 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of Drug Manufacturing License no. Su 20160324 issued by Jiangsu Drug Administration (Huai'an Inspection Branch) valid till 06-12-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted. **Batch No.** | **Invoice No.** | **Quantity Imported** | **Date of approval by DRAP** 2019118 | JXCAVIR-200207 | 25kg | 04-03-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of	Firm has submitted record of digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

	stability chambers (real time and accelerated)	

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.5.6	The section mentions "Not applicable" against pharmacopoeia reference for applied product, whereas BP monograph is available for applied product.	This is to inform you that product registration application of Rivaxo Tablets 2.5mg was submitted on Sep 23, 2021 (receipted copy attached). However, official monograph of Rivaroxaban Tablets has been incorporated in British pharmacopeia 2022 edition. • At the time of dossier submission, official monograph of Rivaroxaban Tablets was not available. Therefore, "Not Applicable" is mentioned against pharmacopeia reference for applied product.
3.2.S.4.1	Submitted specifications and analytical procedure are not as per BP monograph of Rivaroxaban. Test of Enantiomeric purity is not included in the specifications.	This is to inform you that product registration application of Rivaxo Tablets 2.5mg was submitted on Sep 23, 2021 (receipted copy attached). However, official monograph of Rivaroxaban API has been incorporated in British pharmacopeia 2022 edition. At the time of dossier submission, official monograph of Rivaroxaban API was not available. Therefore, submitted specification and analytical procedure are not as per BP monograph of Rivaroxaban and we have adopted specification and testing procedure as provided by API manufacturer. • Firm has submitted updated specification of Rivaroxaban API with the inclusion of test of enantiomer.
3.2.P.2.2.1	Pharmaceutical equivalence & CDP studies have not been conducted against the innovator product.	• This is to inform you that at the time of product development stage, innovator product was not available. However, we have performed Pharmaceutical Equivalence & Comparative Dissolution Profile studies against Xcept 2.5mg Tablets manufactured by M/s PharmEvo (Pvt.) Ltd
3.2.P.5.1	Submitted specifications declare reference as in-house, whereas BP monograph is available for applied product. Submitted specifications and analytical procedure is not as per BP monograph.	This is to inform you that product registration application of Rivaxo Tablets 2.5mg was submitted on Sep 23, 2021 (receipted copy attached). However, official monograph of Rivaroxaban Tablets has been incorporated in British pharmacopeia 2022 edition.

<table>
<tr><td></td><td></td><td>• At the time of dossier submission, official monograph of Rivaroxaban Tablets was not available. Therefore, submitted specifications and analytical procedure declare reference as in-house.</td></tr>
<tr><td>3.2.P.8.3</td><td>• Submitted stability studies have not been conducted as per specification and analytical procedure of BP monograph for Rivaroxaban tablets.</td><td>This is to inform you that we have manufactured 03 batches of Rivaxo Tablets 2.5mg for stability studies as follows:
<table>
<tr><td>Batch No.</td><td>534DS06</td><td>534DS07</td><td>534DS08</td></tr>
<tr><td>Batch Size</td><td>9000 Tablets</td><td>9000 Tablets</td><td>9000 Tablets</td></tr>
<tr><td>Mfg. Date</td><td>17-06-2020</td><td>26-06-2020</td><td>26-06-2020</td></tr>
</table>
06 months accelerated and real time stability studies were completed in Jan-2021 and the dossier was submitted in Sep-2021.

At the time of dossier submission, official monograph of Rivaroxaban Tablets was not available. Therefore, submitted stability studies have been conducted as per In-House specification and analytical procedure.</td></tr>
</table>

Decision of 320th meeting: Approved with BP specifications.

- **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after submission of CDP and pharmaceutical equivalence studies, performed against the innovator's product i..e, Xarelto tablet 2.5mg.**

68.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s The Schazoo Pharmaceutical Laboratories Pvt Ltd. Kalalwala Stop, 20 km Lahore-Jaranwala Road, Distt Sheikhupura, Pakistan**
	Name, address of Manufacturing site.	M/s The Schazoo Pharmaceutical Laboratories Pvt Ltd. Kalalwala Stop, 20 km Lahore-Jaranwala Road, Distt Sheikhupura, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No 25691 dated 15-09-2021
	Details of fee submitted	Rs.30,000/- dated 01-09-2021
	The proposed proprietary name / brand name	**Brinza Eye Drops**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each mL contains: Brinzolamide ..... 10 mg Brimonidine Tartrate ..... 2mg eq. to 1.3mg of Brimonidine
	Pharmaceutical form of applied drug	White to off-white color uniform suspension in white opaque plastic bottles with green-cyan color plastic caps, and finally packed in bleach board carton along with a leaflet.
	Pharmacotherapeutic Group of (API)	**Brinzolamide:** Carbonic anhydrase Inhibitors **Brimonidine Tartrate:** Alpha 2 adrenergic receptor agonist
	Reference to Finished product specifications	Schazoo's specification
	Proposed Pack size	1 x5mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SIMBRINZA 10 mg/mL + 2 mg/mL eye drops, approved by US FDA
	For generic drugs (me-too status)	SIMBRINZA 10 mg/mL + 2 mg/mL eye drops, of Novartis (Reg.# 091907)
	GMP status of the Finished product manufacturer	GMP Certificate #: 162/2019-DRAP (AD-1931718-215) Dated: 28/06/2019
	Evidence of manufacturing facility	GMP Certificate #: 162/2019-DRAP (AD-1931718-215) Dated: 28/06/2019 declares availability
	Name and address of API manufacturer.	**Brimonidine Tartrate:** M/s FARMAK, a.s. Na vlčinci 16/3, Klášterní Hradisko 779 00 Olomouc Czech Republic Phone: ++420/ 587430111, 585547111 **Brinzolamide**: **Duke Chem, S.A.** Pol. Industrial Sant Pere Molanta Avgda. Mare de Déu de Montserrat, 93 - 99 Olèrdola 08799 Barcelona SPAIN DUNS No.: 461001138
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Brinzolamide and Brimonidine tartrate is present in USP 43. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Brimonidine Tartrate:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Brinzolamide**; Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Brimonidine Tartrate:** (12010918, 12020918, 12030918) **Brinzolamide**; (332700600, 332700700, 332700800)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Simbrinza eye drops from SA Alcon-Couvreur NV, Rijksweg 14, BE-2870 Puurs, Belgium by performing quality tests (Identification, sealing of caps, deliverable volume, pH, Osmolality, viscosity, specific gravity, redispersibility, assay and microbiological analysis).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	**Brimonidine Tartrate:** M/s FARMAK, a.s. Na vlčinci 16/3, Klášterní Hradisko 779 00 Olomouc Czech Republic Phone: ++420/ 587430111, 585547111 **Brinzolamide**: **M/s Duke Chem, S.A.** Pol. Industrial Sant Pere Molanta	

	Avgda. Mare de Déu de Montserrat, 93 - 99 Olèrdola 08799 Barcelona SPAIN DUNS No.: 461001138		
API Lot No.	**Brimonidine Tartrate:** (16020620) **Brinzolamide**; (332701800)		
Description of Pack (Container closure system)	**Brimonidine Tartrate:** The stability samples are stored in PE bags inside of PE boxes with screw caps, simulating the actual packaging system of BRIMONIDINE TARTRATE drug substance. **Brinzolamide**: Double transparent polyethylene bags contained inside high-density polyethylene, simulates the packaging proposed for storage and distribution of Brinzolamide		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	**Brimonidine Tartrate:** Real time: 24 months Accelerated: 6 months **Brinzolamide:** Real time: 48 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**BZD/T1/21**	**BZD/T2/21**	**BZD/T3/21**
Batch Size	3 Ltr.	3 Ltr.	3 Ltr.
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	15-04-2021	15-04-2021	15-04-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to Psi report of Valanza tablet conducte don 30th May 2019, wherein following points have been reported: l
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Brimonidine Tartrate**: Copy of EUdra GMP certificate No. sukls1705/2019 valid upto 13-02-2022. **Brinzolamide:** Copy of EUdra GMP certificate No.NCF-II/1924/001/CAT valid upto 28-01-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Brimonidine Tartrate**: Copy of commercial invoice#: TWE-SCH I/04-20 attested by AD DRAP I&E dated 03-02-2021 **Brinzolamide:** Copy of commercial invoice#: TWE/SCH.01.20 attested by AD DRAP I&E dated 03-02-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Section#	Observation	Firm's response
1.6.5	Valid GMP certificate of API manufacturers shall be submitted.	Firm has submitted following: **Brimonidine Tartrate**: Copy of EUdra GMP certificate No. sukls260434/2021 valid upto Nov, 2024. **Brinzolamide:** Copy of GMP certificate No.NCF-II/2121/001/CAT valid upto May, 2024.
3.2.S.4.4	The COA of Brinzolamide from M/s Schazoo declares testing as per BP monograph, whereas drug substance manufacturer has claimed USP specifications.	Firm has submitted that COA of Brinzolamide from M/S Schazoo declares testing on USP rather BP. All tests were performed as per Brinzolamide USP monograph. Method of Analysis and Specification subrnitted were also on USP. The symbol (✓) indicates the new source rather BP. However, COA of Brinzolamide highlighting USP claim is attached for your kind reference.
3.2.S.5	COAs of primary/working standard, applied by the M/s Schazoo, for drug substance analysis shall be submitted.	Submitted.
3.2.P.3.3	• EMA assessment report of innovator product recommends aseptic ball milling of Brinzolamide as well as bulk sterilization of Brinzolamide solution, whereas both the steps have not been included in the submitted manufacturing method. • Submitted manufacturing method neither mentions terminal sterilisation of the filled bottles nor sterile filtration of the final bulk suspension. Justification shall be submitted regarding how the sterility of the finished product will be ensured.	• The technique of aseptic ball milling has been used by the innovator, however, to ensure the particle size of Brinzolamide within range, we have used pre-sized material which is controlled by the drug substance manufacturer. Moreover, to ensure the sterilization of Brinzolamide during manufacturing and finished product, gamma sterilization from Pakistan Radiation Services Lahore and micro-filtration techniques are used. • Moreover, to ensure the sterilization of Brinzolamide during manufacturing and finished product, gamma sterilization from Pa□istan Radiation Services Lahore and micro-filtration techniques are used.
3.2.P.5.1	Submitted drug product specifications does not include tests of boric acid identification, boric acid assay, particle size, as recommended by the literature of innovator product.	Boric acid has been as preservative in the formulation. The contents of boric acid were controlled by performing preservative effectiveness studies throughout stability studies.
3.2.P.5.2	Submitted analytical method determines Brinzolamide &	Firm has submitted that individual chromatograph of Brinzolamide and

	Brimonidine Tartrate simultaneously. Clarification shall be submitted regarding the identification of peak for each drug substance.	Brimonidine, Blank, Excipient only and Product were submitted in Specificity (Analytical Method Validation File-Specificity). Now chromatograph with individual peaks of Brinzolamide & Brimonidine, Blank, Excipient only and product is attached for your kind reference.
3.2.P.5.3	Peak purity parameter has not been assessed in the performance of specificity parameter.	Firm has submitted chromatogram for peak purity parameter.
3.2.P.5.6	Justification of specifications shall be provided.	Firm has submitted that a detailed comparative study of Brinza Eye Drops and Simbrinza Eye Drops were performed. A comparative analysis report was attached in PS. Tests were performed according to the testing data provided by the innovator in literature and USP Chapter 771.
3.2.P.8	• Stability studies have not been conducted at temperature & humidity conditions recommended for the semi-permeable container closure system. • Test of particle size has not been performed during stability studies.	• • Firm hassubmitted that hat Stability study conducted according to ICH Quality Guidelines. Water loss determination data has been submitted along with SOP for Water Loss Determinationin stability study. • Firm has submitted that first of all particle size is controlled at the level of drug substance and secondly at drug product stage it is controlled under pressure of finished product by carefully examining the product for coagulation and agglomeration throughout stability.

Decision of 320th meeting: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that the firm shall revise product specifications for inclusion of test of "Boric Acid Assay"and shall perform the said assay on commercial batches and shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 before issuance of registration letter.**

69.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on 17-07-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 24-06-2019 which specifies SVP general section.

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 6371 dated 08-03-2022
	Details of fee submitted	Rs.30,000/- dated 03-02-2022
	The proposed proprietary name / brand name	**Pacific WFI Injection 5 ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains: Sterile water for injection …… 5ml
	Pharmaceutical form of applied drug	Intravenous (IV) solution
	Pharmacotherapeutic Group of (API)	Pharmacological Class: Water for Injections is a non-isotonic solution. Pharmacotherapeutic group: Solvent/Vehicle ATC code: V07AB(WHO)
	Reference to Finished product specifications	BP specification
	Proposed Pack size	1 x 5 ml
	Proposed unit price	--
	The status in reference regulatory authorities	Approved by TGA of Australia.
	For generic drugs (me-too status)	Otsuka Water for Injection 5ml Otsuka Pakistan Ltd Registration number # 081541
	Name and address of API manufacturer.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted that water for injection in bulk is stored in SS container and is immediately filled in ampoules within 24 hours therefore stability studies are not required to be carried out in this container closure system.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Otsuka sterile Water for Injection 5mL by Otsuka Pakistan Ltd"
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA

Manufacturer of APIs	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore		
API Lot No.	N/A		
Description of Pack (Container closure system)	Low density polyethylene (LDPE) ampoule with twist head cap.		
Stability Storage Condition	Real time: 30°C ± 2°C / 35% HR ±5% Accelerated: 40°C ± 2°C / NMT 25% HR		
Time Period	Real time: 18 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 (Months)		
Batch No.	PDXN0012020	PDXN0022020	PDXN0032020
Batch Size	50 liter	50 liter	50 liter
Manufacturing Date	03/2020	03/2020	03/2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore. GMP certificate issued on 17-07-2020 by DRAP Pakistan.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	N/A
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports on product testing.

6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator[II]:

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

70.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on 17-07-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 24-06-2019 which specifies SVP general section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 6372 dated 08-03-2022
	Details of fee submitted	Rs.30,000/- Dated: 03-02-2022
	The proposed proprietary name / brand name	**Pacific WFI Injection 10 ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains: Sterile water for injection …… 10ml
	Pharmaceutical form of applied drug	Intravenous (IV) solution
	Pharmacotherapeutic Group of (API)	Pharmacological Class: Water for Injections is a non-isotonic solution. Pharmacotherapeutic group: Solvent/Vehicle ATC code: V07AB(WHO)
	Reference to Finished product specifications	BP specification
	Proposed Pack size	1 x 10 ml
	Proposed unit price	--
	The status in reference regulatory authorities	Approved by TGA of Australia
	For generic drugs (me-too status)	Otsuka Water for Injection 10ml Otsuka Pakistan Ltd. Registration number # 048517

		Dosage form: Intravenous (IV) Solution (Non isotonic)
	Name and address of API manufacturer.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted that water for injection in bulk is stored in SS container and is immediately filled in ampoules within 24 hours therefore stability studies are not required to be carried out in this container closure system.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Otsuka Water for Injection 10ml by Otsuka Pakistan Ltd."
	Analytical method validation/verification of product	Firm has submitted Performance Qualification report of WFI.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA	
Manufacturer of APIs	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore
API Lot No.	N/A
Description of Pack (Container closure system)	Low density polyethylene (LDPE) ampoule with twist head cap.
Stability Storage Condition	Real time: 30°C ± 2°C / 35% HR ±5% Accelerated: 40°C ± 2°C / NMT 25% HR
Time Period	Real time: 18 months Accelerated: 6 months

Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 (Months)	
Batch No.		PDXM0012020	PDXM0022020	PDXM0032020
Batch Size		50 liter	50 liter	50 liter
Manufacturing Date		03/2020	03/2020	03/2020
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
#	**Documents To Be Provided**	**Status**	
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	M/s Pacific Pharmaceuticals Ltd. Plot No. 384, Sunder Industrial Estate, Lahore. GMP certificate issued on 17-07-2020 by DRAP Pakistan.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	N/A	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports on product testing.	
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	
Remarks of Evaluator[II]:			
Decision of 320th meeting: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**			
71.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan	
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales	

	Dy. No. and date of submission	Dy.No 19157 dated 08-07-2021
	Details of fee submitted	PKR 30,000/-: dated 21/06/2021
	The proposed proprietary name / brand name	**Soglu-Met 5mg/850mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin ……. 5mg Metformin HCl …….. 850mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	sodium-glucose co-transporter 2 (SGLT2) inhibitors. biguanide class of antidiabetics
	Reference to Finished product specifications	Innovator specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SYNJARDY 5mg/850mg Tablet of Boehringer Ingelheim Canada LTD LTEE. (Health Canada approved)
	For generic drugs (me-too status)	Xenglu-Met 5mg/850mg Tablet of Hilton Pharma Pvt. LTD.
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 03-01-2022 and it is valid till 02-01-2024.
	Name and address of API manufacturer.	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICAL Co.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCl:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months

		Batches: (20160606, 20161017, 20161219)
		Metformin HCl: Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 48 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence and comparative dissolution profile of their developed formulation Soglu-Met 5mg/850mg Tablet (B # ST21A009) with innovator product Synjardy 5mg/850mg Tablet (B #902007) of M/s Boehringer Ingelheim Pharma. in pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of CDP showed that release profile of both test and comparator products were comparable. **The values for f2 factor are in the acceptable range.**
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICALCo.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCl:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155		
API Lot No.	Empagliflozin: E-20190920-D02-E06-01 Metformin HCL: MEF/10030953		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	ST21A009	ST21A010	ST21A011
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	01-2021	01-2021	01-2021

Date of Initiation	28-01-2021	28-01-2021	28-01-2021
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: The firm has submitted GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co., Ltd, China issued by Fuxin Food and Drug Administration. The certificate is valid till 23-08-2023 Metformin HCl: The firm has submitted GMP certificate for AARTI Drugs limited issued by food & drug Control Administration. The certificate is valid till 19-03-2023	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: The firm has submitted attested copy of invoice for the import of empagliflozin (1.5 Kg, Invoice # HN19120501-H) dated 05-12-2019 and attested copy of ADC (I&E) DRAP, Islamabad dated 10-01-2020 Metformin HCL: The firm has submitted attested copy of invoice for the import of Metformin Hcl (1000 Kg, Invoice # EXP/302/20-21) dated 15-5-2020. And attested ADC (I&E) DRAP, Islamabad dated 05-08-2020.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted for HPLC analysis of stability studies.	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.	
Remarks of Evaluator:			
Decision of 320th meeting: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**			

• **Registration Board further advised the firm to follow the relevant guidelines for preparation, standardization and usage of standard for testing of drug substance and product.**		
72.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 18815 dated 05-07-2021
	Details of fee submitted	Rs.30,000/- dated 21-06-2021
	The proposed proprietary name / brand name	**Soglu-Met 12.5mg/850mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….12.5mg Metformin HCl….850mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	sodium-glucose co-transporter 2 (SGLT2) inhibitors. biguanide class of antidiabetics
	Reference to Finished product specifications	Innovator specs
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SYNJARDY 12.5mg/850mg Tablet of Boehringer Ingelheim Canada LTD LTEE. (Health Canada approved)
	For generic drugs (me-too status)	Xenglu-Met 12.5mg/850mg Tablet of Hilton Pharma Pvt. LTD.
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 03-01-2022 and it is valid till 02-01-2024.
	Name and address of API manufacturer.	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICALCo.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (20160606, 20161017, 20161219)
		Metformin HCL: Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence and comparative dissolution profile of their developed formulation Soglu-Met 12.5mg/850mg Tablet (B # ST21A013) with innovator product Synjardy 12.5mg/850mg Tablet (B #803625) of M/s Boehringer Ingelheim Pharma. in pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of CDP showed that release profile of both test and comparator products were comparable. The values for f2 factor are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		

Manufacturer of API	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICALCo.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155		
API Lot No.	Empagliflozin: E-20190920-D02-E06-01 Metformin HCl: MEF/10030953		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	ST21A013	ST21A014	ST21A015
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	15-02-2021	15-02-2021	15-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: The firm has submitted GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co., Ltd, China issued by Fuxin Food and Drug Administration. The certificate is valid till 23-08-2023 Metformin HCl: The firm has submitted GMP certificate for AARTI Drugs limited issued by food & drug Control Administration. The certificate is valid till 19-03-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: The firm has submitted attested copy of invoice for the import of empagliflozin (1.5 Kg, Invoice # HN19120501-H) dated 05-12-2019 and attested copy of ADC (I&E) DRAP, Islamabad dated 10-01-2020 Metformin HCL: The firm has submitted attested copy of invoice for the import of Metformin Hcl (1000 Kg, Invoice # EXP/302/20-21) dated 15-5-2020. And

		attested ADC (I&E) DRAP, Islamabad dated 05-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted for HPLC analysis of stability studies.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
Remarks of Evaluator:		
Decision of 320th meeting: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration Board further advised the firm to follow the relevant guidelines for preparation, standardization adn usage of standard for testing of drug substance and product.**		
73.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 18816 dated 05-07-2021
	Details of fee submitted	Rs.30,000/- dated 25-06-2021
	The proposed proprietary name / brand name	**Soglu-Met 12.5mg/1000mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….12.5mg Metformin HCl……..1000mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	sodium-glucose co-transporter 2 (SGLT2) inhibitors. biguanide class of antidiabetics

	Reference to Finished product specifications	Innovator specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SYNJARDY 12.5mg/1000mg Tablet of Boehringer Ingelheim Canada LTD LTEE. (Health Canada approved)
	For generic drugs (me-too status)	Xenglu-Met 12.5mg/1000mg Tablet of Hilton Pharma Pvt. LTD.
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 03-01-2022 and it is valid till 02-01-2024.
	Name and address of API manufacturer.	**Empagliflozin:** Fuxin Long Rui Pharmaceutical Co.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** Aarti Drugs Limited Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (20160606, 20161017, 20161219)
		Metformin HCL: Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence and comparative dissolution profile of their developed formulation Soglu-Met 12.5mg/1000mg Tablet (B # ST21A021) with innovator product Synjardy 12.5mg/1000mg Tablet (B #002022) of M/s Boehringer Ingelheim Pharma. in pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of CDP showed that release profile of both test and comparator products were comparable. The values for f2 factor are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICALCo.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155		
API Lot No.	Empagliflozin: E-20190920-D02-E06-01 Metformin HCL: MEF/10030953		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	ST21A021	ST21A022	ST21A023
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	15-02-2021	15-02-2021	15-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of

		Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: The firm has submitted GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co., Ltd, China issued by Fuxin Food and Drug Administration. The certificate is valid till 23-08-2023 Metformin HCl: The firm has submitted GMP certificate for AARTI Drugs limited issued by food & drug Control Administration. The certificate is valid till 19-03-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: The firm has submitted attested copy of invoice for the import of empagliflozin (1.5 Kg, Invoice # HN19120501-H) dated 05-12-2019 and attested copy of ADC (I&E) DRAP, Islamabad dated 10-01-2020 Metformin HCL: The firm has submitted attested copy of invoice for the import of Metformin Hcl (1000 Kg, Invoice # EXP/302/20-21) dated 15-5-2020. And attested ADC (I&E) DRAP, Islamabad dated 05-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted for HPLC analysis of stability studies.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
Remarks of Evaluator^{II}:		
Decision of 320th meeting: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration Board further advised the firm to follow the relevant guidelines for preparation, standardization adn usage of standard for testing of drug substance and product.**		
74.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 18814 dated 05-07-2021
	Details of fee submitted	Rs.30,000/- dated 21-06-2021
	The proposed proprietary name / brand name	**Soglu-Met 5mg/1000mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….5mg Metformin HCl……1000mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	sodium-glucose co-transporter 2 (SGLT2) inhibitors. biguanide class of antidiabetics
	Reference to Finished product specifications	Innovator specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SYNJARDY 5mg/1000mg Tablet of Boehringer Ingelheim Canada LTD LTEE. (Health Canada approved)
	For generic drugs (me-too status)	Xenglu-Met 5mg/1000mg Tablet of Hilton Pharma Pvt. LTD.
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 03-01-2022 and it is valid till 02-01-2024.
	Name and address of API manufacturer.	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICALCo.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (20160606, 20161017, 20161219)
		Metformin HCL: Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence and comparative dissolution profile of their developed formulation Soglu-Met 5mg/1000mg Tablet (B # ST21A017) with innovator product Synjardy 5mg/1000mg Tablet (B #902325) of M/s Boehringer Ingelheim Pharma. in pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of CDP showed that release profile of both test and comparator products were comparable. The values for f2 factor are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	**Empagliflozin:** FUXIN LONG RUI PHARMACEUTICALCo.,Ltd. Fluoride industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCl:** AARTI DRUGS LIMITED Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
API Lot No.	Empagliflozin: E-20190920-D02-E06-01 Metformin HCL: MEF/10030953
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)

Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	ST21A017	ST21A018	ST21A019
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	15-02-2021	15-02-2021	15-02-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: The firm has submitted GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co., Ltd, China issued by Fuxin Food and Drug Administration. The certificate is valid till 23-08-2023 Metformin HCl: The firm has submitted GMP certificate for AARTI Drugs limited issued by food & drug Control Administration. The certificate is valid till 19-03-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: The firm has submitted attested copy of invoice for the import of empagliflozin (1.5 Kg, Invoice # HN19120501-H) dated 05-12-2019 and attested copy of ADC (I&E) DRAP, Islamabad dated 10-01-2020 Metformin HCL: The firm has submitted attested copy of invoice for the import of Metformin Hcl (1000 Kg, Invoice # EXP/302/20-21) dated 15-5-2020. And attested ADC (I&E) DRAP, Islamabad dated 05-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted for HPLC analysis of stability studies.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Sr.#	Section#	Observation	Firm's response
1.	**3.2.S.4.2**	Drug substance analytical procedure of Metformin HCl is not as per the latest monograph of USP for Metformin HCl.	Revised analytialprocedure has benesubmitted as per latest monograph of USP for Metformin HCl
2.	**3.2.S.4.3**	Analytical method verification studies shall be submitted from M/s Global Pharmaceuticals for Metformin HCl for the analytical method fo latest monograph of USP.	Analytical method verification studies have been submitted from M/s Global Pharmaceuticals for Metformin HCl as per latest monograph of USP.
3.	**3.2.P.5.1**	• Submitted drug product specifcations does not include test of content uniformity for Empagliflozin. • The USFDA review documents of innovator product i.e., Synjardy declares the dissolution specifications as "NLT Q in 20 minutes", while you have applied dissolution limits of NLT Q in 30minutes. Justification shall be submitted in this regard.	• Firm has submitted as under: "We have performed ontent uniformity at finished dosage form but do not include this in the stability study report. Now firm has submitted analytical record for the content uniformity testing a finished stage and at 15 month time point." • Empagliflozin & metformin HCl are bCS class III drugs (rapidly dissolving drugs) and for rapidly dissolving drugs FDA guideline "Guidance for industry:- Dissolution testing and Acceptance criteria for immediate release solid oral dosage form drug products containing high solubility drug substances menton the dissolution specification NLT 80% after 30 mminutes. We performed and submitted the dissolution testing data with time point i.e., 05,10,15,20& 30 minutes at initial "Finshed stage" and at 6th month time point."
4.	**3.2.P.6**	Date of re-standardization has been declared as 24-01-2021 for the working standard of Empagliflozin, whereas stability study analysis has also been	Firm has submitted re-standardization record for the working standard of Empagliflozin.

		performed subsequent to this date.	

Decision of 320th meeting: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further advised the firm to follow the relevant guidelines for preparation, standardization and usage of standard for testing of drug substance and product.**

75.	Name, address of Applicant / Marketing Authorization Holder	**"M/s High-Q Pharmaceuticals. B-64 KDA-1, Karsaz Road Karachi,"**
	Name, address of Manufacturing site.	M/s High-Q Pharmaceuticals. Plot No.224 & 225/1 Sector 23, Korangi Industrial Area, Karachi-Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 20558 dated 28-07-2021
	Details of fee submitted	PKR 30,000/-: dated 08-06-2021
	The proposed proprietary name / brand name	**Ertagsa 5/100 mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: 6.48 mg ertugliflozin L-pyroglutamic acid equivalent to 5 mg of ertugliflozin and 128.5 mg sitagliptin phosphate monohydrate equivalent to 100 mg sitagliptin
	Pharmaceutical form of applied drug	Pink color, oval shaped, biconvex, film coated tablet with bisect line on one side and other side is plain.
	Pharmacotherapeutic Group of (API)	**Ertugliflozin**: Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Sitagliptin**: Dipeptidyl peptidase-4 (DPP-4) inhibitors
	Reference to Finished product specifications	Manufacturer's Specification
	Proposed Pack size	10's, 14's, 20's, 28's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	"Steglujan 5/100mg Tablet" by Merck & Co., inc. Approved by US FDA

	For generic drugs (me-too status)	Ertuvia 5mg + 100mg Tablet by Ferozsons Laboratories Limited
	GMP status of the Finished product manufacturer	New license granted on 21st Dec, 2021 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**SITAGLIPTIN:** Manufacturing facility name: Fuxin Long Rui Pharmaceutical CO.,Ltd Manufacturing facility address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China Exporting company name: Beijing Sino Hanson Import & Export Co. Ltd Exporting company Address: No 3, Zhonghe Road, Fengtai District, Beijing China 100070 **ERTUGLIFLOZIN-LPGA:** DMF Holder: Shanghai Pansopharm Technology Co., Ltd. Address:2F, Bldg. 7, 333# East Kangqiao Rd., Pudong, Shanghai, China Manufacturer: Chifeng Arker Pharmaceutical Technology Co., Ltd. Manufacturing Site: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng, Inner Mongolia, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Ertugliflozin-LPGA & Sitagliptin are not present in any Pharmacopoeia and the firm has followed manufacturer's specification. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Ertugliflozin-LPGA:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real

		time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 48 months Batches: (D84-161201, D84-161202, D84-170101) **Sitagliptin:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH. The real time stability data is conducted at 30°C ± 2°C / 75% ± 5% RH. Batches: For Accelerated studies (M-20190127-D01-M06-06, M-20190316-D02-M06-07, M-20190127-D01-M06-08) For Real time studies (M-20190127-D01-M06-01, M-20181222-D06-M06-08, M-20181222-D06-M06-09)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	CDP studies against the reference product of Steglujan tablets, in three dissolution mediums has been submitted with acceptable level of f2 results (f2 ≥ 50).
	Analytical method validation/verification of product	Firm has submitted analytical method validation data

STABILITY STUDY DATA

Manufacturer of API	**SITAGLIPTIN:** Fuxin Long Rui Pharmaceutical CO.,Ltd **ERTUGLIFLOZIN-LPGA:** DMF Holder: Shanghai Pansopharm Technology Co., Ltd. Manufacturer:Chifeng Arker Pharmaceutical Technology Co., Ltd.		
API Lot No.	**Sitagliptin phosphate monohydrate:** M-20191228-D07-M06-04 **Ertugliflozin-LPGA:** D84-191001		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3 & 6 (Months) Real Time: 0, 3 & 6 (Months)		
Batch No.	5ESPD01/20	5ESPD02/20	5ESPD03/20
Batch Size	2500 tab	2500 tab	2500 tab

<table>
<tr><td colspan="2">Manufacturing Date</td><td>04-2020</td><td>04-2020</td><td>04-2020</td></tr>
<tr><td colspan="2">Date of Initiation</td><td>09-04-2020</td><td>09-04-2020</td><td>09-04-2020</td></tr>
<tr><td colspan="2">No. of Batches</td><td colspan="3">03</td></tr>
<tr><td colspan="5">Administrative Portion</td></tr>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td colspan="3">Attached</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td colspan="3">Ertugliflozin-LPGA: Copy of GMP certificate issued by CFDA in the name of M/s Chifeng Arker Pharmaceutical Technology Co., Ltd., China provided
Sitagliptin phosphate monohydrate: Copy of GMP Certificate issued by the CFDA in the name of M/s Fuxin Long Rui
Pharmaceutical Co., Ltd., Liaoning Province, China. valid upto May/25/2024.</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td colspan="3">Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
Sitagliptin phosphate monohydrate:
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported.</th><th>Date of approval by DRAP</th></tr>
<tr><td>M-20191228-D07-M06-04</td><td>MR200219-H</td><td>200Kg</td><td>26-02-2020</td></tr>
</table>
Ertugliflozin-LPGA:
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<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported.</th><th>Date of approval by DRAP</th></tr>
<tr><td>Not Available</td><td>PSPW-191025</td><td>1Kg</td><td>12-11-2019</td></tr>
</table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms,
Raw data sheets, COA, summary data sheets etc.</td><td colspan="3">Submitted</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td colspan="3">Submitted</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td colspan="3">Yes</td></tr>
<tr><td rowspan="2">76.</td><td>Name, address of Applicant / Marketing Authorization Holder</td><td colspan="3">"M/s High-Q Pharmaceuticals. B-64 KDA-1, Karsaz Road Karachi,"</td></tr>
<tr><td>Name, address of Manufacturing site.</td><td colspan="3">M/s High-Q Pharmaceuticals.</td></tr>
</table>

		Plot No.224 & 225/1 Sector 23, Korangi Industrial Area, Karachi-Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 20559 dated 28-07-2021
	Details of fee submitted	PKR 30,000/-: dated 08-06-2021
	The proposed proprietary name / brand name	**Ertagsa 15/100 mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: 19.43mg Ertugliflozin L-pyroglutamic acid equivalent to 15 mg of Ertugliflozin and 128.5 mg Sitagliptin phosphate monohydrate equivalent to 100 mg Sitagliptin
	Pharmaceutical form of applied drug	Brown colored, oval shaped, biconvex, film coated tablet with bisect line on one side and plain on other side
	Pharmacotherapeutic Group of (API)	**Ertugliflozin**: Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Sitagliptin**: Dipeptidyl peptidase-4 (DPP-4) inhibitors
	Reference to Finished product specifications	Manufacturer's Specification
	Proposed Pack size	10's, 14's, 20's, 28's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	"Steglujan 15/100mg Tablet" by Merck & Co., inc. Approved by US FDA
	For generic drugs (me-too status)	Ertuvia 15mg + 100mg Tablet by Ferozsons Laboratories Limited
	GMP status of the Finished product manufacturer	New license granted on 21st Dec, 2021 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**SITAGLIPTIN:** Manufacturing facility name: Fuxin Long Rui Pharmaceutical CO.,Ltd Manufacturing facility address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China Exporting company name: Beijing Sino Hanson Import & Export Co. Ltd Exporting company Address: No 3, Zhonghe Road, Fengtai District, Beijing China 100070 **ERTUGLIFLOZIN-LPGA:** DMF Holder: Shanghai Pansopharm Technology Co., Ltd.

		Address:2F, Bldg. 7, 333# East Kangqiao Rd., Pudong, Shanghai, China Manufacturer: Chifeng Arker Pharmaceutical Technology Co., Ltd. Manufacturing Site: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng, Inner Mongolia, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Ertugliflozin-LPGA & Sitagliptin are not present in any Pharmacopoeia and the firm has followed manufacturer's specification. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Ertugliflozin-LPGA:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 48 months. Batches: (D84-161201, D84-161202, D84-170101) **Sitagliptin:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH. The real time stability data is conducted at $30^oC \pm 2^oC$ / 75% ± 5% RH. Batches: For Accelerated studies (M-20190127-D01-M06-06, M-20190316-D02-M06-07, M-20190127-D01-M06-08) For Real time studies (M-20190127-D01-M06-01, M-20181222-D06-M06-08, M-20181222-D06-M06-09)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	CDP studies against the reference product of Steglujan tablets, in three dissolution mediums has been submitted with acceptable level of f2 results (f2 ≥ 50).
	Analytical method validation/verification of product.	Firm has submitted analytical method validation data

STABILITY STUDY DATA

Manufacturer of API	**SITAGLIPTIN:** Fuxin Long Rui Pharmaceutical CO.,Ltd **ERTUGLIFLOZIN-LPGA:** DMF Holder: Shanghai Pansopharm Technology Co., Ltd. Manufacturer:Chifeng Arker Pharmaceutical Technology Co., Ltd.		
API Lot No.	**Sitagliptin phosphate monohydrate:** M-20191228-D07-M06-04 **Ertugliflozin-LPGA:** D84-191001		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3 & 6 (Months) Real Time: 0, 3 & 6 (Months)		
Batch No.	1ESPD01/20	1ESPD02/20	1ESPD03/20
Batch Size	2380 Tablets	2380 Tablets	2380 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	09-04-2020	09-04-2020	09-04-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Attached
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin-LPGA:** Copy of GMP certificate issued by CFDA in the name of M/s Chifeng Arker Pharmaceutical Technology Co., Ltd., China provided **Sitagliptin phosphate monohydrate:** Copy of GMP Certificate issued by the CFDA in the name of M/s Fuxin Long Rui Pharmaceutical Co., Ltd., Liaoning Province, China. valid upto May/25/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted. **Sitagliptin phosphate monohydrate:**

Batch No.	**Invoice No.**	**Quantity Imported.**	**Date of approval by DRAP**

		M-20191228-D07-M06-04 | MR200219-H | 200Kg | 26-02-2020 **Ertugliflozin-LPGA:** **Batch No.** | **Invoice No.** | **Quantity Imported.** | **Date of approval by DRAP** Not Available | PSPW-191025 | 1Kg | 12-11-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Yes

Remarks of Evaluator[II]:

Sr.#	Section#	Observation	Firm's response
1.	1.6.5	Valid GMP certificate of the manufacturer of Ertugliflozin L-PGA shall be submitted.	Submitted from Changzhou Pharmaceutical Profession Association wghich is not relevant regulatory authority.
		Ertugliflozin L-Pyroglutamic acid	
2.	3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Pro duct manufacturer is required. • Submitted specifications and analytical procedure by drug substance manufacturer describes the test for content of "Ertugliflozin L-pyroglutamic acid, whereas the Innovator's product literature recommends test of "Ertugliflozin potency" in the drug substance specifications. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product	• Submitted. • As per the manufacturer: Ertugliflozin potency = Ertugliflozin LPGA Assay - LPGA content. So, they have shown only two test results of them on the COA, instead of all three, because the third outcome can be calculated out. • Analytical method verification report has been submitted. *As per submitted analytical record various chromatograms have been analysed with retention time of 20 minutes whereas analytical procedure recommends gradient run time of 45 minutes.* • Submitted. • Firm has submitted Revised CoA with Ertugliflozin content is submitted.

		manufacturer shall be submitted. • Analytical record i.e., Raw data sheet, FTIR spectrum, chromatograms etc., shall be submitted for the analysis of 'Ertugliflozin L-pyroglutamic Acid' performed by M/s High-Q Pharmaceuticals. • COA from drug substance manufacturer does not declare the "Ertugliflozin potency" as recommended by the innovator product. • COA from of drug substance from drug product manufacturer does not include test of L-Pyroglutamic acid content.	• Revised CoA of material with test of L-pyroglutamic acid content is submitted. The test for L-PGA was performed after the submission, considering that theoretical factor calculated using molecular weights can serve the purpose for small size trial batches. This test has now been performed on the retention sample of API and included in the specification for routine testing of API for commercial batches of the product
3.	3.2. S.5	• COA of reference standard of L-Pyroglutamic acid shall be submitted. • Submitted COAs of reference standard of Ertugliflozin L-PGA does not mention any manufacturing date, validity date & batch no. • Submitted COA of reference standard does not declare the content of L-pyroglutamic acid.	• CoA of Reference standard of L-pyroglutamic acid is submitted. • Updated CoA of Reference standard with L-pyroglutamic acid content is attached. Batch number: B34-191001 Mfg Date: Oct 26, 2019 Retest Date: Oct 25, 2021
4.	3.2. S.7	Justification shall be submitted for not performing test of L-PGA content throughout the stability studies.	Firm has submitted declaration from drug substance manufacturer: On the stability data of Ertugliflozin L-PGA, L-PGA content is only shown in month 0 and month 24, because L-PGA is very stable, and doesn't degrade within 3-4 years, so we tested it every two years in the stability studies initially. If customer insist to have L-PGA content data in each column, then we'll add the test results from next stability batch.
Sitagliptin phosphate monohydrate			
5.	3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity,	Firm has submitted specifications, analytical procedure, analytical method verification report, analytical record for Drug substance analysis and COAs.

		accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted. • Analytical record i.e., Raw data sheet, FTIR spectrum, chromatograms etc., shall be submitted performed by M/s High-Q Pharmaceuticals. • Provide Certificate of Analysis (CoA) of relevant batch(es) of Drug Substance performed by Drug substance manufacturer used during product development and stability studies.	
6.	3.2.S.5	• Submitted COA of working standard declares the expire date as 24-07-2018, whereas the drug substance analysis has been performed subsequent to this date.	Revised COA of working standard has been submitted with expiry date of 14-02-2023.
7.	3.2.S.7	• Long term stability studies have been submitted for 6 months only.	Long term stability data as per Zone IVa conditions has been submitted for 24 months.
8.	3.2.P.1	• Excipients used in the proposed formulation are different form that used by the Innovator. Justification shall be submitted in this regard. • Clarification shall be submitted regarding composition of "Quick tab" used in the formulation.	• Firm has referred to drug excipient compatibility study as justification. • Quick Tab is a pre-mix used as Binder, filler and disintegrant.
9.	3.2.P.3.5	Sampling plan of compression stage, presented in the submitted process validation protocol, does not include test of content uniformity. Justification shall be submitted in this regard.	Revised Process validation protocol submitted.
10.	3.2. P.5.1	• Drug substance specifications have been submitted instead of the drug product specifications. • Dissolution parameters of apparatus (paddle instead of basket), dissolution medium (v/0.1N HCl instead of pH 4.5acetate buffer) & dissolution volume (1000ml instead of 900ml), proposed in analytical procedure, are different from that recommended by the US FDA in the innovator's product	• Firm has submitted drug product specifications. • There was a typo error; the actual paddle speed is 50 rpm as mentioned in Comparative Dissolution Profile documents (Biowaiver Studies Protocol), already submitted. The testing was done following that procedure. • The medium (0.1N HCI pH 1.2) was selected as both ertugliflozin and sitagliptin

		literature review. Justifications shall be submitted in this regard. • You have applied Paddle speed = 100 rpm in dissolution parameters. You are advised to justify the speed of paddle apparatus with reference to USP general chapter <1092> (The Dissolution Procedure; Development and Validation). • Submitted analytical procedure does not include test of content uniformity.	meet the requirements of BCS Class I drug due to high solubility across physiological pH range and high permeability. Ertugliflozin / sitagliptin tablets display rapid in vitro dissolution characteristics over the pH range of 1.2 — 6.8. • The control methods of Ertagsa 5mg/100 mg & Ertagsa 15 mg/100 mg have been corrected to show Paddle speed as 50 rpm and Dissolution volume as 500 ml. The analysis of commercial batches shall be carried out according to the revised methods for Ertagsa 5mg/100mg & 10mg/10mg Tablets. The actual testing of trial batches were carried out with 1000 ml dissolution volume instead of 500 ml but since both the APIs are high solubility and the Tablets have low disintegration time, therefore, it can be assumed that dissolution results would not be significantly impacted. • Dissolution medium and volume in revised drug product method is still not as per US FDA.
11.	3.2. P.5.4	Test of content uniformity by way of Assay has not been performed during batch analysis.	Firm ha submitted performance on the retention samples of all the three trial batches for content uniformity. The CoAs along with related chromatograms and work sheets
12.	3.2. P.6	• Dates of standardization of working standard of Sitagliptin & Ertugliflozin are April & August 2020, whereas the product analysis has also been performed prior to these dates. Clarification shall be submitted regarding reference standards applied for the analysis of product samples, performed prior to the date of standardization of working standards. • Submitted COA of working standard of Ertugliflozin-LPGA does not declare the content of LPGA and also the potency in	Sitagliptin USP, batch no. M-20191228-D07-M06-04, was received with expiry date as 14/02/2023. Same was standardized on 16/03/2020 against USP Reference Standard (Lot # R07630) and declared as working standard since the results were comparable with the RS. The re-standardization date given was 15/03/2021. Same lot was again tested on 27/07/2020 due to malfunctioning of the refrigerator, in which reference and working standards are stored, and since no change in potency and water contents observed therefore its re-standardization date revised accordingly as 26/07/2021 with no

		terms of Ertugliflozin has not been determined.	change in potency. In the documents submitted, the revised CoA was attached, by mistake. Ertugliflozin, batch no. D-84-191001, was received on 29/10/2019. Same was standardized on 17/01/2020 against Working Standard (B34-191001) supplied by the manufacturer. This lot was also qualified as Working Standard with re-standardization date as 16/01/2021. Same lot was again tested on 17/08/2020 due to consumption of entire quantity of working standard retained. A fresh sample was taken from the available material of batch no. D-84-191001 and standardized with re-standardization date as 16/08/2021 with no change in potency. In the documents submitted, the revised CoA was attached, by mistake. • Reviewed COA of working standard has been submitted.
13.	3.2. P.8	• Submitted commercial invoice for Sitagliptin phosphate monohydrate does not reveal the name of manufacturer, hence Form 3 & 7 shall be submitted. • Justification shall be submitted for applying the theoretical factor of LPGA, instead of applying the actual potency of Ertugliflozin in working standard.	• Firm has submitted Form 3 & Form 7 for the imported batch of Sitaglitpin form M/s Fuxin Long Rui., China. • Theoretical factor was used as the actual contents of L-pyroglutamic acid were not determined at that time. The API has been retested (on 15/02/2022) in order to determine the potencies of Ertugliflozin L-PGA, Ertugliflozin and L-PGA separately to see the impact on quantity of Ertuglifolzin L-PGA used in trial batches. The difference between the theoretical and actual L-PGA contents as declared in the CoA from the supplier, is not that much that could significantly impact the quantity of Ertugliflozin L-PGA dispensed for small size trial batches. In commercial batches the quantity of Ertugliflozin L-PGA per batch shall be calculated on the basis of actual %age of L-PGA content in the API

14.		• You are advised to justify the quantity of "Ertugliflozin-LPGA" dispensed for formulation of each trial, with reference to the %age content of "Ertugliflozin" in the drug substance of "Ertugliflozin-LPGA".	According to the data of potency determined in COA of Ertugliflozin-LPGA, the difference between quantity dispensed and the actual quantity that should have been dispensed, is nominal, however in commercial batches the quantity of Ertugliflozin L-PGA per batch shall be calculated on the basis of actual %age of L-PGA content in the API in order to achieve the desired label claim of Ertugliflozin.

Decision: Registration Board deliberated that the selected dissolution parameters for the applied products including apparatus, dissolution medium, volume etc are different from the parameters described in the literature review of the product approved by US FDA. Therefore, the Board decided to defer the applications for Ertagsa 15/100 mg Tablet & Ertagsa 5/100 mg Tablet for submission of of stability studies data of two batches of each strength at accelerated and long term conditions for initial and 1 month time point, wherein dissolution tests shall be performed as per the dissolution paarmeters recommended by US FDA in the literature review of innovator drug product i.e, Steglujan tablet.

77.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot**
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter No. F.1-19/2014-Lic. from Secretary CLB for issuance of DML, declaring availability of "tablet general section".
	Dy. No. and date of submission	Dy. No 23837 dated 31-08-2021
	Details of fee submitted	Rs.30,000/- dated 04-08-2021
	The proposed proprietary name / brand name	**Celezib 200mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Celecoxib ……200mg
	Pharmaceutical form of applied drug	Clear and colorless solution filled in clear glass ampoules with red and blue ACF rings and blue color OPC mark
	Pharmacotherapeutic Group of (API)	Non-steroidal Anti inflammatory (NSAID)

	Reference to Finished product specifications	BP
	Proposed Pack size	20's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Celecoxib 200 mg capsules, hard by M/s Macleods Pharma UK Limited, approved by MHRA of UK.
	For generic drugs (me-too status)	Celbex 200mg capsule by M/s Getz Pharma (Pvt) Limited Reg. No. 028693
	GMP status of the Finished product manufacturer	New DML was granted after inspection vide letter No. F. 1-19/2014-Lic (Vol-1) Dated: 29-08-2018, including Capsule general section
	Name and address of API manufacturer.	M/s AARTI DRUGS LIMITED, Plot No. E-21/22, M.I.D.C, Tarapur, Maharashtra, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5% RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches:(KM-1102215, KM-1102315, KM-1102415)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Comparative dissolution profile has been established against the Clebrex capsule of M/s Pfizer in three buffer mediums i.e., ph1.2, pH 4.5 & ph 6.8 with acceptable results.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s AARTI DRUGS LIMITED, Plot No. E-21/22, M.I.D.C, Tarapur, Maharashtra, India		
API Lot No.	Ceb/10040077		
Description of Pack (Container closure system)	Alu-PVC		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20CRn009	21CRn001	21CRn002
Batch Size	2000 capsules	2000 capsules	2000 capsules
Manufacturing Date	12-2021	01-2021	01-2021
Date of Initiation	02-2021	02-2021	02-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. (New Section)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	--
3	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.14850/2020/DRAP-AD-VIII (I&E) dated 16/10/2020 is submitted wherein the permission to import different APIs including for the purpose of test/analysis and stability studies is granted. • AirWay Bill No. 176-26046624 Dated: 21/12/2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	• HPLC system digital log has been submitted excluding for the intial time point analysis.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.6.5	Valid GMP certificate issued by the relevant regulatory authority shall be	Submitted GMP certificate is of another site of AARTI drugs ltd (PLOT NO. W-60(B)W-61(B)W-

	submitted for the drug substance manufacturer.	62(B)W-71(B)W-72(B)W-73(B),MIDC, Tarapur Thane, India), instead of the site (Plot No. E-21/22, M.I.D.C, Tarapur, Maharashtra, India) from which drug substance has been imported.
3.2.S.4.2	• Submitted drug substance analytical method from M/s Islam pharma does not include details of system suitability parameters in Assay test.	Revised analytical method containing details of system suitability parameters has been submitted.
3.2.S.4.3	• Drug substance analytical method from M/s Aarti Drugs, declare retention time of Celecoxib at about 27 minutes, whereas the Analytical method verification report submitted from M/s Islam Pharma declares the retention time as about 16 minutes. Clarifications hall be submitted in this regard.	USP method for celecoxib do not mentions/declare the retention time of celecoxib, the retention time may vary depending on HPLC system, column condition and source of chemicals.
3.2. S.4.4	• The COA of drug substance manufacturer declares compliance with USP, whereas COA of drug product manufacturer declares the compliance with BP monograph. Clarification shall be submitted in this regard. • Analytical record for the drug substance analysis performed by M/s Islam Pharma shall be submitted.	• As monograph for celecoxib API is available in both USP and BP but drug product is only available in BP, so we M/s Islam pharma chosen the BP method and specifications. Method of analysis and specification for celecoxib API are same in both USP and BP monographs. • Analytical record for the drug substance analysis has been submitted.
3.2.S.6	Drug substance is of USP standard whereas reference standard of BP grade has been submitted.	As the drug substance is available in both USP and BP and have same specifications and analytical procedure. Drug product is available only in BP so we chosen BP standard and used it for analysis.
3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted.	• Firm has submitted Pharmaceutical equivalence report against the celebrex capsule of M/s Pfizer, wherein instead of dissolution test of batch relase, CDP study reusulst have been submitted. Submitted chromatograms declares file created date i.e., 18-02-2021 which is subsequent to the acquired date mentioned on each chromatogram i.e., 21-01-2021.

3.2.P.3.5	Submitted process validation protocol does not include sampling plan.	Process validation protocol including sampling plan has been submitted.
3.2.P.5.3	Submitted analytical method verification studies include details of "Montisim tablet."	In method verification report, under section C (Method precision), by a typographic mistake "montisim tablet" was written which is corrected
3.2.P.8.3	• Documents for the procurement of API with approval from DRAP (in case of import) shall be submitted. • Raw data sheets for complete stability studies shall be submitted. • Submitted analytical record does not reflect the performance of system suitability test during Assay analysis as recommended by BP monograph of Celcoxib capsules. • Stability studies data for 6th month time point shall be submitted. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) shall be submitted.	• Firm has submitted copy of commercial invoice# SAMP/1002//20-21-23/10/2020 frrom M/s AARTI drugs ltd., in the name of islam Pharma for the 2.5 Kg of Celecoxib. The submitted invoice is not attested by DRAP I&E office. • Firm has also submitted copy of Air WayBill. • 6th month data of stability studies has been submitted. • Firm has performed system suitability test by establishing the RSD of standard replicates, while BP monograph recommends performance of system suitability with the help of impurity standards. • Record of digital data logger has been submitted.

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

78.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot**
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter No. F.1-19/2014-Lic. from Secretary CLB for issuance of DML, declaring availability of "tablet general section".

	Dy. No. and date of submission	Dy.No 23835 dated 31-08-2021
	Details of fee submitted	Rs.20,000/- dated 22-04-2021
	The proposed proprietary name / brand name	**Caltis 250mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated tablet Contains: Clarithromycin ……. 250mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Clarithromycin 250mg tablet, Teva Pharmaceutical, MHRA Approved.
	For generic drugs (me-too status)	Rithmo 250mg tablet, Sami Pharmaceuticals (Pvt.) Limited.
	GMP status of the Finished product manufacturer	New DML was granted after inspection vide letter No. F. 1-19/2014-Lic (Vol-1) Dated: 29-08-2018, including Capsule general section
	Name and address of API manufacturer.	Zhejiang Better Pharmaceuticals Co., Ltd. Sanjiang Road, Paojiang Industrial Zone, Shaoxing, Zhejiang, P.R. China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5% RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Klacid 250mg tablet by Abbvie S.r.l Italy by performing quality tests. CDP has been performed against the Klacid 250mg tablet by Aesica Queenborough UK in Acid media (pH 1.0-1.2) & Acetate buffer 4.5pH and Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Better Pharmaceuticals Co., Ltd. Sanjiang Road, Paojiang Industrial Zone, Shaoxing, Zhejiang, P.R. China.		
API Lot No.	A022006051		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20TRn019	21TRn001	21TRn002
Batch Size	2000 tab	1000 tab	1000 tab
Manufacturing Date	12-2020	01-2021	01-2021
Date of Initiation	06-01-2021	12-01-2021	12-01-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. (New Section)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	--
3	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.12086/2020/DRAP-AD-G (I&E) dated 28/08/2020 is submitted wherein the permission to import different APIs including Clarithromycin for the purpose of test/analysis and stability studies is granted. • **DHL No.** 2020-11-16 XMLPI 6.2/90-1604 WAYBILL 41 0121 2102
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	--
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	--

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.1	Differential fee of Rs. 10,000/- shall be submitted as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	Differential fee of Rs. 10,000/- has been paid vide deposit slip# 9995357177 dated 20-06-2022
1.6.5	Valid GMP certificate issued by the relevant regulatory authority shall be submitted for the drug substance manufacturer.	Firm has submitted a document for " Written confirmation for active substances exported to EU' instead of GMP certificate, Zheijiang Food & Drug Administration.
3.2.S.4.2	Submit drug substance analytical record performed by M/s Islam pharma.	Submitted
3.2.P.2.2.1	In Pharmaceutical equivalence studies dissolution test has not been performed as per the USP monograph of Clarithromycin tablets.	Firm has submitted Dissolution test performance in continuation to Pharmaceutical equivalence studies.
3.2.P.3.2	• Justify the proposed quantity of Clarithromycin of 257.334mg per tablet in the batch formula against the label claim of 250mg per tablet. • A batch formula for proposed commercial batch size shall be provided	• Firmhas justified proposed quantity against the actual potency of drug substance determined on as is basis. • Commerical batch formula is submitted.
3.2.P.3.5	Submitted process validation protocol does not include sampling plan.	Revised process valiation protocol has been submitted.
3.2.P.8.3	➢ Submitted chromatograms of initial time point analysis declares file created date i.e., 18-02-2021 which is subsequent to the acquired date mentioned on each chromatogram. Clarification shall be submitted in this regard. ➢ Justification shall be submitted for calculating dissolution results based upon one value for standard peak area. ➢ Following shall be submitted: ➢ Compliance Record of HPLC software 21CFR & audit trail reports on product testing ➢ Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	• Laptop attached to the HPLC stopped working due to some fault and its hard disc was corrupted in Feb-2021 due to which new laptop was installed with HPLC. Previous data was recovered and transferred on 18-02-2021 to new laptop. • A new set of chromatograms print out for DRAP submission was taken after above incident so the chromatograms are showing file created date as 18-02-2021 (which is date if saved data transfer to new laptop) after the acquired date • HPLC system digital log has been submitted excluding for the intial time point analysis.

		Documents for the procurement of API with approval from DRAP (in case of import) shall be submitted.	• Record of Digital data logger for temperature and humidity monitoring of stability chamber is submitted. • Firm has submitted copy of commercialinvice which is not attested by DRAP I&E office.

Decision: Deferred for following:

- **Submission of valid GMP certificate of the drug substance manufacturer issued by the relevant regulatory authority.**
- **Onsight verification for the claim of the firm regarding disparity between date of acquisition & date of file creation in the submitted chromatograms.**

79.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot**
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter No. F.1-19/2014-Lic. from Secretary CLB for issuance of DML, declaring availability of "tablet general section".
	Dy. No. and date of submission	Dy.No 23834 dated 31-08-2021
	Details of fee submitted	Rs.20,000/- dated 22-04-2021
	The proposed proprietary name / brand name	**Caltis 500mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated tablet Contains: Clarithromycin ……. 500mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Clarithromycin 500mg tablet, Teva Pharmaceutical, MHRA Approved.
	For generic drugs (me-too status)	Rithmo 500mg tablet, Sami Pharmaceuticals (Pvt.) Limited.
	GMP status of the Finished product manufacturer	New DML was granted after inspection vide letter No. F. 1-19/2014-Lic (Vol-1) Dated: 29-08-2018, including Capsule general section

	Name and address of API manufacturer.	Zhejiang Better Pharmaceuticals Co., Ltd. Sanjiang Road, Paojiang Industrial Zone, Shaoxing, Zhejiang, P.R. China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5% RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Klacid 500mg tablet by Aesica Queenborough UK by performing quality tests. CDP has been performed against the Klacid 500mg tablet by Aesica Queenborough UK in Acid media (pH 1.0-1.2) & Acetate buffer 4.5pH and Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Better Pharmaceuticals Co., Ltd. Sanjiang Road, Paojiang Industrial Zone, Shaoxing, Zhejiang, P.R. China.
API Lot No.	A022006051
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 06 months Accelerated: 06 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20TRn018	20TRn024	20TRn025
Batch Size	2000 tab	1000 tab	1000 tab
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	04-01-2021	04-01-2021	04-01-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. (New Section)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	--
3	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.12086/2020/DRAP-AD-G (I&E) dated 28/08/2020 is submitted wherein the permission to import different APIs including Clarithromycin for the purpose of test/analysis and stability studies is granted. • **DHL No.** 2020-11-16 XMLPI 6.2/90-1604 WAYBILL 41 0121 2102
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	--
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	--

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.1	Differential fee of Rs. 10,000/- shall be submitted as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	Differential fee of Rs. 10,000/- has been paid vide deposit slip# 94806947378 dated 20-06-2022
1.6.5	Valid GMP certificate issued by the relevant regulatory authority shall be submitted for the drug substance manufacturer.	Firm has submitted a document for " Written confirmation for active substances exported to EU' instead of GMP certificate, Zheijiang Food & Drug Administration.
3.2.S.4.2	Submit drug substance analytical record performed by M/s Islam pharma.	• Submitted • Firm has submitted Dissolution test performance in continuation to

		Pharmaceutical equivalence studies.
3.2.P.2.2.1	• In Pharmaceutical equivalence studies dissolution test has not been performed as per the USP monograph of Clarithromycin tablets. • In Pharmaceutical equivalence studies submitted chromatograms of initial time point analysis declares file created date i.e., 18-02-2021 which is earlier to the acquired date mentioned on each chromatogram.	• Laptop attached to the HPLC stopped working due to some fault and its hard disc was corrupted in Feb-2021 due to which new laptop was installed with HPLC. Previous data was recovered and transferred on 18-02-2021 to new laptop. • A new set of chromatograms print out for DRAP submission was taken after above incident so the chromatograms are showing file created date as 18-02-2021 (which is date if saved data transfer to new laptop) after the acquired date 29-12-2020.
3.2.P.3.2	• Justify the proposed quantity of Clarithromycin of 514.668mg per tablet in the batch formula against the label claim of 500mg per tablet. • A batch formula for proposed commercial batch size shall be provided	• Firm has justified proposed quantity against the actual potency of drug substance determined on as is basis. • Commerical batch formula is submitted.
3.2.P.3.5	Submitted process validation protocol does not include sampling plan.	Revised process valiation protocol has been submitted.
3.2.P.8.3	➢ Submitted chromatograms of initial time point analysis declares file created date i.e., 18-02-2021 which is earlier to the acquired date mentioned on each chromatogram. Clarification shall be submitted in this regard. ➢ Justification shall be submitted for calculating dissolution results based upon one value for standard peak area. ➢ Following shall be submitted: ➢ Compliance Record of HPLC software 21CFR & audit trail reports on product testing ➢ Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated). Documents for the procurement of API with approval from DRAP (in case of import) shall be submitted.	• Laptop attached to the HPLC stopped working due to some fault and its hard disc was corrupted in Feb-2021 due to which new laptop was installed with HPLC. Previous data was recovered and transferred on 18-02-2021 to new laptop. • A new set of chromatograms print out for DRAP submission was taken after above incident so the chromatograms are showing file created date as 18-02-2021 (which is date if saved data transfer to new laptop) after the acquired date. • All of three batches on stability studies were tested on same day at each time point so only one standard solution for dissolution was injected and calculations were made against same one standard value.

			• HPLC system digital log has been submitted excluding for the intial time point analysis. • Record of Digital data logger for temperature and humidity monitoring of stability chamber is submitted. • Firm has submitted copy of commercialinvice which is not attested by DRAP I&E office.

Decision: Deferred for following:

- **Submission of valid GMP certificate of the drug substance manufacturer issued by the relevant regulatory authority.**
- **Onsight verification for the claim of the firm regarding disparity between date of acquisition & date of file creation in the submitted chromatograms.**

80.	Name, address of Applicant / Marketing Authorization Holder	**M/s Novamed Pharmaceuticals(Pvt.)Ltd Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.)Ltd ., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 25004 dated 09-09-2021
	Details of fee submitted	PKR 30,000/-: dated 09/08/2021
	The proposed proprietary name / brand name	**Rivamed Tablet 20 mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Rivaroxaban…….20mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Rivaroxaban inhibits free FXa and prothrombinase activity.
	Reference to Finished product specifications	In-House
	Proposed Pack size	10’s,14’s 20’s,28’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xeralto Tablet 20mg of M/s Janssen Pharms, approved by US FDA.
	For generic drugs (me-too status)	Xcept of M/s Pharmevo

	GMP status of the Finished product manufacturer	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Name and address of API manufacturer.	**Name**: Nantong Chanyoo Pharmatech Co., Ltd **Address**:No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal economic development zone nangton Jiangsu province
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(RB-190401, RB-190402, RB-190403)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence & Comparative dissolution profile has been established against the Xarelto tablets 10mg in three buffer mediums i.e., ph1.2, pH 4.5 & phH6.8 with acceptable results.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Name**: Nantong Chanyoo Pharmatech Co., Ltd **Address**: No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal
API Lot No.	RD-RB-202003271
Description of Pack (Container closure system)	Alu-Alu blisters, each containing Blue colored, round shape, biconvex, film coated tablets, Plain on both sides One side of blister is printed with labeling specification.

	After primary packing blister is packed in specific hard card unit carton along with Patient information leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Ti me: 0, 3, 6 (Months)		
Batch No.	**RD/PR20-030/T1/S1**	**RD/PR20-030/T1/S2**	**RD/PR20-030/T1/S3**
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	08-12-2020	08-12-2020	08-12-2020
No. of Batches	03		

81.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novamed Pharmaceuticals(Pvt.) Ltd., 28km Ferozepur Road Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.) Ltd., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of approval of manufacturing facility	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Dy. No. and date of submission	Dy.No 23878 dated 31-08-2021
	Details of fee submitted	Rs.30,000/- dated 09-08-2021
	The proposed proprietary name / brand name	**Rivamed 15mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Rivaroxaban ……15mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Rivaroxaban inhibits free FXa and prothrombinase activity.
	Reference to Finished product specifications	In-House
	Proposed Pack size	10’s,14’s 20’s,28’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xeralto Tablet 10mg of M/s Janssen Pharms, approvedby US FDA.
	For generic drugs (me-too status)	Xcept of M/s Pharmevo

	GMP status of the Finished product manufacturer	GMP certificate granted on 31/08/2021.
	Name and address of API manufacturer.	M/s Nantong Chanyoo Pharmatech Co., Ltd **Address**:No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal economic development zone nangton Jiangsu province
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5% RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches:(KM-1102215, KM-1102315, KM-1102415)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical requivalence & Comparative dissolution profile has been established against the Xarelto tablets 10mg in three buffer mediums i.e., ph1.2, pH 4.5 & ph 6.8 with acceptable results.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	**Name**: Nantong Chanyoo Pharmatech Co., Ltd	

	Address: No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal		
API Lot No.	RD-RB-202003271		
Description of Pack (Container closure system)	Alu-Alu blisters		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**RD/PR20-029/T1/S1**	**RD/PR20-029/T1/S2**	**RD/PR20-029/T1/S3**
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	08-12-2020	08-12-2020	08-12-2020
No. of Batches	03		

82.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novamed Pharmaceuticals(Pvt.) Ltd., 28km Ferozepur Road Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.) Ltd., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of approval of manufacturing facility	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Dy. No. and date of submission	Dy.No 23877 dated 31-08-2021
	Details of fee submitted	Rs.30,000/- dated 09-08-2021
	The proposed proprietary name / brand name	**Rivamed 10mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Rivaroxaban ……10mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Rivaroxaban inhibits free FXa and prothrombinase activity.
	Reference to Finished product specifications	In-House
	Proposed Pack size	10's,14's 20's,28's

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xeralto Tablet 10mg of M/s Janssen Pharms, approved by US FDA.
	For generic drugs (me-too status)	Xcept of M/s Pharmevo
	GMP status of the Finished product manufacturer	GMP certificate granted on 31/08/2021.
	Name and address of API manufacturer.	M/s Nantong Chanyoo Pharmatech Co., Ltd **Address**:No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal economic development zone nangton Jiangsu province
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5% RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches:(KM-1102215, KM-1102315, KM-1102415)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence & Comparative dissolution profile has been established against the Xarelto tablets 10mg in three buffer mediums i.e., ph1.2, pH 4.5 & ph 6.8 with acceptable results.

	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Name**: Nantong Chanyoo Pharmatech Co., Ltd **Address**: No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal		
API Lot No.	RD-RB-202003271		
Description of Pack (Container closure system)	Alu-Alu blisters, each containing Yellow colored, round shape, biconvex, film coated tablets, Plain on both sides One side of blister is printed with labeling specification. After primary packing blister is packed in specific hard card unit carton along with Patient information leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**RD/PR20-028/T1/S1**	**RD/PR20-028/T1/S2**	**RD/PR20-028/T1/S3**
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	27-11-2020	27-11-2020	27-11-2020
No. of Batches	03		

83.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novamed Pharmaceuticals(Pvt.) Ltd., 28km Ferozepur Road Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.) Ltd., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of approval of manufacturing facility	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Dy. No. and date of submission	Dy.No 23876 dated 31-08-2021
	Details of fee submitted	Rs.30,000/- dated 09-08-2021
	The proposed proprietary name / brand name	**Rivamed 2.5mg Tablet**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Rivaroxaban …… 2.5mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Rivaroxaban inhibits free FXa and prothrombinase activity.
	Reference to Finished product specifications	In-House
	Proposed Pack size	10's,14's 20's,28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xeralto Tablet 10mg of M/s Janssen Pharms, approvedby US FDA.
	For generic drugs (me-too status)	Xcept of M/s Pharmevo (Reg No: 076157)
	GMP status of the Finished product manufacturer	GMP certificate granted on 31/08/2021.
	Name and address of API manufacturer.	M/s Nantong Chanyoo Pharmatech Co., Ltd **Address**:No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal economic development zone nangton Jiangsu province
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5% RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches:(KM-1102215, KM-1102315, KM-1102415)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical requivalence & Comparative dissolution profile has been established against the Xarelto tablets in three buffer mediums i.e., ph1.2, pH 4.5 & ph 6.8 with acceptable results.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Name**: Nantong Chanyoo Pharmatech Co., Ltd **Address**: No.2 Tonghai Si road Yangkou chemical industrial park rudong coastal		
API Lot No.	RD-RB-202003271		
Description of Pack (Container closure system)	Alu-Alu blisters, each containing Yellow colored, round shape, biconvex, film coated tablets, Plain on both sides One side of blister is printed with labeling specification. After primary packing blister is packed in specific hard card unit carton along with Patient information leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**RD/PR20-027/T1/S1**	**RD/PR20-027/T1/S2**	**RD/PR20-027/T1/S3**
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	27-11-2020	27-11-2020	27-11-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate Nantong Chemical & Medical Industry Association has been submitted valid upto 05-05-2022.
3	Documents for the procurement of API with approval from DRAP (in case of import).	--
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.5.6	The said section declares Pharmacopoeial reference as In-Hose, whereas BP monograph is available for applied product.	Since the BP monograph of the Rivaroxaban was not available at the time of Product Development So the specification and analytical method follows In-House standard as per FDA guideline and same method has been validated. Both the Raw material and Product is Included in recent volume of BP
1.6.5	Valid GMP certificate issued by the relevant regulatory authority shall be submitted for the drug substance manufacturer.	GMPcertificate from nanytong chemical & medical Industry Association valid till 21-02-2026 has been submitted.
3.2.S.4.1	• The specifications and analytical procedure submitted from drug substance manufacturer is of In-house standard whereas BP monograph is available for applied formulation. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance / by Drug Product manufacturer is required.	• Since the BP monograph of the Rivaroxaban was not available at the time of Product Development So the specification and analytical method follows In-House standard FDA guideline and same method has been validated Analytical method validation studies were performed for In-House method as the BP Monograph was not available for applied formulation till its development and submission.
3.2.S.4.3	Analytical method verification studies shall be submitted for BP monograph of Rivaroxaban, performed by M/s Novamed.	Analytical method validation studies were performed for In-House method as the BP Monograph was not available for applied formulation till its development and submission
3.2.S.5	COA of primary / secondary reference standard, applied by M/s Novamed for drug substance analysis, including source and lot number shall be provided.	COA of working standard submitted.
3.2.P.2.2.1	Dissolution test has not been performed in Pharmaceutical equivalence studies.	Comparative dissolution profile against the Innovator Xeralto was performed and Pharmaceutical equivalence was established Through CDP and rest of the testing parameters are covered under PE testing
3.2.P.5.1	• Drug product specifications and analytical procedures have been referred as In-house , where as BP	• BP Since the BP monograph of the Rivaroxaban was not available at the time of Product

	monograph is available fro "Rivaroxaban tablets". • BP monograph of Rivaroxaban tablets specify limits of Assay test as 95.0% - 105.0%, whereas firm has applied limits of 90.0% - 110.0%. Justification shall be submitted in this regard. • Test of content uniformity has not been included in the drug product specifications.	Development So the specification and analytical method follows In-House standard FDA guideline and same method has been validated. Both the Raw material and Product is Included in recent volume of BP. • Since the BP monograph of the Rivaroxaban was not available at the time of Product Development So the specification and analytical method follows In-House standard FDA guideline and assay limit was set as 90-110% and same method has been validated. • The Content uniformity has been performed and results are submitted.
3.2.P.5.2	• Submitted analytical procedure for Assay & Dissolution test is not as per the BP monograph of Rivaroxaban tablet. • Limits for dissolution test mentioned in analytical procedure (NLT 80% (Q) in 45 minutes)) is not as per the BP monograph (NLT 80% (Q) in 30 minutes)).	• Since the BP monograph of the Rivaroxaban was not available at the time of Product Development So the specification and analytical method & Dissolution follows In-House standard based on FDA guideline and same method has been validated. • The limits for dissolution is as per In-house Standard since the BP monograph was not available at the time of its development and submission.
3.2.P.5.3	Analytical method verification studies shall be submitted for BP monograph of Rivaroxaban tablet, performed by M/s Novamed.	Analytical method validation studies were performed for In-House method as the BP Monograph was not available for applied formulation till its development and submission.
3.2.P.5.4	• Submitted batch analysis record does not include test of content uniformity. • Submitted batch analysis record reflects performance of Dissolution test with specifications different from BP monograph.	• The Content uniformity has been performed and results are submitted. • The dissolution test is performed as per In-house standard based on FDA guideline as the BP method is not available at the time of its development.
3.2.P.8.3	• Documents for the procurement of API with approval from DRAP (in case of import) shall be submitted.	Copy of commercial invoice# CY20121 attested by AD DRAP I&E Lahore dated 30-07-2020fo

	• Stability studies have not been conducted according to the BP monograph of Rivaroxaban Tablet. Justification shall be submitted in this regard.	rimport of 1 Kg of Rivaroxaban ha sbeen submitted. Since the BP monograph of the Rivaroxaban was not available at the time of Product Development So the specification follows In-House standard based on FDA guideline and stability studies performed accordingly.

Decision of 320th meeting: Registration Board approved Rivamed Tablet 20 mg, Rivamed 15mg Tablet, Rivamed 10mg Tablet & Rivamed 2.5mg Tablet with BP specifications.

- **The firm shall submit fee of Rs. 7500/- for each strength for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

84.	Name, address of Applicant / Marketing Authorization Holder	**M/s Novamed Pharmaceuticals(Pvt.)Ltd Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.)Ltd ., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 23875 dated 31-08-2021
	Details of fee submitted	PKR 30,000/-: dated 07/06/2021
	The proposed proprietary name / brand name	**Apixo Tablet 2.5 mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Apixaban ……. 2.5mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Apixaban (Anticoagulant and direct inhibitor of factor Xa.
	Reference to Finished product specifications	In-House
	Proposed Pack size	10’s,20’s,30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Eliquis Tablet 2.5mg, Company: Bristol Myers Squibb,USA

	For generic drugs (me-too status)	Apixaget 2.5mg by Getz Pharma Reg No: 105247
	GMP status of the Finished product manufacturer	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Name and address of API manufacturer.	**Name**: Changzhou Pharmaceuticals Factory **Address**:518 Laodong East Road, Changzhou, Jianngsu Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(ZSAP171104,ZSAP171105,ZSAP171106)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Eliquis Tablet 2.5mg** by performing quality tests (Identification, Assay, Dissolution, pH). **CDP** was applicable and has been submitted.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity, robustness and Limit of Quantification.

STABILITY STUDY DATA	
Manufacturer of API	**Name**: Changzhou Pharmaceuticals Factory **Address**: 518 Laodong East Road,Changzhou,Jianngsu Province, China.
API Lot No.	AP191204

Description of Pack (Container closure system)	Alu-PVC blisters, each containing 10 Green colored, round shape, biconvex, film coated tablets, Plain on both sides One side of blister is printed with labeling specification. After primary packing blister is packed in specific hard card unit carton along with Patient information leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**RD/PR20-001/T1/S1**	**RD/PR20-001/T1/S2**	**RD/PR20-001/T1/S3**
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	24-08-2020	24-08-2020	24-08-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted copy of Last inspection Report conducted on 24/01/2018 (Daclatasvir), 06/03/2017 (Sofosbuvir)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by CFDA, People's republic of china Changzhou Jiangsu valid till 21/10/2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.6139/2020/DRAP-AD-CD(I&E) dated 15/05/2020 is submitted wherein the permission to import API Apixaban for the purpose of test/analysis and stability studies is granted. AD I&E (Lahore) Attested invoice CYI20200 Dated.28/05/2020 is also submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.6.5	Valid GP certificate issued by relevant regulatory authority shall be submitted, for drug substance manufacturer.	Firm has submitted GMP certificate valid upto 15-11-2024, issud by the Jiangsu Changzhou Drug Administration, which is not a state

		or provincial level regulatory authority.
3.2.P.2.2.1	Dissolution test has not been performed in Pharmaceutical Equivalences studies. Clarification shall be submitted for declaring dissolution results above 85% in CDP studies, without using surfactant i.e., SLS in dissolution medium.	• CDP againt the Innovator was performed and Pharmaceutical equivalence was established through CDP and rest of the testing parameters are covered under PE testing. • Surfactant SLS is mistakenly not mentioned n CDP reports while it is used in dissolution medium, which is evident from testing method.
3.2.P.5.1	• Innovator product approved by US FDA has recommended dissolution limits of NLT Q in 30minutes whereas firm has proposed dissolution time of 45 minutes. • Test of content uniformity has not been included in finished drug product specifications.	• Firm has referred to the EM Aassesment report for Apixaban tablet wherein resulst of 80% dissolved in 45 minutes have been mentioned for the coparative profile of refernec eand test product, whereas observation was made regarding dissolution test limits recommended for batch release by US FDA for innovator product. • Firm has submitted results for the performance of content uniformity test.

Decision of 320th meeting: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

85.	Name, address of Applicant / Marketing Authorization Holder	**M/s Novamed Pharmaceuticals(Pvt.)Ltd Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.)Ltd ., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 25003 dated 31-08-2021
	Details of fee submitted	PKR 30,000/-: dated 07/06/2021

	The proposed proprietary name / brand name	**Apixo Tablet 5 mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Apixaban ……. 5mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Apixaban (Anticoagulant and direct inhibitor of factor Xa.
	Reference to Finished product specifications	In-House
	Proposed Pack size	10's,20's,30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Eliquis Tablet 2.5mg, Company: Bristol Myers Squibb,USA
	For generic drugs (me-too status)	Apixaget 2.5mg by Getz Pharma Reg No: 105247
	GMP status of the Finished product manufacturer	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Name and address of API manufacturer.	**Name**: Changzhou Pharmaceuticals Factory **Address**:518 Laodong East Road,Changzhou,Jianngsu Province,China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(ZSAP171104,ZSAP171105,ZSAP171106)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard,

		container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence & CDP have been established against the **Eliquis Tablet 5mg.**
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity, robustness.

STABILITY STUDY DATA

Manufacturer of API	**Name**: Changzhou Pharmaceuticals Factory **Address**: 518 Laodong East Road,Changzhou,Jianngsu Province, China.		
API Lot No.	AP191204		
Description of Pack (Container closure system)	Alu-PVC blisters, each containing 10 Green colored, round shape, biconvex, film coated tablets, Plain on both sides One side of blister is printed with labeling specification. After primary packing blister is packed in specific hard card unit carton along with Patient information leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**RD/PR20-002/T2/S1**	**RD/PR20-002/T2/S2**	**RD/PR20-002/T2/S3**
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	24-08-2020	24-08-2020	24-08-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted copy of Last inspection Report conducted on 24/01/2018 (Daclatasvir), 06/03/2017 (Sofosbuvir)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by CFDA, People's republic of china Changzhou Jiangsu valid till 21/10/2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.6139/2020/DRAP-AD-CD(I&E) dated 15/05/2020 is submitted wherein the permission to import API Apixaban for the purpose of test/analysis and stability studies is granted. AD I&E (Lahore) Attested invoice CYI20200 Dated.28/05/2020 is also submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
1.6.5	Valid GMP certificate issued by relevant regulatory authority shall be submitted, for drug substance manufacturer.	Firm has submitted GMP certificate valid upto 15-11-2024, issud by the Jiangsu Changzhou Drug Administration, which is not a state or provincial level regulatory authority.
3.2.P.2.2.1	Dissolution test has not been performed in Pharmaceutical Equivalences studies. Clarification shall be submitted for declaring dissolution results above 85% in CDP studies, without using surfactant i.e., SLS in dissolution medium.	• CDP againt the Innovator was performed and Pharmaceutical equivalence was established through CDP and rest of the testing parameters are covered under PE testing. • Surfactant SLS is mistakenly not mentioned n CDP reports while it is used in dissolution medium, which is evident from testing method.
3.2.P.5.1	• Innovator product approved by US FDA has recommended dissolution limits of NLT Q in 30minutes whereas firm has proposed dissolution time of 45 minutes. • Test of content uniformity has not been included in finished drug product specifications.	• Firm has referred to the EMA Aassesment report for Apixaban tablet wherein resulst of 80% dissolved in 45 minutes have been mentioned for the coparative profile of refernec eand test product, whereas observation was made regarding dissolution test limits recommended for batch release by US FDA for innovator product. • Firm has submitted results for the performance of content uniformity test.

Decision of 320th meeting: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

86.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.**
	Name, address of Manufacturing site.	M/s SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 23868 dated 31-08-2021
	Details of fee submitted	PKR 30,000/- dated 14/07/2021
	The proposed proprietary name / brand name	**OMDIN 100mcg/ml Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Dexmedetomidine hydrochloride equivalent to Dexmedetomidine ……. 100mcg
	Pharmaceutical form of applied drug	Clear colorless solution for injection
	Pharmacotherapeutic Group of (API)	Hypnotics and Sedatives ATC Code: N05CM18
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	2ml; 1's, 2's, 5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	PRECEDEX 100mcg/ml Injection approved by USFDA
	For generic drugs (me-too status)	Precidex 100mcg/ml Injection by M/s Brookes Pharma (Reg.#088249)
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	M/s Jiangsu Hengrui Medicine Co., Ltd. 22 Jinqiao Road, Dapu Industrial park, Economical & Technological Development Zone Lianyungang, Jiangsu 222002, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (6601506012, 6601507012, 6601507022)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Precidex 100mcg/ml Injection by M/s Brookes Pharma by performing quality tests (Appearance, pH, Assay, impurity profiling, BET, sterility test). CDP is not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision (repeatability), specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Jiangsu Hengrui Medicine Co., Ltd.		
API Lot No.	6601908012		
Description of Pack (Container closure system)	Unprinted Clear ampoule 2ml USP type 1		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-1	Lab-2	Lab-3
Batch Size	2000 ml	2000 ml	2000 ml
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	16-05-2020	16-05-2020	16-05-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Reference of last onsite panel inspection for instant dosage form conducted during last two years i.e. **IBRUO** (Ibuprofen) 800mg/8ml injection which was presented in 289th meeting of the registration board & hence approved & registered by registration board Date of inspection: 28th January 2019 The inspection report confirms following points • The HPLC software is 21CFR Compliant • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled

		and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate no. JS20191012 of M/s Jiangsu Hengrui Medicine Co., Ltd.is valid until 27/02/2024 issued by Jiangsu Drug Administration, China Food and Drug Administration
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice (Invoice#19QN265 dated 14-2-2020 with received quantity of 4gm) for the purchase of Dexmedetomidine HCl from M/s Jiangsu Hengrui Medicine Co., Ltd. with attestation of DRAP dated 27-02-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
3.2.P.2.2.1	Pharmaceutical equivalence studies have not been performed against Innovator.	• As innovator product is not available in Pakistan, therefore, we tried to arrange the innovator product from outside the Pakistan, however since this product is only used in Hospitals/Institutions before and/or during surgical and other procedures and therefore not available at Pharmacy level; we conducted, comparative analysis with the comparator product •As per the DRAP's "Frequently Asked Questions" uploaded on its official website, it has been permitted by the Authority that in case of non-availability of the innovator pack, comparative analysis can be performed with the brand leader/generic product (Reference document attached) •It is further submitted that as per WHO technical report Series No. 902, 2002: "If the innovator product is not available on the local market, pharmaceutical companies should obtain from the market a product that is the best representative innotao rproduct fro

		mth epoint of view of its quality, safety & efficacy." Hence, due to non-availability of the innovator pack in the local market, we conducted the comparative analysis with comparator product .i.e. PRECIDEX (Dexmedetomidine) 100mcg/ml Injection (Reg. No. 088249} being manufactured by M/s. Brookes Pharma, Karachi
3.2.P.5.2	Exact Limits of Endotoxin test shall be mentioned instead of referring to the general USP chapter	Firm has submitted revised test method with numerical limits of Endotoxin test.
3.2.P.5.4	Submitted COA does not include performance of test of "Fill volume".	Firm has submitted revised COA indicating the extractable volume with declaration that we have performed this test however was not mentioned in the COA since it's an in-process test.

Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

87.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 28733 dated 20-10-2021
	Details of fee submitted	Rs.75,000/- dated 13-07-2021
	The proposed proprietary name / brand name	**Limaxone 1g IV/IM Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 1gm
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef 1g Injection of M/s. Pride Pharmaceuticals 025878
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Rocephin Injection 1g IM.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	124	125	126
Batch Size	10,000 Vials	12170 Vials	12170 Vials
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	28-08-2020	28-08-2020	28-08-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin Injection 1 gm IV/IM later approved as Trophin Injection 1 gm IV
Batch No. of drug product	124, 125, 126
Case No.	3
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.
- **Firm has applied for both IV/IM injection however the data of contract manufacturer i.e. M/s Gray's Pharmaceuticals already considered and approved in 316th meeting was for 1gm IV Injection.**

Decision of 320th meeting: Approved with IV route of administration.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after on-site inspection of capacity assessment of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad, for the manufacturing & Quality control facility.**

88.	Name, address of Applicant / Marketing Authorization Holder	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 29008 dated 25-10-2021
	Details of fee submitted	Rs.75,000/- dated 06-10-2020
	The proposed proprietary name / brand name	**Limaxone 250mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 250mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef Injection of Ceftriaxone Sodium by Pride Pharmaceuticals 025876
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40 ^{O} ± 2 ^{O} C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2 ^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Oxidil 250mg Injection IV.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	103	115	120
Batch Size	5,000 packs	5,000 packs	5,000 packs
Manufacturing Date	10-2019	05-2020	06-2020
Date of Initiation	09-10-2019	05-05-2020	04-06-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin injection 250mg IV
Batch No. of drug product	103, 115, 120
Case No.	7
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision of 320th meeting: Approved with IV route of administration.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after on-site inspection of capacity assessment of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad, for the manufacturing & Quality control facility.**

89.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Quaper Pharmaceuticals Plant 26-A Small Industrial Esatte Lahore Road Sargodha**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad

	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 27303 dated 04-10-2021
	Details of fee submitted	Rs.30,000/- dated 27-09-2021
	The proposed proprietary name / brand name	**Q-NEM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.

	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 001	Noopem Injection 001
Batch Size	7,000 Vials	7,000 Vials	7,000 Vials
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	28-06-2019	28-06-2019	28-06-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	P5001 (8,600 vials), P5002 (8,600vials), P5003 (10,630 vials)
Case No.	608
Registration Board meeting	316th meeting of Registration Board held on (15-18 March, 2022)

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Decision of 320th meeting: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

90.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Quaper Pharmaceuticals Plant 26-A Small Industrial Esatte Lahore Road Sargodha**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 27304 dated 04-10-2021
	Details of fee submitted	Rs.30,000/- dated 27-09-2021
	The proposed proprietary name / brand name	**Q-Nem 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem …… 1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and

		its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10,500 Vials	13,000 Vials	5,500 Vials
Manufacturing Date	06-2019	09-2019	09-2019

Date of Initiation	30-06-2019	30-09-2019	26-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 1g Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	821
Registration Board meeting	316th meeting of Registration Board

Decision of 320th meeting: Approved.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
91.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Aptcure Pvt Ltd. 8- Pharma City, 30 km Multan Road, Lahore**
	Name, address of Manufacturing site.	M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 32566 dated 13-12-2021
	Details of fee submitted	Rs.75,000/- dated 03-11-2021
	The proposed proprietary name / brand name	**Greeninject 50mg/ml Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Iron as Ferric Carboxymaltose…50mg/ml
	Pharmaceutical form of applied drug	IV Liquid injection
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	10ml;1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by MHRA of UK
	For generic drugs (me-too status)	Ferotox 50mg/ml Injection of M/s Wilshire Laboratories Reg.# 108356
	GMP status of the Finished product manufacturer	GMP certificate issued on the basis of inspection conducted on 17& 18-01-2019
	Evidence of manufacturing facility.	GMP certificate issued on the basis of inspection conducted on 17& 18-01-2019, declares availability of Liquid injectable vial & ampoule section.
	Name and address of API manufacturer.	M/s Nanjing Hancer Pharmaceutical Co., Ltd., China, No. 18 Hichang Road, Lishui Economi Technlogical Development one Jiangsu, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, , specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Ferinject Injection.
	Analytical method validation/verification of product	--

STABILITY STUDY DATA			
Manufacturer of API	M/s Nanjing Hancer Pharmaceutical Co., Ltd., China, No. 18 Hichang Road, Lishui Economi Technlogical Development one Jiangsu, China.		
API Lot No.	R210302		
Description of Pack (Container closure system)	Type I glass vial.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,3,6 (Months) Real Time: 0,3,6 (Months)		
Batch No.	FRI-001	FRI-002	FRI-003
Batch Size	5000 packs	10,000 packs	10,000 packs
Manufacturing Date	07-2021	07-2021	07-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No.JS20180811 issued by NMPA China valid till 06-05-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of commercial invoice no. HC2IT09T001-01 attested by AD DRAP I&E Lahore dated 02-07-2021 for the import of 50Kg Ferric Carboxymaltose..
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
3.2.S.4.2	• Drug substance analytical procedure applied by drug substance manufacturer shall be submitted. • Limits for the Content of Iron declared in the analytical procedure for Assay is not as per those submitted in drug substance specifications.	• Firm has submitted analytical procedure from drug substance manufacturer. • Revised analytical procedure has been submitted wherein limit for Assay test has been declared in term of 5age of iron.
3.2.S.4.3	Analytical method verification studies for the Assay test procedure of drug substance shall be submitted form M/s English Pharmaceuticals.	Submitted.
3.2.P.3.5	Submitted process validation protocol does not identifies Mixing stage as critical process parameter.	Firm has submitted revised process validation protocol including mixing stage as critical process parameter.
3.2.P.5.3	Analytical method validation studies for the Assay test of Iron content shall be submitted.	Firm has submitted analytical method validation studies for the titration method of Assay for drug product.
3.2.P.8	• Digital data logger record for accelerated stability chamber shall be submitted. • Dispensed quantity of Ferric carboxymaltose, during batch manufacturing shall be justified against the label claim of Iron.	Submitted. Firm has justified dispensed quantity of ferric carboxymaltose considering the %age Assay results calculated on "as is basis."

Decision of 320th meeting: Approved with Innovator's specifications and change of brand name.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
92.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Daneen Pharma Private Limited 27-Sundar Industrial Estate, Sundar Raiwind Road, Lahore**
	Name, address of Manufacturing site.	M/s Genix Pharma Private Limited 44-45B Korangi creek road Karachi
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ **Is involved in none of the above (contract giver)**
	Status of application	☐ **New Drug Product (NDP)** ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ **Domestic and Export sales**
	Dy. No. and date of submission	Dy.No 33644 dated 24-12-2021
	Details of fee submitted	Rs.75,000/- dated 03-11-2021
	The proposed proprietary name / brand name	**Danforge-A Tablets 10mg/160mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Amlodipine eq. to Amlodipine Besylate…..10mg Valsartan……..160mg
	Pharmaceutical form of applied drug	Round, Biconvex, Light Orange color, film coated tablet, engraved "GENIX" on one side & break line on other side.
	Pharmacotherapeutic Group of (API)	Antihypertensive
	Reference to Finished product specifications	U.S.P Specification
	Proposed Pack size	7's, 14's & 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Exforge tablet by M/s Novartis USFDA Approved.
	For generic drugs (me-too status)	Covam Tablets by M/s Getz Pharma
	GMP status of the Finished product manufacturer	New GMP granted on 07/10/2021 Tablet section (General & Psycotropic) approved.
	Name and address of API manufacturer.	**Amlodipine:** Amsal Chem Private Limited, A-1/401/2/3, GIDC Industrial Estate Ankleshwar - 393 002, District Bharuch, Gujarat, India **Valsartan:** Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its

		verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Amlodipine:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (13002/APL,13003/APL& 13004/APL) **Valsartan:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (201207301, 201207302& 201207303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the relevant strength of **Covam Tablet** by M/s Getz Pharma by performing quality tests (Identification, Assay, Dissolution) CDP has been performed against the same brand that is **Covam Tablet** by Getz Pharma in Acid media (0.1N HCl), Acetate buffer of pH 4.5 & Phosphate Buffer (pH 6.8). The f2 value was in acceptable range.
	Analytical method validation/verification of product	Method verification studies have been submitted including justification of system suitability, specificity, linearity, accuracy, precision-repeatability.

STABILITY STUDY DATA	
Manufacturer of API	**Amlodipine:** Amsal Chem Private Limited, A-1/401/2/3, GIDC Industrial Estate Ankleshwar - 393 002, District Bharuch, Gujarat, India **Valsartan:** Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China
API Lot No.	Amlodipine: 17019/AB, Valsartan: 10200-171201
Description of Pack (Container closure system)	Alu/alu blister
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 6 months

Frequency		Accelerated:0,3 & 6(Months) Real Time: 0,3, 6, 9 ,12,18 & 24 (Months)	
Batch No.		001T199	002T199	003T199
Batch Size		100,000 Tablets	100,000 Tablets	100,000 Tablets
Manufacturing Date		04-2018	04-2018	04-2018
Date of Initiation		07-05-2018	07-05-2018	07-05-2018
No. of Batches		03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Amlodipine: Copy of GMP certificate No. 1991611 issued by Food & Drugs control administration, Gujarat, India valid till 23/09/2022 Valsartan: Copy of GMP certificate No. ZJ20180033 issued by CFDA valid till 14/03/2023	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Amlodipine: Copy of Purchase invoice No.AE/2122/0090 attested by AD DRAP I&E dated 30/07/2021is submitted Valsartan: Copy of Purchase invoice No.TY121560 attested by AD DRAP I&E dated 09/07/2021 is submitted	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	
93.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Daneen Pharma Private Limited 27-Sundar Industrial Estate, Sundar Raiwind Road, Lahore**	
	Name, address of Manufacturing site.	M/s Genix Pharma Private Limited 44-45B Korangi creek road Karachi	
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ **Is involved in none of the above (contract giver)**	
	Status of application	☐ **New Drug Product (NDP)** ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ **Domestic and Export sales**	
	Dy. No. and date of submission	Dy. No 34243 dated 31-12-2021	
	Details of fee submitted	Rs.75,000/- dated 03-11-2021	

	The proposed proprietary name / brand name	**Danforge-A Tablets 5mg/160mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Amlodipine eq. to Amlodipine Besylate ……. 5mg Valsartan ……. 160mg
	Pharmaceutical form of applied drug	Round, Biconvex, Light Orange color, film coated tablet, engraved "GENIX" on one side & break line on other side.
	Pharmacotherapeutic Group of (API)	Antihypertensive
	Reference to Finished product specifications	U.S.P Specification
	Proposed Pack size	7's, 14's & 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Exforge tablet by M/s Novartis USFDA Approved.
	For generic drugs (me-too status)	Covam Tablets by M/s Getz Pharma
	GMP status of the Finished product manufacturer	New GMP granted on 07/10/2021 Tablet section (General & Psycotropic) approved.
	Name and address of API manufacturer.	**Amlodipine:** Amsal Chem Private Limited, A-1/401/2/3, GIDC Industrial Estate Ankleshwar - 393 002, District Bharuch, Gujarat, India **Valsartan:** Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Amlodipine:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (13002/APL,13003/APL& 13004/APL) **Valsartan:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

		Batches: (201207301, 201207302& 201207303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the relevant strength of **Covam Tablet** by M/s Getz Pharma by performing quality tests (Identification, Assay, Dissolution) CDP has been performed against the same brand that is **Covam Tablet** by Getz Pharma in Acid media (0.1N HCl), Acetate buffer of pH 4.5 & Phosphate Buffer (pH 6.8). The f2 value was in acceptable range.
	Analytical method validation/verification of product	Method verification studies have been submitted including justification of system suitability, specificity, linearity, accuracy, precision-repeatability.

STABILITY STUDY DATA

Manufacturer of API	**Amlodipine:** Amsal Chem Private Limited, A-1/401/2/3, GIDC Industrial Estate Ankleshwar - 393 002, District Bharuch, Gujarat, India **Valsartan:** Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China		
API Lot No.	Amlodipine: 17019/AB, Valsartan: 10200-171201		
Description of Pack (Container closure system)	Alu/alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated:0,3 & 6(Months) Real Time: 0,3, 6, 9 ,12,18 & 24 (Months)		
Batch No.	001T198	002T198	003T198
Batch Size	100,000 Tablets	100,000 Tablets	100,000 Tablets
Manufacturing Date	04-2018	04-2018	04-2018
Date of Initiation	02-05-2018	02-05-2018	02-05-2018
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Amlodipine: Copy of GMP certificate No. 1991611 issued by Food & Drugs control administration, Gujarat, India valid till 23/09/2022 Valsartan: Copy of GMP certificate No. ZJ20180033 issued by CFDA valid till 14/03/2023

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Amlodipine: Copy of Purchase invoice No.AE/2122/0090 attested by AD DRAP I&E dated 30/07/2021is submitted Valsartan: Copy of Purchase invoice No.TY121560 attested by AD DRAP I&E dated 09/07/2021 is submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
94.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Daneen Pharma Private Limited 27-Sundar Industrial Estate, Sundar Raiwind Road, Lahore**
	Name, address of Manufacturing site.	M/s Genix Pharma Private Limited 44-45B Korangi creek road Karachi
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ **Is involved in none of the above (contract giver)**
	Status of application	☐ **New Drug Product (NDP)** ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ **Domestic and Export sales**
	Dy. No. and date of submission	Dy.No 34241 dated 31-12-2021
	Details of fee submitted	Rs.75,000/- dated 03-11-2021
	The proposed proprietary name / brand name	**Danforge-A Tablets 5mg/80mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Amlodipine eq. to Amlodipine Besylate…..5mg Valsartan……..80mg
	Pharmaceutical form of applied drug	Round, Biconvex, Light Orange color, film coated tablet, engraved "GENIX" on one side & break line on other side.
	Pharmacotherapeutic Group of (API)	Antihypertensive
	Reference to Finished product specifications	U.S.P Specification
	Proposed Pack size	7's, 14's & 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Exforge tablet by M/s Novartis USFDA Approved.
	For generic drugs (me-too status)	Covam 5mg/80mg Tablets by M/s Getz Pharma

	GMP status of the Finished product manufacturer	New GMP granted on 07/10/2021 Tablet section (General & Psycotropic) approved.
	Name and address of API manufacturer.	**Amlodipine:** Amsal Chem Private Limited, A-1/401/2/3, GIDC Industrial Estate Ankleshwar - 393 002, District Bharuch, Gujarat, India **Valsartan:** Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Amlodipine:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (13002/APL,13003/APL& 13004/APL) **Valsartan:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (201207301, 201207302& 201207303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the relevant strength of **Covam Tablet** by M/s Getz Pharma by performing quality tests (Identification, Assay, Dissolution) CDP has been performed against the same brand that is **Covam Tablet** by Getz Pharma in Acid media (0.1N HCl), Acetate buffer of pH 4.5 & Phosphate Buffer (pH 6.8). The f2 value was in acceptable range.
	Analytical method validation/verification of product	Method verification studies have been submitted including justification of system suitability, specificity, linearity, accuracy, precision-repeatability.

STABILITY STUDY DATA			
Manufacturer of API	**Amlodipine:** Amsal Chem Private Limited, A-1/401/2/3, GIDC Industrial Estate Ankleshwar - 393 002, District Bharuch, Gujarat, India **Valsartan:** Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China		
API Lot No.	Amlodipine: 17019/AB, Valsartan: 10200-171201		
Description of Pack (Container closure system)	Alu/alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated:0,3 & 6(Months) Real Time: 0,3, 6, 9 ,12,18 & 24 (Months)		
Batch No.	001T197	002T197	003T197
Batch Size	100,000 Tablets	100,000 Tablets	100,000 Tablets
Manufacturing Date	04-2018	04-2018	04-2018
Date of Initiation	03-05-2018	03-05-2018	03-05-2018
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Amlodipine: Copy of GMP certificate No. 1991611 issued by Food & Drugs control administration, Gujarat, India valid till 23/09/2022 Valsartan: Copy of GMP certificate No. ZJ20180033 issued by CFDA valid till 14/03/2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Amlodipine: Copy of Purchase invoice No.AE/2122/0090 attested by AD DRAP I&E dated 30/07/2021is submitted Valsartan: Copy of Purchase invoice No.TY121560 attested by AD DRAP I&E dated 09/07/2021 is submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observation	Firm's response
1.6.5	Name of manufacturing site of M/s Amsal Chem, mentioned in section 1.6.5 & 3.2.S.2.1 is different form that declared on GMP certificate.	The mentioned address in section 1.6.5 & 3.2.S.1 is of administrative office. Howver, name of manufacturer is same as mentioned on GMP certificate i.e., M/s Amsal Che, Pvt. Ltd, Mumbai, India, A-1,401,402,403 G.I.D.C industrial Estate, Ankleshwar-393002, District, Bharuch, Gujarat, India.
3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	Submitted.
3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacture.	Submitted.
3.2.S.5	Submit COAs of working standard used for the batch release for drug substance used in the formulation of stability batches of drug product.	Firm has submitted COA of working standard of both drug substances from relevant manufacturer.
3.2.P.2.2.1	Justification shall be submitted for not performing Comparative dissolution & Pharmaceutical equivalence studies against the innovator product.	Firm has submitted that due to unavailability of innovator sample in Pakistan, CDP was conducted against Covam tablets of M/s Getz Pharma.
3.2.P.8.3	Submitted commercial invoices for the import of drug substances are of subsequent dates from the date of manufacturing of stability batches.	Firm has now submitted following: • Amlodipine: Copy of Purchase Invoice No. AE/227/17-18 attested by AD DRAP I&E dated 21/12/2017 for batch# 17019/AB • Valsartan: Copy of Purchase invoice No. TYI18026 attested by AD DRAP I&E dated 30/01/2018.

- Comparative dissolution & Pharmaceutical equivalence studies have been performed on the recent batches manufactured by M/s Genix, instead of the stability batches.

Decision of 320th meeting: Registration Board approved Danforge-A Tablets 10mg/160mg, Danforge-A Tablets 5mg/160mg & Danforge-A Tablets 5mg/80mg.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued upon submission of Pharmaceutical equivalence & CDP studies for each strength against the innovator drug product.**

95.	**Name, address of Applicant / Marketing Authorization Holder**	**Asian Continental (Pvt) Ltd., D/32 SITE Super Highway Karachi.**
	Name, address of Manufacturing site.	M/s Wimits Pharmaceuticals (Pvt.) Ltd. Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 32419 dated 29-11-2021
	Details of fee submitted	Rs.75,000/- dated 18-10-2021
	The proposed proprietary name / brand name	**Vintera 30mg/ml Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml Contains: Ketorolac Tromethamine …… 30mg
	Pharmaceutical form of applied drug	Injectable solution
	Pharmacotherapeutic Group of (API)	Anti-inflammatory agent, non-steroid
	Reference to Finished product specifications	USP
	Proposed Pack size	1ml×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ketorolac Tromethamine injection 30mg/ml by M/s Peckforton Pharmaceuticals Limited Crewe Hall, Crewe, Cheshire, CW1 6UL, United Kingdom, MHRA Approved.
	For generic drugs (me-too status)	Toradol Injection 30mg/ml by M/s Barrett Hodgson Pakistan (Pvt.) Ltd. Reg. No. 015000
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 08-11-2019.
	Name and address of API manufacturer.	M/s. Satyadivis Pharmaceuticals Pvt. Ltd., Survey No. 10, Gaddapotaram (V), Khazipally I.D.A., Jinnaram (M), Sangareddy Dist.-502 319. T.S. INDIA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities,

		specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, t, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Toradol 30mg/ml Injection of Barret Hodgsosn
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Satyadivis Pharmaceuticals Pvt. Ltd., Survey No. 10, Gaddapotaram (V), Khazipally I.D.A., Jinnaram (M), Sangareddy Dist.-502 319. T.S. INDIA		
API Lot No.	0070320		
Description of Pack (Container closure system)	Glass ampoules		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	KL021	KL022	KL023
Batch Size	100,000 ampoules	100,000 ampoules	100,000 ampoules
Manufacturing Date	07-2020	07-2020	07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	--
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of commercial invoice# E023/KET for import of 10Kg of Ketorolac tromethamine, attested by AD DRAP I&E Lahore dated 20-07-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	N/A

Remarks of Evaluator:

Sr.#	Observations	Firm's response
1.6.5	Valid GMP certificate of the drug substance manufacturer shall be submitted.	Firm has submitted GMP certificate no. 75331/TS/2022 issued by Drug Control Administration Government of Telangana valid until 21/01/2023.
3.2.S.4.4	Microbial report for the sterility testing of drug substance by M/s Wimits shall be submitted.	Firm has submitted Sterility test/Bacterial Endotoxin test report for the drug substance Batch# 0070320.
3.2.P.2.2.1	Justification shall be submitted for not performing Pharmaceutical equivalence studies against the innovator product.	Firm has submitted Pharmaceutical Equivalence studies against Toradol injection of M/s Barret Hodgson.
3.2.P.5.1	Justification shall be submitted for additional fill volume in each ampoule.	Firm has referred to USP General Chapter <1151> wherein excess volume of 0.1ml is allowed for 1ml injection.
3.2.P.5.3	Concentrations in term of mg/ml shall be provided for three concentration levels tested in performance of Accuracy parameter	Firm has submitted concentration in terms of mg/ml for each concentration level of Accuracy parameter performance.
3.2.P.6	COA of working standard used for the analysis of drug product stability batches shall be submitted.	Firm has submitted COA of working standard "Ketorolac tromethamine USP" valid upto Feb-2023.

Decision of 320th meeting: Approved.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**		
96.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 32577 dated 30-11-2021
	Details of fee submitted	Rs.75,000/- dated 28-10-2021
	The proposed proprietary name / brand name	**Elmet XR 25/25/1000 mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated extended-release tablet contains: Empagliflozin …….. 25mg Linagliptin …… 25 mg (as immediate release coating) Metformin HCl …… 1000mg (as extended release core)
	Pharmaceutical form of applied drug	Film-coated extended-release tablet
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** sodium-glucose co-transporter 2 (SGLT2) inhibitors **Linagliptin:** dipeptidyl peptidase-4 (DPP-4) inhibitors **Metformin HCl:** antihyperglycemic drug
	Reference to Finished product specifications	Innovator
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Trijardy® XR Tablets by M/s Boehringer Ingelheim, FDA Approved.
	For generic drugs (me-too status)	Not Available
	Evidence of manufacturing facility	GMP certificate granted on basis of inspection conducted on 18.06.2020 endorses tablet general section.
	GMP status of the Finished product manufacturer	GMP certificate granted on basis of inspection conducted on 18.06.2020.

	Name and address of API manufacturer.	**Linagliptin:** **M/s Lee Pharma Limited, India** HuaiNan ShunLong Pharmaceutical CO, LTD. No. 9 Yongxing Road, Econonmic and Technological Development Development Zone, Huainan City, Anhui Province China. **Empagliflozin:** HuaiNan ShunLong Pharmaceutical CO, LTD. No. 9 Yongxing Road, Econonmic and Technological Development Development Zone, Huainan City, Anhui Province China. **Metformin Hydrochloride:** Shandong Keyuan Pharmaceutical Co., Ltd. Keyuan Street, Shandong shanghe Economic Zone, Jinan city, Shandong Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data on CTD format related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications and analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies of Drug substance	**Empagliflozin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Linagliptin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Metformin HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturing process and process control, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Trijardy XR Tablets 25/25/1000mg approved by US-FDA. CDP has been performed against the same brand that is Trijardy XR Tablets 12.5/2.5/1000mg approved by US-FDA in Acid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)		
	Analytical method validation/verification of product	Method validation studies have submitted including, Specificity, linearity, range, accuracy, precision Repeatability, Intermediate precision, Robustness, System Suitability.		
STABILITY STUDY DATA				
Manufacturer of API		**Linagliptin:** **M/s Lee Pharma Limited, India** Sy No. 10/G-1, Gadda Potharam (VillageJinnaram (Mandal), Medak (District) Telangana, 502319, INDIA. **Empagliflozin:** Jiangsu Yongan Pharmaceuticals Co., Limited. No.18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu, China. **Metformin Hydrochloride:** IOL Chemicals and Pharmaceuticals Limited 85 Industrial Area 'A' Ludhiana-141003 Punjab. India.		
API Lot No.		**Empagliflozin:** 20200705 **Linagliptin:** 20200701 **Metformin HCl:** P5102004020		
Description of Pack (Container closure system)		Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 03 months Accelerated: 03 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		MLEH-001	MLEH-002	--
Batch Size		5000 tab	5000 tab	--
Manufacturing Date		02-2021	02-2021	--
Date of Initiation		02-2021	02-2021	--
No. of Batches		02		
97.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore**		
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore		
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)		
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)		

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 30935 dated 11-11-2021
	Details of fee submitted	Rs.75,000/- dated 28-10-2021
	The proposed proprietary name / brand name	**Elmet XR 10/5/1000 mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated extended-release tablet contains: Empagliflozin …….. 10mg Linagliptin …… 5 mg (as immediate release coating) Metformin HCl …… 1000mg (as extended release core)
	Pharmaceutical form of applied drug	Film-coated extended-release tablet
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** sodium-glucose co-transporter 2 (SGLT2) inhibitors **Linagliptin:** dipeptidyl peptidase-4 (DPP-4) inhibitors **Metformin HCl:** antihyperglycemic drug
	Reference to Finished product specifications	Innovator
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Trijardy® XR Tablets by M/s Boehringer Ingelheim, FDA Approved.
	For generic drugs (me-too status)	Not Available
	Evidence of manufacturing facility	GMP certificate granted on basis of inspection conducted on 18.06.2020 endorses tablet general section.
	GMP status of the Finished product manufacturer	GMP certificate granted on basis of inspection conducted on 18.06.2020.
	Name and address of API manufacturer.	**Linagliptin:** **M/s Lee Pharma Limited, India** HuaiNan ShunLong Pharmaceutical CO, LTD. No. 9 Yongxing Road, Econonmic and Technological Development Development Zone, Huainan City, Anhui Province China. **Empagliflozin:** HuaiNan ShunLong Pharmaceutical CO, LTD. No. 9 Yongxing Road, Econonmic and Technological Development Development Zone, Huainan City, Anhui Province China. **Metformin Hydrochloride:** Shandong Keyuan Pharmaceutical Co., Ltd. Keyuan Street, Shandong shanghe Economic Zone, Jinan city, Shandong Province, China

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data on CTD format related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications and analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies of Drug substance	**Empagliflozin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Linagliptin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Metformin HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturing process and process control, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Trijardy XR Tablets 10/5/1000mg approved by US-FDA. CDP has been performed against the same brand that is Trijardy XR Tablets 12.5/2.5/1000mg approved by US-FDA inAcid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)
	Analytical method validation/verification of product	Method validation studies have submitted including, Specificity, linearity, range, accuracy, precision Repeatability, Intermediate precision, Robustness, System Suitability.
STABILITY STUDY DATA		
Manufacturer of API	**Linagliptin:** **M/s Lee Pharma Limited, India** Sy No. 10/G-1, Gadda Potharam (VillageJinnaram (Mandal), Medak (District) Telangana, 502319, INDIA. **Empagliflozin:** Jiangsu Yongan Pharmaceuticals Co., Limited.	

	No.18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu, China. **Metformin Hydrochloride:** IOL Chemicals and Pharmaceuticals Limited 85 Industrial Area 'A' Ludhiana-141003 Punjab. India.		
API Lot No.	**Empagliflozin:** 20200705 **Linagliptin:** 20200701 **Metformin HCl:** P5102004020		
Description of Pack (Container closure system)	Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 03 months Accelerated: 03 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MLEL-001	MLEL-002	--
Batch Size	5000 tab	5000 tab	--
Manufacturing Date	02-2021	02-2021	--
Date of Initiation	02-2021	02-2021	--
No. of Batches	02		

98.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 30935 dated 11-11-2021
	Details of fee submitted	Rs.75,000/- dated 28-10-2021
	The proposed proprietary name / brand name	**Elmet XR 12.5/2.5/1000 mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated extended-release tablet contains: Empagliflozin …….. 12.5mg Linagliptin …… 2.5 mg (as immediate release coating) Metformin HCl …… 1000mg (as extended release core)
	Pharmaceutical form of applied drug	Film-coated extended-release tablet

	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	Innovator
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Trijardy® XR Tablets 12.5mg/2.5mg/1000mg by M/s Boehringer Ingelheim, FDA Approved.
	For generic drugs (me-too status)	Not Available
	Evidence of manufacturing facility	GMP certificate granted on basis of inspection conducted on 18.06.2020 endorses tablet general section.
	GMP status of the Finished product manufacturer	GMP certificate granted on basis of inspection conducted on 18.06.2020.
	Name and address of API manufacturer.	**Linagliptin:** **M/s Lee Pharma Limited, India** HuaiNan ShunLong Pharmaceutical CO, LTD. No. 9 Yongxing Road, Econonmic and Technological Development Development Zone, Huainan City, Anhui Province China. **Empagliflozin:** HuaiNan ShunLong Pharmaceutical CO, LTD. No. 9 Yongxing Road, Econonmic and Technological Development Development Zone, Huainan City, Anhui Province China. **Metformin Hydrochloride:** Shandong Keyuan Pharmaceutical Co., Ltd. Keyuan Street, Shandong shanghe Economic Zone, Jinan city, Shandong Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data on CTD format related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications and analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies of Drug substance	**Empagliflozin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Linagliptin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Metformin HCl:**

		Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturing process and process control, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Trijardy XR Tablets 12.5/2.5/1000mg approved by US-FDA. CDP has been performed against the same brand that is Trijardy XR Tablets 12.5/2.5/1000mg approved by US-FDA in Acid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)
	Analytical method validation/verification of product	Method validation studies have submitted including, Specificity, linearity, range, accuracy, precision Repeatability, Intermediate precision, Robustness, System Suitability.

STABILITY STUDY DATA

Manufacturer of API	**Linagliptin:** **M/s Lee Pharma Limited, India** Sy No. 10/G-1, Gadda Potharam (VillageJinnaram (Mandal), Medak (District) Telangana, 502319, INDIA. **Empagliflozin:** Jiangsu Yongan Pharmaceuticals Co., Limited. No.18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu, China. **Metformin Hydrochloride:** IOL Chemicals and Pharmaceuticals Limited 85 Industrial Area 'A' Ludhiana-141003 Punjab. India.		
API Lot No.	**Empagliflozin:** 20200705 **Linagliptin:** 20200701 **Metformin HCl:** P5102004020		
Description of Pack (Container closure system)	Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 03 months Accelerated: 03 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MLEM-001	MLEM-002	--
Batch Size	5000 tab	5000 tab	--
Manufacturing Date	02-2021	02-2021	--
Date of Initiation	02-2021	02-2021	--
No. of Batches	02		

Documents submitted along with stability data

<table>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td>Firm has referred to onsite inspection report of their product:

EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) & Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) which was conducted on 1st June, 2021 and was presented in 307th meeting of Registration Board held on 08-10th June , 2021.
Registration Board decided to approve registration of

EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) &Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) by M/s. Horizon Healthcare (Pvt) Ltd. Lahore. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

Following two observations were reported in the report:
i. The HPLC software is 21 CFR compliant.
ii. Audit trail on the testing reports of EMPAZON 10mg and 25mg Tablets, Dayzol 30mg and 60mg Capsules is available.
iii. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>• Firm had provided valid GMP (No. AH20180451) & DML (No. 20160342) Certificate of M/s HuaiNan ShunLong Pharmaceutical CO, LTD.
Issued by China Food & Drug Administration
DML Valid upto: 31-12-2025
GMP Valid upto: 07-04-2023
• Firm had provided valid GMP(No. SD 20170595) & DML (No. LU202000453) Certificate of M/s Shandong Keyuan Pharmaceutical Co., Ltd.
Issued by China Food & Drug Administration
DML Valid upto: 30-07-2025
GMP Valid upto: 14-08-2022</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted.
Empagliflozin:
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>20200705</td><td>JF20201013</td><td>0.700kgs</td><td>07-12-2020</td></tr>
</table>
5 Linagliptin:
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
</table></td></tr>
</table>

		20200701 | JF20201014 | 0.2 00kgs | 07-12-2020 **Metformin HCl:** **Batch No.** | **Invoice No.** | **Quantity Imported** | **Date of approval by DRAP** P5102004020 | SDKY2020084403 | 100kgs | 27-08-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Audit trail reports have been submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Digital data logger record has been submitted for temperature & humidity conditions of both accelerated and long-term stability chambers.

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
3.2.S.4	Copies of the Drug substance specifications used for routine testing of the Drug substance by Drug Product manufacturer is required.	Firm has submitted drug substance specifications adopted by M/s Horizon.
3.2.P.5.3	Specificity studies shall be submitted for the Analysis method of Metformin in Dissolution test, wherein it could be established that the UV absorbance results for Metformin HCl are not interfered with the presence of other two Drug substances in the sample aliquot.	Firm has submitted UV spectra for the performance of Specificity parameter for dissolution test revealing that absorbance of Linagliptin and empagliflozin has not been interfered
3.2.P.6	• Submitted COA of working standard of Metformin HCl declares retest date as May 2021, whereas stability studies have also been performed subsequent to this date. • Submitted COA of working standard of Empagliflozin declares retest date as March 2021, whereas stability studies have also been performed subsequent to this date.	Firm has submitted COA of working standards of Metformin HCl & Empagliflozin with retest date as of May 2023 & March 2023 respectively.
• Submit details of excess Active coating solution used to achieve desired content of Empagliflozin & Linagliptin.		Firm has submitted that we use excess active coating solution due to process loss process loss details of which have been submitted.

Decision of 320th meeting: Registration Board approved Elmet XR 25/25/1000 mg Tablet, Elmet XR 10/5/1000 mg Tablet & Elmet XR 12.5/2.5/1000 mg Tablet with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Deferred cases

99.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Usawa Pharmaceuticals. 146 S.I.Z. Risalpur, KPK, Pakistan**
	Name, address of Manufacturing site.	M/s Bio Labs Pvt Ltd. Plot # 145, Industrial Triangle, Kahuta Road, Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 23-07-2012 which specifiesLyophilized vials (General) for M/s Bio-Labs Pharma
	Dy. No. and date of submission	Dy. No 7860 dated 10-03-2021
	Details of fee submitted	Rs.50,000/- dated 25-06-2021
	The proposed proprietary name / brand name	**UswaTig 50mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Tigecycline (Lyophilized powder)……50mg
	Pharmaceutical form of applied drug	Lyophilized Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibacterial agent
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Tigewel Injection of M/s Welwrd Pharma (Reg.# 082530)
	GMP status of the Finished product manufacturer	GMP certificate issued on 13-08-2020.

	Name and address of API manufacturer.	Fuan Pharmaceutical Group Chongqing Bosen Pharmaceutical Co. Ltd .No .1 human Yi Road, Changshou District, Chongqing 401254,P.R China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: $6^{o}C \pm 2\ ^{o}C$, RH for 36 months Accelerated: $25^{o}C \pm 2^{o}C/60\% \pm 5\%$RH for 6 months Batches: (Til00701V, Til00702V, Til00703V)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. BTig 50mg injection by Bosch pharmaceuticals.
	Analytical method validation/verification of product	Method verification studies have been submitted.
STABILITY STUDY DATA		

Manufacturer of API	Fuan Pharmaceutical Group Chongqing Bosen Pharmaceutical Co. Ltd. No .1 human Yi Road, Changshou District, Chongqing 401254, P.R China.		
API Lot No.	Ti191201		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9,12,18,24(Months)		
Batch No.	L-131	L-138	L-242
Batch Size	1000 Vials	1000 Vials	700 vials
Manufacturing Date	01-2018	01-2018	08-2019
Date of Initiation	20-03-18	12-03-18	01-10-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. CQ20180031) issued by Chongqing food and drug administration valid upto 09-10-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Licenses to Import Drug substance Tigecycline issued by AD I&E DRAP, Islamabad dated 05-08-2019 & 02-04-2020.
4	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Section#	Observations	Firm's response
3.2. S.4	mits for test of pH submitted in the drug ecifications is not as per the USP r "Tigecycline". of coloumn temperature, mobile phase ystem suitability solution mentioned in the	• Firm has submitted revised documents submitted without justifying the deviations observed in previously submitted data. • Temperature for autosampler not reflected in analytical method.

	ethod by Drug substance manufacturer is USP monograph for "Tigecycline".)A from M/s Bio-labs reflect that tests of ıdotoxin & sterility have not been he Drug substance specifications and ɔcedures used for routine testing of the ce /Active Drug Product manufacturer is Method Verification studies including accuracy and repeatability (method formed by the Drug Product manufacturer itted. s of analysis of relevant batch(es) of Drug rformed by Drug Product manufacturer roduct development and stability studies, ertificate of Analysis (CoA) of the same)rug Substance / /Active Pharmaceutical nufacture. availability of Auto sampler in HPLC, C temperature conditions could be	• Firm has submitted Bioburden test report from M/s Bio Lab for another batch than that submitted earlier. • Drug substance specifications and analytical procedure has been submitted from M/s Bio-Labs, but these documents are not formal and does not bear any document no., issue date or effective date. • Analytical method verification studies have been submitted from M/s Bio-Labs. • COA from API manufacturer has been submitted, which declares the product name as "Tigecycline lyophilized", whereas COA of M/s Bio-Lab declares it as "Tigecycline" only. • No Evidence of availability of Auto sampler in HPLC, wherein 10°C temperature conditions could be maintained.
3.2. S.5	imary / secondary reference standard rce and lot number shall be provided.	COA of working standard has been submitted from M/s Fuan Pharmaceutical, China.
3.2. S.7	• The USP monograph for "Tigecycline" recommends storage condition as at refrigerated temperature, whereas stability studies data has been submitted as per room temperature conditions. • Specifications for pH & specific optical rotation applied in stability studies is different from that submitted in section 3.2.S.4.4.	Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as reuired for a refrigerated item, while the analytical values for all the tests are same as presented earlier.
3.2.P.1	• Inclusion of lactose monohydrate in the composition shall be justified since innovator product approved by US FDA & EMA is formulated without use of any excipient.	MHRA approved reference given.
3.2.P.2.1	• Compatibility studies of the Drug Substance(s) with Lactose shall be provided since innovator product approved by US FDA & EMA is formulated without use of any excipient.	MHRA approved reference given.
3.2. P.5	; of fill weight/vial shall be submitted. ; does not include test of "Particulate availability of Auto sampler in HPLC, C temperature conditions could be	: given ; of fill weight/vial shall be submitted. availability of Auto sampler in HPLC, C temperature conditions could be ion is not proper, since it does not the base line.

	ameter has not been performed in the hod verification studies. vant batches for which stability studies data nitted, shall be provided.	re not formal and does not bear any , issue date or effective date.)As does no tinclude test of particulate ommended by the USP monograph of for injection"
3.2.P.6	orking standard COA reflect date of -12-2019, whereas stability batches have prior to this date.	COA of working standard submitted with date of analysis as 25-12-2017, wherein the reference standard (lot# F0M325) used for its standardization was valid upto 30-09-2017.
3.2. P.8	mitted copy of Licenses to Import Drug gecycline issued by AD I&E DRAP, ted 05-08-2019 & 02-04-2020, whereas ues have been manufactured prior to these shall be submitted whether submitted es data is of trial batches or commercial eets for stability studies, reflecting the ndard weight, Sample dilution preparation, eference standard and Calculation formula e Assay test shall be submitted. ted stability studies data, test of particulate ot been performed, justification shall be his regard. ng written in the stability summary sheets me points, does not relate with the relevant onths. • As per submitted BMRs potency adjustment has not been done for the Drug substance, based upon the actual Assay results. • As per submitted BMRs, lactose monohydrate has been used in the formulation, whereas innovator product has been formulated without use of any excipient. Justification shall be submitted in this regard. • Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches shall be submitted shall be submitted. • Submitted BMRs have not been filled completely.	d are still subsequent to the date of of two batches. i.e. L-131 & L-138 turing date of 03-2018, whereas oice is of 08-2019. oice is for "Tigecycline lyophilized". ubmitted that provided data is of atches. ets submitted. ity study sheets have been submitted. • BMR was written with standard batch formula and now it been revised with potency adjustment as per potency of drug substance. • Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas asper submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis. • Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage. • Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.

Decision of 316th meeting: Deferred for following:

- **S**ubmission of formal documents for drug substance specifications & analytical procedures form M/s Bio-Labs, wherein details of document no., issue date or effective date shall have been mentioned.
- Evidence of availability of Auto sampler in HPLC, wherein 10°C temperature conditions could be maintained.
- Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.

- Specifications of fill weight/vial shall be submitted.
- Peak integration is not proper, since it does not coincide with the base line.
- Submitted commercial invoices for the procurement of drug substance are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date of 03-2018, whereas submitted invoice is of 08-2019.
- Scientific justification shall be submitted for use of Lyophilized powder of drug substance for the manufacture of finished drug product by way of lyophilization.
- Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis.
- Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage.
- Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.
- Submitted COAs of drug product does not include test of particulate matter as recommended by the USP monograph of "Tigecycline for injection"

Firm's reply:

Observation	**Firm's Reply**
• **S**ubmission of formal documents for drug substance specifications & analytical procedures form M/s Bio-Labs, wherein details of document no., issue date or effective date shall have been mentioned.	Firm has submitted analytical procedure, wherein mobile phase composition is different from that proposed by the drug substance manufcaturer.
Evidence of availability of Auto sampler in HPLC, wherein 10^{o}C temperature conditions could be maintained.	Fimr has submitted specification sof of auto sampler assembled with HPLC of Perkin Almer 200LC, wherein operating conditions for "Ambient temperature" are mentioned as 10- 30^{o}C.
Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.	The stability data has been done as per recommended storage conditions. There was typographic error in the data.
Specifications of fill weight/vial shall be submitted.	The product is in lyophilized form. For this 2 ml solution per vial was filled and then lyophilized. *It is pertinent to mention that vials are filled with 2 ml solution at an intermediate stage, whereas final dosage form of the applied product is in the powder form hence fill weight specifications are necessary to establish uniformity of dosage.*
Peak integration is not proper, since it does not coincide with the base line.	Firm has submitted chromatograms again with justification that the attenuation is increased which results in the proper coinciding of baseline.
• Submitted commercial invoices for the procurement of drug substance are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date	No reply submitted.

of 03-2018, whereas submitted invoice is of 08-2019.	
• Scientific justification shall be submitted for use of Lyophilized powder of drug substance for the manufacture of finished drug product by way of lyophilization.	The bulk and raw material of tigecycline is also available in lyophilized/sterilized form. The raw material was then formulated into solution form which is then filled and lyophilized.
• Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis.	Firm has declared it as a typographic error, and has submitted revised COA of drug substance wherein Assay value has been declared as 99% on anhydrous basis, which still does not justify the dispensed amount on basis of "as is potency", since water content has been declared as 1.3%.
Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage	The solution is filled in the vials. The volume variation/checklist is attached.
• Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.	The solution is filled in glass beaker (5Ltr) whose minimum handling capacity is 500ml.
Submitted COAs of drug product does not include test of particulate matter as recommended by the USP monograph of "Tigecycline for injection".	Firm has submitted revised COAs of drug product for complete stability studies, wherein test of "Particular matter" has now been included.

Decision of 320th meeting: Deferred for following:

- **Submission of commercial invoices attested by AD DRAP I&E, for the procurement of drug substance used to manufacture drug product batches. i.e. L-131 & L-138.**
- **Specifications for the fill weight/vial shall be submitted.**
- **Evidence of performance of sterility testing at the time of batch release shall be submitted.**
- **Scientific justification shall be submitted for using glass beaker (5Ltr) for the compounding the commercial scale batches.**
- **Verification of the claim of the firm regarding submitted HPLC chromatograms that "attenuation is increased which results in the proper coinciding of baseline."**

100.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Gray's Pharmaceuticals. Plot No. 2, street No.N-3, National Industrial Zone, Rawat Islmabad.**
	Name, address of Manufacturing site.	M/s Bio Labs Pvt Ltd. Plot # 145, Industrial Triangle, Kahuta Road, Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 23-07-2012 which specifiesLyophilized vials (General) for M/s Bio-Labs Pharma

	Dy. No. and date of submission	Dy. No 7458 dated 08-03-2021
	Details of fee submitted	Rs.50,000/- dated 25-02-2021
	The proposed proprietary name / brand name	**Bacticil 50mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Tigecycline (Lyophilized powder) …… 50mg
	Pharmaceutical form of applied drug	Lyophilized Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibacterial agent
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Tigewel Injection of M/s Welwrd Pharma (Reg.# 082530)
	GMP status of the Finished product manufacturer	GMP certificate issued on 13-08-2020.
	Name and address of API manufacturer.	Fuan Pharmaceutical Group Chongqing Bosen Pharmaceutical Co. Ltd .No .1 human Yi Road, Changshou District, Chongqing 401254,P.R China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 6ºC ± 2 ºC,RH for 36 months Accelerated: 25ºC ± 2ºC/60% ± 5%RH for 6 months Batches: (Til00701V, Til00702V, Til00703V)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. BTig 50mg injection by Bosch pharmaceuticals.
	Analytical method validation/verification of product	Method verification studies have been submitted.

STABILITY STUDY DATA

Manufacturer of API	Fuan Pharmaceutical Group Chongqing Bosen Pharmaceutical Co. Ltd. No .1 human Yi Road, Changshou District, Chongqing 401254, P.R China.		
API Lot No.	Ti191201		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9,12,18,24(Months)		
Batch No.	L-131	L-138	L-242
Batch Size	1000 Vials	1000 Vials	700 vials
Manufacturing Date	01-2018	01-2018	08-2019
Date of Initiation	20-03-18	12-03-18	01-10-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. CQ20180031) issued by Chongqing food and drug administration valid upto 09-10-2023.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Licenses to Import Drug substance Tigecycline issued by AD I&E DRAP, Islamabad dated 05-08-2019 & 02-04-2020.
4	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Section#	Observations	Firm's response
3.2. S.4	mits for test of pH submitted in the drug ecifications is not as per the USP r "Tigecycline". of coloumn temperature, mobile phase ystem suitability solution mentioned in the ethod by Drug substance manufacturer is USP monograph for "Tigecycline".)A from M/s Bio-labs reflect that tests of dotoxin & sterility have not been he Drug substance specifications and ocedures used for routine testing of the ce /Active Drug Product manufacturer is Method Verification studies including accuracy and repeatability (method formed by the Drug Product manufacturer itted. s of analysis of relevant batch(es) of Drug rformed by Drug Product manufacturer roduct development and stability studies, ertificate of Analysis (CoA) of the same Drug Substance / /Active Pharmaceutical nufacture. availability of Auto sampler in HPLC, C temperature conditions could be	• Firm has submitted revised documents submitted without justifying the deviations observed in previously submitted data. • Temperature for autosampler not reflected in analytical method. • Firm has submitted Bioburden test report from M/s Bio Lab for another batch than that submitted earlier. • Drug substance specifications and analytical procedure has been submitted from M/s Bio-Labs, but these documents are not formal and does not bear any document no., issue date or effective date. • Analytical method verification studies have been submitted from M/s Bio-Labs. • COA from API manufacturer has been submitted, which declares the product name as "Tigecycline lyophilized", whereas COA of M/s Bio-Lab declares it as "Tigecycline" only. • No Evidence of availability of Auto sampler in HPLC, wherein 10°C temperature conditions could be maintained.
3.2.S.5	imary / secondary reference standard rce and lot number shall be provided.	COA of working standard has been submitted from M/s Fuan Pharmaceutical, China.
3.2. S.7	• The USP monograph for "Tigecycline" recommends storage condition as at refrigerated	Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been

	temperature, whereas stability studies data has been submitted as per room temperature conditions. • Specifications for pH & specific optical rotation applied in stability studies is different from that submitted in section 3.2.S.4.4.	changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.
3.2.P.1	• Inclusion of lactose monohydrate in the composition shall be justified since innovator product approved by US FDA & EMA is formulated without use of any excipient.	MHRA approved reference given.
3.2.P.2.1	• Compatibility studies of the Drug Substance(s) with Lactose shall be provided since innovator product approved by US FDA & EMA is formulated without use of any excipient.	MHRA approved reference given.
3.2. P.5	• Specifications of fill weight/vial shall be submitted. • Specifications does not include test of "Particulate matter". • Evidence of availability of Auto sampler in HPLC, wherein $10^{o}C$ temperature conditions could be maintained. • Precision parameter has not been performed in the analytical method verification studies. • COAs of relevant batches for which stability studies data has been submitted, shall be provided.	• Following not given • Specifications of fill weight/vial shall be submitted. • Evidence of availability of Auto sampler in HPLC, wherein $10^{o}C$ temperature conditions could be maintained. • Peak integration is not proper, since it does not coincide with the base line. • Documents are not formal and does not bear any document no., issue date or effective date. • Submitted COAs does not include test of particulate matter as recommended by the USP monograph of "Tiogecycline for injection"
3.2.P.6	• Submitted working standard COA reflect date of analysis as 14-12-2019, whereas stability batches have been analysed prior to this date.	COA of working standard submitted with date of analysis as 25-12-2017, wherein the reference standard (lot# F0M325) used for its standardization was valid upto 30-09-2017.
3.2. P.8	• Firm has submitted copy of Licenses to Import Drug substance Tigecycline issued by AD I&E DRAP, Islamabad dated 05-08-2019 & 02-04-2020, whereas stability batches have been manufactured prior to these dates. • Clarification shall be submitted whether submitted stability studies data is of trial batches or commercial batches. • Raw data sheets for stability studies, reflecting the details of Standard weight, Sample dilution preparation, Potency of Reference standard and	• Invoices shared are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date of 03-2018, whereas submitted invoice is of 08-2019. • Submitted invoice is for "Tigecycline lyophilized". • Firm has submitted that provided data is of commercial batches. • Raw data sheets submitted. • Revised stability study sheets have been submitted.

	Calculation formula applied for the Assay test shall be submitted. • As per submitted stability studies data, test of particulate matter has not been performed, justification shall be submitted in this regard. • Dates of testing written in the stability summary sheets for different time points, does not relate with the relevant duration in months. • As per submitted BMRs potency adjustment has not been done for the Drug substance, based upon the actual Assay results. • As per submitted BMRs, lactose monohydrate has been used in the formulation, whereas innovator product has been formulated without use of any excipient. Justification shall be submitted in this regard. • Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches shall be submitted shall be submitted. • Submitted BMRs have not been filled completely.	• BMR was written with standard batch formula and now it has been revised with potency adjustment as per potency of drug substance. • Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis. • Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage. • Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.

Decision of 316th meeting: Deferred for following:

- **S**ubmission of formal documents for drug substance specifications & analytical procedures form M/s Bio-Labs, wherein details of document no., issue date or effective date shall have been mentioned.
- Evidence of availability of Auto sampler in HPLC, wherein 10°C temperature conditions could be maintained.
- Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.
- Specifications of fill weight/vial shall be submitted.
- Peak integration is not proper, since it does not coincide with the base line.
- Submitted commercial invoices for the procurement of drug substance are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date of 03-2018, whereas submitted invoice is of 08-2019.
- Scientific justification shall be submitted for use of Lyophilized powder of drug substance for the manufacture of finished drug product by way of lyophilization.
- Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis.
- Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage.
- Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.
- Submitted COAs of drug product does not include test of particulate matter as recommended by the USP monograph of "Tigecycline for injection"

Firm's reply:

Observation	Firm's Reply
• **S**ubmission of formal documents for drug substance specifications & analytical procedures form M/s Bio-Labs, wherein details of document no., issue date or effective date shall have been mentioned.	Firm has submitted analytical procedure; wherein mobile phase composition is different from that proposed by the drug substance manufacturer.
Evidence of availability of Auto sampler in HPLC, wherein 10^{o}C temperature conditions could be maintained.	Fimr has submitted specification sof of auto sampler assembled with HPLC of Perkin Almer 200LC, wherein operating conditions for "Ambient temperature" are mentioned as 10- 30^{o}C.
Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.	The stability data has been done as per recommended storage conditions. There was typographic error in the data.
Specifications of fill weight/vial shall be submitted.	The product is in lyophilized form. For this 2 ml solution per vial was filled and then lyophilized. *It is pertinent to mention that vials are filled with 2 ml solution at an intermediate stage, whereas final dosage form of the applied product is in the powder form hence fill weight specifications are necessary to establish uniformity of dosage.*
Peak integration is not proper, since it does not coincide with the base line.	Firm has submitted chromatograms again with justification that the attenuation is increased which results in the proper coinciding of baseline.
• Submitted commercial invoices for the procurement of drug substance are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date of 03-2018, whereas submitted invoice is of 08-2019.	No reply submitted.
• Scientific justification shall be submitted for use of Lyophilized powder of drug substance for the manufacture of finished drug product by way of lyophilization.	The bulk and raw material of tigecycline is also available in lyophilized/sterilized form. The raw material was then formulated into solution from which is then filled and lyophilized.
• Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis.	Firm has declared it as a typographic error, and has submitted revised COA of drug substance wherein Assay value has been declared as 99% on anhydrous basis, which still does not justify the dispensed amount on basis of "as is potency", since water content has been declared as 1.3%.

Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage	The solution is filled in the vials. The volume variation/checklist is attached.
• Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.	The solution is filled in glass beaker (5Ltr) whose minimum handling capacity is 500ml.
Submitted COAs of drug product does not include test of particulate matter as recommended by the USP monograph of "Tigecycline for injection".	Firm has submitted revised COAs of drug product for complete stability studies, wherein test of "Particular matter" has now been included.

Decision of 320th meeting: Deferred for following:

- **Submission of commercial invoices attested by AD DRAP I&E, for the procurement of drug substance used to manufacture drug product batches. i.e. L-131 & L-138.**
- **Specifications for the fill weight/vial shall be submitted.**
- **Evidence of performance of sterility testing at the time of batch release shall be submitted.**
- **Scientific justification shall be submitted for using glass beaker (5Ltr) for the compounding the commercial scale batches.**
- **Verification of the claim of the firm regarding submitted HPLC chromatograms that "attenuation is increased which results in the proper coinciding of baseline."**

101.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novartana Pharmaceuticals (Pvt). Ltd 87-B Plot of Sundar Industrial Area, Raiwind Road, Lahore Pakistan.**
	Name, address of Manufacturing site.	M/s Bio Labs Pvt Ltd. Plot # 145, Industrial Triangle, Kahuta Road, Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 23-07-2012 which specifiesLyophilized vials (General) for M/s Bio-Labs Pharma
	Dy. No. and date of submission	Dy. No 8006 dated 11-03-2021
	Details of fee submitted	Rs.50,000/- dated 08-03-2021
	The proposed proprietary name / brand name	**Novartig 50mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Tigecycline (Lyophilized powder)……50mg
	Pharmaceutical form of applied drug	Lyophilized Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibacterial agent

	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Tigewel Injection of M/s Welwrd Pharma (Reg.# 082530)
	GMP status of the Finished product manufacturer	GMP certificate issued on 13-08-2020.
	Name and address of API manufacturer.	Fuan Pharmaceutical Group Chongqing Bosen Pharmaceutical Co. Ltd .No .1 human Yi Road, Changshou District, Chongqing 401254,P.R China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 6^{o}C ± 2 ^{o}C,RH for 36 months Accelerated: 25^{o}C ± 2^{o}C/60% ± 5%RH for 6 months Batches: (Til00701V, Til00702V, Til00703V)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. BTig 50mg injection by Bosch pharmaceuticals.
	Analytical method validation/verification of product	Method verification studies have been submitted.

STABILITY STUDY DATA

Manufacturer of API	Fuan Pharmaceutical Group Chongqing Bosen Pharmaceutical Co. Ltd. No .1 human Yi Road, Changshou District, Chongqing 401254, P.R China.		
API Lot No.	Ti191201		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9,12,18,24(Months)		
Batch No.	L-131	L-138	L-242
Batch Size	1000 Vials	1000 Vials	700 vials
Manufacturing Date	01-2018	01-2018	08-2019
Date of Initiation	20-03-18	12-03-18	01-10-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. CQ20180031) issued by Chongqing food and drug administration valid upto 09-10-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Licenses to Import Drug substance Tigecycline issued by AD I&E DRAP, Islamabad dated 05-08-2019 & 02-04-2020.
4	Data of stability batches will be supported by attested respective documents like chromatograms, Raw	Submitted

	data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Section#	Observations	Firm's response
3.2. S.4	• Acceptance limits for test of pH submitted in the drug substance specifications is not as per the USP monograph for "Tigecycline". • The details of coloumn temperature, mobile phase preparation, system suitability solution mentioned in the Assay test method by Drug substance manufacturer is not as per the USP monograph for "Tigecycline". • Submitted COA from M/s Bio-labs reflect that tests of Bacterial Endotoxin & sterility have not been performed. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted. • Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. • Evidence of availability of Auto sampler in HPLC, wherein 10^{o}C temperature conditions could be maintained.	• Firm has submitted revised documents submitted without justifying the deviations observed in previously submitted data. • Temperature for autosampler not reflected in analytical method. • Firm has submitted Bioburden test report from M/s Bio Lab for another batch than that submitted earlier. • Drug substance specifications and analytical procedure has been submitted from M/s Bio-Labs, but these documents are not formal and does not bear any document no., issue date or effective date. • Analytical method verification studies have been submitted from M/s Bio-Labs. • COA from API manufacturer has been submitted, which declares the product name as "Tigecycline lyophilized", whereas COA of M/s Bio-Lab declares it as "Tigecycline" only. • No Evidence of availability of Auto sampler in HPLC, wherein 10^{o}C temperature conditions could be maintained.
3.2.S.5	• COA of primary / secondary reference standard including source and lot number shall be provided.	COA of working standard has been submitted from M/s Fuan Pharmaceutical, China.

3.2. S.7	• The USP monograph for "Tigecycline" recommends storage condition as at refrigerated temperature, whereas stability studies data has been submitted as per room temperature conditions. • Specifications for pH & specific optical rotation applied in stability studies is different from that submitted in section 3.2.S.4.4.	Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as reuired for a refrigerated item, while the analytical values for all the tests are same as presented earlier.
3.2.P.1	• Inclusion of lactose monohydrate in the composition shall be justified since innovator product approved by US FDA & EMA is formulated without use of any excipient.	MHRA approved reference given.
3.2.P.2.1	• Compatibility studies of the Drug Substance(s) with Lactose shall be provided since innovator product approved by US FDA & EMA is formulated without use of any excipient.	MHRA approved reference given.
3.2. P.5	• Specifications of fill weight/vial shall be submitted. • Specifications does not include test of "Particulate matter". • Evidence of availability of Auto sampler in HPLC, wherein 10°C temperature conditions could be maintained. • Precision parameter has not been performed in the analytical method verification studies. • COAs of relevant batches for which stability studies data has been submitted, shall be provided.	: given ; of fill weight/vial shall be submitted. availability of Auto sampler in HPLC, C temperature conditions could be ion is not proper, since it does not the base line. re not formal and does not bear any , issue date or effective date. Submitted COAs does no tinclude test of particulate matter as recommended by the USP monograph of "Tiogecycline for injection"
3.2.P.6	• Submitted working standard COA reflect date of analysis as 14-12-2019, whereas stability batches have been analysed prior to this date.	COA of working standard submitted with date of analysis as 25-12-2017, wherein the reference standard (lot# F0M325) used for its standardization was valid upto 30-09-2017.
3.2. P.8	• Firm has submitted copy of Licenses to Import Drug substance Tigecycline issued by AD I&E DRAP, Islamabad dated 05-08-2019 & 02-04-2020, whereas stability batches have been manufactured prior to these dates. • Clarification shall be submitted whether submitted stability studies data is of trial batches or commercial batches. • Raw data sheets for stability studies, reflecting the details of Standard weight, Sample dilution preparation, Potency of Reference standard and Calculation formula applied for the Assay test shall be submitted.	ɛd are still subsequent to the date of ʒ of two batches. i.e. L-131 & L-138 turing date of 03-2018, whereas oice is of 08-2019. oice is for "Tigecycline lyophilized". ubmitted that provided data is of atches. ɛts submitted. ity study sheets have been submitted.

	• As per submitted stability studies data, test of particulate matter has not been performed, justification shall be submitted in this regard. • Dates of testing written in the stability summary sheets for different time points, does not relate with the relevant duration in months. • As per submitted BMRs potency adjustment has not been done for the Drug substance, based upon the actual Assay results. • As per submitted BMRs, lactose monohydrate has been used in the formulation, whereas innovator product has been formulated without use of any excipient. Justification shall be submitted in this regard. • Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches shall be submitted shall be submitted. • Submitted BMRs have not been filled completely.	• BMR was written with standard batch formula and now it sbeen revised with potency adjustment as per potency of drug substance. • Revised BMR mentions the dispensed quantity of APi on the basis of 99% potency, whereas asper submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis. • Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage. Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.

Decision of 316th meeting: Deferred for following:

- **S**ubmission of formal documents for drug substance specifications & analytical procedures form M/s Bio-Labs, wherein details of document no., issue date or effective date shall have been mentioned.
- Evidence of availability of Auto sampler in HPLC, wherein 10°C temperature conditions could be maintained.
- Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.
- Specifications of fill weight/vial shall be submitted.
- Peak integration is not proper, since it does not coincide with the base line.
- Submitted commercial invoices for the procurement of drug substance are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date of 03-2018, whereas submitted invoice is of 08-2019.
- Scientific justification shall be submitted for use of Lyophilized powder of drug substance for the manufacture of finished drug product by way of lyophilization.
- Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis.
- Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage.
- Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.
- Submitted COAs of drug product does not include test of particulate matter as recommended by the USP monograph of "Tigecycline for injection"

Firm's reply:

Observation	Firm's Reply
• **S**ubmission of formal documents for drug substance specifications & analytical procedures form M/s Bio-Labs, wherein details of document no., issue date or effective date shall have been mentioned.	Firm has submitted analytical procedure; wherein mobile phase composition is different from that proposed by the drug substance manufacturer.
Evidence of availability of Auto sampler in HPLC, wherein 10^{o}C temperature conditions could be maintained.	Firm has submitted specifications of auto sampler assembled with HPLC of Perkin Almer 200LC, wherein operating conditions for "Ambient temperature" are mentioned as 10- 30^{o}C.
Firm has submitted stability studies data of drug substance for the same batches as submitted earlier, wherein only conditions of storage have been changed as required for a refrigerated item, while the analytical values for all the tests are same as presented earlier.	The stability data has been done as per recommended storage conditions. There was typographic error in the data.
Specifications of fill weight/vial shall be submitted.	The product is in lyophilized form. For this 2 ml solution per vial was filled and then lyophilized. *It is pertinent to mention that vials are filled with 2 ml solution at an intermediate stage, whereas final dosage form of the applied product is in the powder form hence fill weight specifications are necessary to establish uniformity of dosage.*
Peak integration is not proper, since it does not coincide with the base line.	Firm has submitted chromatograms again with justification that the attenuation is increased which results in the proper coinciding of baseline.
• Submitted commercial invoices for the procurement of drug substance are still subsequent to the date of manufacturing of two batches. i.e. L-131 & L-138 with manufacturing date of 03-2018, whereas submitted invoice is of 08-2019.	No reply submitted.
• Scientific justification shall be submitted for use of Lyophilized powder of drug substance for the manufacture of finished drug product by way of lyophilization.	The bulk and raw material of tigecycline is also available in lyophilized/sterilized form. The raw material was then formulated into solution from which is then filled and lyophilized.
• Revised BMR mentions the dispensed quantity of API on the basis of 99% potency, whereas as per submitted COA of drug substance from M/s Bio-Labs, the potency of API is 98.4% on as is basis.	Firm has declared it as a typographic error, and has submitted revised COA of drug substance wherein Assay value has been declared as 99% on anhydrous basis, which still does not justify the dispensed amount on basis of "as is potency", since water content has been declared as 1.3%.

Submitted BMRs does not reflect any test of filled weight per vial, sterility testing at any stage	The solution is filled in the vials. The volume variation/checklist is attached.
• Details of the minimum handling capacity of the compounding vessel used for manufacturing of stability batches have not been submitted.	The solution is filled in glass beaker (5Ltr) whose minimum handling capacity is 500ml.
Submitted COAs of drug product does not include test of particulate matter as recommended by the USP monograph of "Tigecycline for injection".	Firm has submitted revised COAs of drug product for complete stability studies, wherein test of "Particular matter" has now been included.

Decision of 320th meeting: Deferred for following:

- Submission of commercial invoices attested by AD DRAP I&E, for the procurement of drug substance used to manufacture drug product batches. i.e. L-131 & L-138.
- Specifications for the fill weight/vial shall be submitted.
- Evidence of performance of sterility testing at the time of batch release shall be submitted.
- Scientific justification shall be submitted for using glass beaker (5Ltr) for the compounding the commercial scale batches as lyophilization is performed after filling the solution in vials.
- Verification of the claim of the firm regarding submitted HPLC chromatograms that "attenuation is increased which results in the proper coinciding of baseline."

Case no. 02 Registration applications of newly granted DML or New section (Human)

New DML

102.	Name, address of Applicant / Marketing Authorization Holder	M/s Carer Pharmaceuticals plot No. 27 main RCCI road Rawat Industrial estate Islamabad Pakistan.
	Name, address of Manufacturing site.	M/s Carer Pharmaceuticals plot No. 27 main RCCI road Rawat Industrial estate Islamabad Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 4969 dated 22-02-2022
	Details of fee submitted	Rs.30,000/- dated 19-01-2022
	The proposed proprietary name / brand name	**Clarithromycin 250mg/5ml Dry Powder suspension.**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Clarithromycin ……. 250mg
	Pharmaceutical form of applied drug	White to off white Powder filled in 60ml Amber Glass Bottle.
	Pharmacotherapeutic Group of (API)	Macrolide (Antibiotics)
	Reference to Finished product specifications	USP
	Proposed Pack size	60ml Dry Powder suspension.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved.
	For generic drugs (me-too status)	Klaricid 250mg suspension by M/s ABBOTT Laboratories, Reg. No. 076148
	GMP status of the Finished product manufacturer	New license granted on 07/06/2021 Tablet, Capsule, Dry powder and ampoules (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/S Vision Pharmaceuticals Plot No: 22-23, Kahuta Industrial Triangle, Kahuta Rd, Islamabad,
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions:

		Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CTM0510, CTM0511, CTM0513)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Klaricid Dry Powder by ABBOTT Laboratories.
	Analytical method validation/verification of product	Method verification studies have been submitted.

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals Plot No: 22-23, Kahuta Industrial Triangle, Kahuta Rd, Islamabad, 44000		
API Lot No.	CTM0681		
Description of Pack (Container closure system)	60ml Bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	500 Bottles	500 Bottles	500 Bottles
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	15-06-2021	15-06-2021	15-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. F. 3-26/2019 issued by DRAP valid till 10/02/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local Purchase from M/S Vision Pharmaceuticals Plot No: 22-23, Kahuta Industrial Triangle, Kahuta Rd, Islamabad.

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
103.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Carer Pharmaceuticals plot No. 27 main RCCI road Rawat Industrial estate Islamabad Pakistan.**
	Name, address of Manufacturing site.	M/s Carer Pharmaceuticals plot No. 27 main RCCI road Rawat Industrial estate Islamabad Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8310 dated 30-03-2022
	Details of fee submitted	Rs.30,000/- dated 31-01-2022
	The proposed proprietary name / brand name	**Clarithromycin 125mg Dry Powder**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Clarithromycin ……. 125mg
	Pharmaceutical form of applied drug	White to off white Powder filled in 60ml Amber Glass Bottle.
	Pharmacotherapeutic Group of (API)	Macrolide (Antibiotics)
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved.
	For generic drugs (me-too status)	Klaricid 125 mg suspension by M/s ABBOTT Laboratories, Reg. No. 015104
	GMP status of the Finished product manufacturer	New license granted on 07/06/2021 Tablet, Capsule, Dry powder and ampoules (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals Plot No: 22-23, Kahuta Industrial Triangle, Kahuta Rd, Islamabad,

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CTM0510, CTM0511, CTM0513)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Klaricid 125mg Dry Powder by ABBOTT Laboratories.
	Analytical method validation/verification of product	Method verification studies have been submitted.

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals Plot No: 22-23, Kahuta Industrial Triangle, Kahuta Rd, Islamabad, 44000
API Lot No.	CTM0681
Description of Pack (Container closure system)	60ml Bottle
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	500 Bottles	500 Bottles	500 Bottles
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	15-06-2021	15-06-2021	15-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. F. 3-26/2019 issued by DRAP valid till 10/02/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local Purchase from M/S Vision Pharmaceuticals Plot No: 22-23, Kahuta Industrial Triangle, Kahuta Rd, Islamabad.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section#	Observations	Firm's response
3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.	Submitted.
3.2.S.4.4	• Submitted COA of Clarithromycin pellets form M/s Carer Pharma does not mention the batch# of drug substance. • Manufacturing date mentioned on the COAs of drug substance from M/s Vision pharma & M/s Carer pharma are different. • Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance.	Firm has submitted revised COA of batch# CTM 0681, wherein date of manufacturing has been corrected as per COA from M/s Vision Pharmaceuticals.

3.2.P.3.2	Justify the proposed quantity of Clarithromycin per 5 ml in the submitted batch formula.	Firm has justified the proposed quantity on basis of %age content fof the Clarithromycin taste masked pellets used in the formulation.
3.2.P.5.2	Detailed analytical procedures used for testing the drug product shall be provided instead of submitting the USP monograph print.	Firm has submitted drug product testing method adopted by M/s Carer Pharma based upon the USP monograph.
3.2.P.5.3	Performance of precision parameter shall be submitted in the analytical method verification studies.	Submitted.
3.2.P.8	• Copy of commercial invoice for procurement of pellets from M/s Vision shall be submitted.	Firm has submitted copy of commercial invoice# 801551 from M/s Vision pharma for procurement of 25 Kg Clarithromycin taste masked pellets.

Decision: Registration Baord approved Clarithromycin 125mg Dry Powder & Clarithromycin 250mg/5ml Dry Powder suspension.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

a. **New Sections**

104.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 11279 dated 13-04-2021

	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**Cetron 1gm IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone as Sodium ……. 1gm
	Pharmaceutical form of applied drug	Parenteral (Injectable)
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Triject IV 1gm Injection of M/s Nabiqasim
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Rocephin Injection 1gm" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA

Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	00421/014/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20D04	20D05	20D06
Batch Size	1600 vials	1600 vials	1600 vials
Manufacturing Date	04-2020	04-2020	04-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr.#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued on basis of inspection conducted on 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	N/A

Batch No.	**Invoice No.**	**Quantity Imported**	**Date of approval by DRAP**
00421-03/014/2020	2540	10Kg 5.8 Kg	N/A

Remarks of Evaluator:

Section	**Observation**	**Firm's response**

3.2. S.4.1	• Drug substance specifications submitted by M/s Jupiter Pharma declare specification's reference as USP 43, whereas limits for Assay test & Related substances are not as per the USP monograph of "Ceftriaxone sodium". • Reference for specifications of Assay test must be clarified by Drug substance manufacturer, whether it is USP or BP, since both limits could not be applied.	• Firm has referred to the USP monograph of ceftriaxone sodium for Drug substance specifications and has submitted revised specifications & analutical procedure accordingly.	
3.2.S.4.3	• Chromatographic conditions applied for the analytical method validation is not as per those recommended by USP monograph for "Ceftriaxone sodium". • Details of the performance of specificity parameter have not been submitted	Firm has submitted revised analytical method verification report as per USP monograph.	
3.2.S.5	Firm has submitted COA of working standard from M/s Pharmagen for "Ceftriaxone sodium" which declares the "use before date" as 19-11-2016, whereas the stability batches have been manufactured and analysed in 2020.	Firm has submitted COA of working standard from M/s Pharmagen valid till January 2021.	
3.2.P.1	• Equivalency factor of the Ceftriaxone sodium shall be defined for Ceftriaxone. • Reconstitution diluent has been submitted as 5ml Water for Injection, which is not as recommended by the reference product.	• Firm has justified the proposed quantity per vial with reference to the equivalency factor for sodium salt. • Firm has submitted that it was a typographic error and in commercialpacks same diluent will be provided as recommended by reference product i.e., 10ml WFI.	
3.2.P.3.5	• Submitted process validation protocol does not identify Critical process parameters and critical Quality attributes. • Acceptable limits given in the sampling plan are different from that declared in section 3.2. P.5.1	• Firm has submitted revised process validation protocol.	
3.2. P.5.1	• A signed copy of Drug product specifications and analytical procedure, used for the batch release and stability studies of applied product, shall be submitted.	• Submitted.	
3.2.P.8	• Submit raw data sheets reflecting the details of Standard weight, Sample weight, Dilution	• Frim has submitted raw data sheets along with relevant chormatograms for stabiltiy	

	preparation, Potency of Reference standard and Calculation formula applied for the Assay test. • Chromatograms for the complete analysis of stability studies of each batch have not been submitted. • Submitted BMR does not declare the target fill weight/vial, calculated on the basis of the established potency of drug substance. • Submitted BMRs reflect the same batch no. against the entry for "Previous product" & "Clearance granted for", in the Line clearance sheet of filling step.	studies. • Frim has submitted revised BMRs decalring target fill weight & correction of Line clearance details.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

105.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12475 dated 27-04-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**Cetron 250mg IM Injection**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone as Sodium ……. 250mg
	Pharmaceutical form of applied drug	Parenteral (Injectable)
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Exit 250mg IV of M/s City Pharma
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Oxidil Injection 250mg" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA

Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	00421/014/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20D16	20D17	20D18
Batch Size	1287vials	1287 vials	1287 vials
Manufacturing Date	04-2020	04-2020	04-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr.#	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued on basis of inspection conducted on 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	N/A

Batch No.	**Invoice No.**	**Quantity Imported**	**Date of approval by DRAP**
00421-03/014/2020	2540	10Kg 5.8 Kg	N/A

Remarks of Evaluator:

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

106.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12476 dated 27-04-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**Cetron 250mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone as Sodium ……. 250mg
	Pharmaceutical form of applied drug	Parenteral (Injectable)
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Exit 250mg IV of M/s City Pharma
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.

	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Oxidil Injection 250mg" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA			
Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	00421/014/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20D13	20D14	20D15
Batch Size	1287vials	1287 vials	1287 vials
Manufacturing Date	04-2020	04-2020	04-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr.#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer	GMP certificate issued on basis of inspection conducted on 08-01-2019.

<table>
<tr><td></td><td>issued by concerned regulatory authority of country of origin.</td><td></td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
<table><tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>00421-03/014/2020</td><td>2540</td><td>10Kg
5.8 Kg</td><td>N/A</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Firm has submitted audit trail reports on product testing.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td>N/A</td></tr>
</table>

Remarks of Evaluator:

Section	Observation	Firm's response
3.2. S.4.1	• Drug substance specifications submitted by M/s Jupiter Pharma declare specification's reference as USP 43, whereas limits for Assay test & Related substances are not as per the USP monograph of "Ceftriaxone sodium". • Reference for specifications of Assay test must be clarified by Drug substance manufacturer, whether it is USP or BP, since both limits could not be applied.	• Firm has referred to the USP monograph of ceftriaxone sodium for Drug substance specifications and has submitted revised specifications & analutical procedure accordingly.
3.2.S.4.3	• Chromatographic conditions applied for the analytical method validation is not as per those recommended by USP monograph for "Ceftriaxone sodium". • Details of the performance of specificity parameter have not been submitted	• Firm has submitted revised analytical method verification report as per USP monograph.
3.2.S.4.4	• Submitted COA of drug substance from M/s Jupiter does not declare the results for the tests of "Sterility" & "Bacterial Endotoxin". • Limits for the test of "Description/Appearance" is different between the COA of M/s Pharmagen & M/s Jupiter. • Submit analytical record i.e., Chromatograms, FTIR spectrum and raw data sheets for the drug substance analysis performed by M/s Jupiter pharma	• Firm has submitted revised COA wherein limts for description have been corrected, test of BET & Sterility has been included along with result for Assay test has as per the USP specifications. • Submitted.
3.2.S.5	Relevant information has not been submitted.	Firm has submitted COA of working standard from M/s Pharmagen for "Ceftriaxone sodium" which declares the "use before date" as 19-11-2016, whereas the stability batches have been manufactured and analysed in 2020.
3.2. P.1	• Equivalency factor of the Ceftriaxone sodium shall be defined for Ceftriaxone.	• Firm has justified the proposed quantity per vial with reference to the equivalency factor for sodium salt.
3.2. P.3.5	• Submitted process validation protocol does not identify Critical process parameters and critical Quality attributes. • Acceptable limits given in the sampling plan are different from that declared in section 3.2. P.5.1	• Firm has submitted revised process validation protocol.
3.2. P.5.1	• A signed copy of Drug product specifications and analytical procedure,	• Firm has submitted copy of Drug product specifications &

	used for the batch release and stability studies of applied product, shall be submitted. • Submitted specification does not include test of "Constituted solution". • Submitted specifications mention only one Assay limit of 90- 115%, whereas USP monograph of "Ceftriaxone for injection" mandates two Assay limits.	analytical procedure as per USP monograph.
3.2. P.5.3	• The concentration of standard solution mentioned in the analytical procedure is not as per the USP monograph of "Ceftriaxone for injection". • Parameter of specificity test mentions the use of placebo. You are advised to clarify the composition of placebo.	• Firm has submitted revised analytical method verification report as per USP monograph.
3.2.P.8	• Submitted stability studies report reflect that Assay test has been performed for reconstituted injection only, whereas USP monograph of "Ceftriaxone for injection" also requires performance of another Assay test with acceptance limit of "Ceftriaxone for Injection contains an amount of Ceftriaxone Sodium equivalent to NLT 776 µg/mg of Ceftriaxone." Justification shall be submitted in this regard. • Submit raw data sheets reflecting the details of Standard weight, Sample weight, Dilution preparation, Potency of Reference standard and Calculation formula applied for the Assay test. • Chromatograms for the complete analysis of stability studies of each batch have not been submitted. • Reports of the microbiological testing for the tests of "Sterility" and "Bacterial Endotoxin" have not been submitted. • Submitted BMR does not declare the target fill weight/vial, calculated on the basis of the established potency of drug substance..	• We have just filled the raw material in glass vials. Before filling the raw material is completely teste. And during stability studies all the test paarmeters were found within acceptable limits. • Reports of the microbiological testing for the tests of "Sterility" and "Bacterial Endotoxin" have been submitted. • Firm has submitted raw data sheets along with relevant chormatograms for stabiltiy studies. • Firm has submitted revised BMRs decalring target fill weight.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

107.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**

	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 14699 dated 28-05-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021 & Rs.10,000/- dated 27-05-2021
	The proposed proprietary name / brand name	**Cetron 2gm IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone as Sodium ……. 2gm
	Pharmaceutical form of applied drug	Parenteral (Injectable)
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Triject IV 1gm Injection of M/s Nabiqasim
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Oxidil 2gm IV" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA			
Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	00421/014/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20D01	20D02	20D03
Batch Size	588 vials	588 vials	588 vials
Manufacturing Date	04-2020	04-2020	04-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr.#	**Documents To Be Provided**	**Status**

<table>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td>N/A</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>GMP certificate issued on basis of inspection conducted on 08-01-2019.</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP,
Karachi, has been submitted.

<table><tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>00421-03/014/2020</td><td>2540</td><td>10Kg
5.8 Kg</td><td>N/A</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>N/A</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
</table>

Remarks of Evaluator:

Section	Observation	Firm's response
3.2. S.4.1	• Drug substance specifications submitted by M/s Jupiter Pharma declare specification's reference as USP 43, whereas limits for Assay test & Related substances are not as per the USP monograph of "Ceftriaxone sodium". • Reference for specifications of Assay test must be clarified by Drug substance manufacturer, whether it is USP or BP, since both limits could not be applied.	• Firm has referred to the USP monograph of ceftriaxone sodium for Drug substance specifications and has submitted revised specifications & analutical procedure accordingly.
3.2.S.4.4	• Submitted COA of drug substance from M/s Jupiter does not declare the results for the tests of "Sterility" & "Bacterial Endotoxin".	• Firm has submitted revised COA wherein limts for description have been corrected, test of BET & Sterility has been included along with result for Assay test has as per the USP specifications.

	• Limits for the test of "Description/Appearance" is different between the COA of M/s Pharmagen & M/s Jupiter. • Submit analytical record i.e., Chromatograms, FTIR spectrum and raw data sheets for the drug substance analysis performed by M/s Jupiter pharma	• Submitted.	
3.2.S.5	Relevant information has not been submitted.	Firm has submitted COA of working standard from M/s Pharmagen valid till January 2021.	
3.2.P.1	• Reconstitution diluent has been submitted as 5ml Water for Injection, which is not as recommended by the reference product.	• Firm has submitted that it was a typographic error and in commercialpacks same diluent will be provided as recommended by reference product i.e., 10ml WFI.	
3.2.P.3.5	• Submitted process validation protocol does not identify Critical process parameters and critical Quality attributes. • Acceptable limits given in the sampling plan are different from that declared in section 3.2. P.5.1	• Firm has submitted revised process validation protocol.	
3.2. P.5.1	• A signed copy of Drug product specifications and analytical procedure, used for the batch release and stability studies of applied product, shall be submitted. • Submitted specification does not include test of "Constituted solution". • Submitted specifications mention only one Assay limit of 90- 115%, whereas USP monograph of "Ceftriaxone for injection" mandates two Assay limits.	• Firm has submitted drug product analytical method, as per the USP monograph of "Cefrtriaxone for injection".	
3.2. P.5.3	• The concentration of standard solution mentioned in the analytical procedure is not as per the USP monograph of "Ceftriaxone for	• Firm has submitted revised analytical method verification report as per USP monograph.	

	injection". • Parameter of specificity test mentions the use of placebo. You are advised to clarify the composition of placebo.	
3.2.P.8	• Submitted stability studies report reflect that Assay test has been performed for reconstituted injection only, whereas USP monograph of "Ceftriaxone for injection" also requires performance of another Assay test with acceptance limit of "Ceftriaxone for Injection contains an amount of Ceftriaxone Sodium equivalent to NLT 776 µg/mg of Ceftriaxone." Justification shall be submitted in this regard. • Submit raw data sheets reflecting the details of Standard weight, Sample weight, Dilution preparation, Potency of Reference standard and Calculation formula applied for the Assay test. • Chromatograms for the complete analysis of stability studies of each batch have not been submitted. • Reports of the microbiological testing for the tests of "Sterility" and "Bacterial Endotoxin" have not been submitted. • Submitted BMR does not declare the target fill weight/vial, calculated on the basis of the established potency of drug substance.	• We have just filled the raw material in glass vials. Before filling the raw material is completely teste. And during stability studies all the test paarmeters were found within acceptable limits. • Reports of the microbiological testing for the tests of "Sterility" and "Bacterial Endotoxin" have been submitted. • Frim has submitted raw data sheets along with relevant chormatograms for stabiltiy studies. • Frim has submitted revised BMRs decalring target fill weight.

- No fee has been submitted for the submitted variations.

Decision: Approved. Registration Board further decided that registration letter will be issued after submission of fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

108.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12478 dated 27-04-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**Cetron 500mg IM Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone as Sodium ……. 500mg
	Pharmaceutical form of applied drug	Parenteral (Injectable)
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	El-cef Injection 500mg IM of M/s Linear Pharmaceuticals.
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Rocephin Injection 500mg" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA	
Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore
API Lot No.	00421/014/2020
Description of Pack (Container closure system)	Type II glass vial
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

<table>
<tr><td colspan="2">Batch No.</td><td>20D10</td><td>20D11</td><td>20D12</td></tr>
<tr><td colspan="2">Batch Size</td><td>1000 vials</td><td>1000 vials</td><td>1000 vials</td></tr>
<tr><td colspan="2">Manufacturing Date</td><td>04-2020</td><td>04-2020</td><td>04-2020</td></tr>
<tr><td colspan="5">DOCUMENTS / DATA PROVIDED BY THE APPLICANT</td></tr>
<tr><td>Sr.#</td><td>Documents To Be Provided</td><td colspan="3">Status</td></tr>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td colspan="3">Not submitted</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td colspan="3">GMP certificate issued on basis of inspection conducted on 08-01-2019.</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td colspan="3">Copy of commercial invoice attested by AD I&E DRAP,
Karachi, has been submitted.
<table><tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>00421-03/014/2020</td><td>2540</td><td>10Kg
5.8 Kg</td><td>N/A</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td colspan="3">Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td colspan="3">Firm has submitted audit trail reports on product testing.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td colspan="3">N/A</td></tr>
<tr><td colspan="5">Remarks of Evaluator:</td></tr>
<tr><td colspan="5">Decision: Approved.
• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.
• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.</td></tr>
<tr><td>109.</td><td colspan="2">Name, address of Applicant / Marketing Authorization Holder</td><td colspan="2">M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi</td></tr>
<tr><td></td><td colspan="2">Name, address of Manufacturing site.</td><td colspan="2">M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi</td></tr>
<tr><td></td><td colspan="2">Status of the applicant</td><td colspan="2">☒ Manufacturer
☐ Importer
☐ Is involved in none of the above (contract giver)</td></tr>
<tr><td></td><td colspan="2">GMP status of the firm</td><td colspan="2">GMP certificate issued on basis of inspection conducted on 18-11-2020.</td></tr>
</table>

	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12477 dated 27-04-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**Cetron 500mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone as Sodium ……. 500mg
	Pharmaceutical form of applied drug	Parenteral (Injectable)
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Cefnig Injection 500mg (Ceftriaxone as sodium) of M/s Global Pharmaceuticals.
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Rocephin Injection 500mg" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA			
Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	00421/014/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20D07	20D08	20D09
Batch Size	1000 vials	1000 vials	1000 vials
Manufacturing Date	04-2020	04-2020	04-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr.#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued on basis of inspection conducted on 08-01-2019.

<table>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP,
Karachi, has been submitted.
<table><tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>00421-03/014/2020</td><td>2540</td><td>10Kg
5.8 Kg</td><td>N/A</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>N/A</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td>N/A</td></tr>
</table>

Remarks of Evaluator:

Section	Observation	Firm's response
3.2.S.4.1	• Drug substance specifications submitted by M/s Jupiter Pharma declare specification's reference as USP 43, whereas limits for Assay test & Related substances are not as per the USP monograph of "Ceftriaxone sodium". • Reference for specifications of Assay test must be clarified by Drug substance manufacturer, whether it is USP or BP, since both limits could not be applied.	• Firm has referred to the USP monograph of ceftriaxone sodium for Drug substance specifications and has submitted revised specifications & analutical procedure accordingly.
3.2.S.4.3	• Chromatographic conditions applied for the analytical method validation is not as per those recommended by USP monograph for "Ceftriaxone sodium". • Details of the performance of specificity parameter have not been submitted	Firm has submitted revised analytical method verification report as per USP monograph.
3.2.S.4.4	• Submitted COA of drug substance from M/s Jupiter does not declare the results for the tests of "Sterility" & "Bacterial Endotoxin". • Limits for the test of "Description/Appearance" is different between the COA of M/s Pharmagen & M/s Jupiter.	• Firm has submitted revised COA wherein limits for description have been corrected, test of BET & Sterility has been included along with result for Assay test has as per the USP specifications. • Submitted.

	• Submit analytical record i.e., Chromatograms, FTIR spectrum and raw data sheets for the drug substance analysis performed by M/s Jupiter pharma	
3.2.P.1	Equivalency factor of the Ceftriaxone sodium shall be defined for Ceftriaxone.	• Firm has justified the proposed quantity per vial with reference to the equivalency factor for sodium salt. • Firm has submitted that it was a typographic error and in commercialpacks same diluent will be provided as recommended by reference product i.e., 10ml WFI.
3.2.P.3.5	• Submitted process validation protocol does not identify Critical process parameters and critical Quality attributes. • Acceptable limits given in the sampling plan are different from that declared in section 3.2. P.5.1	Firm has submitted revised process validation protocol.
3.2. P.5.1	• A signed copy of Drug product specifications and analytical procedure, used for the batch release and stability studies of applied product, shall be submitted. • Submitted specification does not include test of "Constituted solution". • Submitted specifications mention only one Assay limit of 90- 115%, whereas USP monograph of "Ceftriaxone for injection" mandates two Assay limits.	Revised drug product specification sand analytical procedure has been submitted as per USP momnograph.
3.2. P.5.3	• The concentration of standard solution mentioned in the analytical procedure is not as per the USP monograph of "Ceftriaxone for injection". • Parameter of specificity test mentions the use of placebo. You are advised to clarify the composition of placebo.	Firm has submitted revised analytical method verification report as per USP monograph.
3.2. P.5.4	• Batch size mentioned on submitted COAs is different from that declared in BMRs.	Firm has declared it typographical error and has submitted revised COAs.
3.2.P.8	• Submitted stability studies report reflect that Assay test has been performed for reconstituted injection only, whereas USP monograph of "Ceftriaxone for injection" also requires performance of another Assay test with acceptance limit of	• We have just filled the raw material in glass vials. Before filling the raw material is completely teste. And during stability studies all the test paarmeters were found within acceptable limits. • Reports of the microbiological testing for the tests of "Sterility" and

		"Ceftriaxone for Injection contains an amount of Ceftriaxone Sodium equivalent to NLT 776 µg/mg of Ceftriaxone." Justification shall be submitted in this regard. • Chromatograms for the 6th month time point of stability studies of batch no. 20D07 has not been submitted. • Submit raw data sheets reflecting the details of Standard weight, Sample weight, Dilution preparation, Potency of Reference standard and Calculation formula applied for the Assay test. • Chromatograms for the complete analysis of stability studies of batch# 20D08 have not been submitted. • Chromatograms for the complete analysis of stability studies of batch# 20D09 have not been submitted. • Repots of the microbiological testing for the tests of "Sterility" and "Bacterial Endotoxin" have not been submitted. • Submitted BMR does not declare the target fill weight/vial, calculated on the basis of the established potency of drug substance.	"Bacterial Endotoxin" have been submitted. • Frim has submitted raw data sheets along with relevant chormatograms for stabiltiy studies. • Frim has submitted revised BMRs decalring target fill weight.
Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**			

110.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin)

		Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 9892 dated 30-03-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**M-Xime 100mg/5ml Dry Suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension contains: Cefixime as Trihydrate …… 100mg
	Pharmaceutical form of applied drug	Dry suspension oral
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's x 30ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Cefspan DS dry suspension of M/s Barret Hodgson Karachi (Reg.#024634)
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time

		stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Cefspan dry suspension of M/s Barret Hodgson Karachi" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA			
Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	004243/022/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20DST04	20DST05	20DST06
Batch Size	200 bottles	200 bottles	200 bottles
Manufacturing Date	02-2020	02-2020	02-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr.#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued on basis of inspection conducted on 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice for 10Kg of Cefixime (micronized) has been submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	N/A

6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)
111.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Jupiter Pharma. Plot No. 25, Street # S-6, National Industrial Zone, Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 27-06-2019, declaring grant following additional sections: "Capsule (Cephalosporin) Dry powder suspension (Cephalosporin) Dry Powder injection (Cephalosporin)"
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 9891 dated 30-03-2021
	Details of fee submitted	Rs.20,000/- dated 05-01-2021
	The proposed proprietary name / brand name	**M-Xime Plus 200mg/5ml Dry Suspension 30ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension contains: Cefixime as Trihydrate …… 200mg
	Pharmaceutical form of applied drug	Dry suspension oral
	Pharmacotherapeutic Group of (API)	Third-Generation Cephalosporin's
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's x 30ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Cefspan DS dry suspension of M/s Barret Hodgson Karachi (Reg.#024634)
	Name and address of API manufacturer.	M/s Pharmagen Ltd., Ferozpur Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities,

		specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence Studies against the reference product of "Cefspan DS dry suspension of M/s Barret Hodgson Karachi" has been submitted.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.

STABILITY STUDY DATA			
Manufacturer of APIs	M/s Pharmagen Ltd., Ferozpur Road, Lahore		
API Lot No.	004243/022/2020		
Description of Pack (Container closure system)	Type II glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20DST04	20DST05	20DST06
Batch Size	200 bottles	200 bottles	200 bottles
Manufacturing Date	02-2020	02-2020	02-2020

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr.#	**Documents To Be Provided**	**Status**

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued on basis of inspection conducted on 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice for 10Kg of Cefixime (micronized) has been submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	N/A
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator:

Section	Observation	Firm's response
3.2. S.4.3	• Details of the performance of specificity parameter have not been submitted	Performance of specificty parameter has been submitted.
3.2. S.4.4	• Limits for the test of "Description/Appearance" & Assay are different between the COA of M/s Pharmagen & M/s Jupiter. • Submit analytical record i.e., Chromatograms, FTIR spectrum and raw data sheets for the drug substance analysis performed by M/s Jupiter pharma	Firm has submitted revised COA along with analytical record.
3.2. S.5	Relevant information has not been submitted.	COA of USP reference standard of cefixime has been submitted.
3.2.P.2.5	• Quantities of preservatives used in formulation shall be justified for per unit dose with reference to the relevant guidelines/standards. • Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	• Firm has referred to literature from hand book of pharmaceutical excipients as rationale for the quantities of preservative used. • Microbial enumeration report has been submitted for preservative effectiveness studies.
3.2. P.5.1	• A signed copy of Drug product specifications and analytical procedure, used for the batch release and stability studies of applied product, shall be submitted. • Test for content of antimicrobial	Firm has submitted revised drug product analytical procedure including test of preservative effectiveness.

	preservative & efficacy of preservative, as recommended by ICH Q1 (R2) guidelines & USP chapter <51>, has not been included in the finished product specifications. You are advised to submit justification in this regard.	
3.2. P.5.6	• This section refers to JP specifications, whereas section 3.2.P.5.1 declares finished product specifications of USP standard.	Firm has declared it a typographic error and has referred to USP monograph as drug product specifications.
3.2. P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	COA of USP reference standard of cefixime has been submitted for Lot# G01139
3.2. P.8	• Chromatograms for the 6th month time point of stability studies have not been submitted. • Submitted Chromatograms are not readable, hence a clear readable copy of chromatograms shall be submitted. • Test for content of antimicrobial preservative & efficacy of preservative, as recommended by ICH Q1 (R2) guidelines, has not been performed during stability studies. You are advised to submit justification in this regard. • Summary of additional stability studies i.e., in-use studies re-constituted product, along with proposed in-use storage statement and in-use shelf-life shall be provided. • Justify the quantity of API dispensed for each trial batch, considering the declared potency and equivalency factor of API.	• Firm has submitted analytical record including raw data sheets and chromatograms for 6th moth time point also. • Firm has justified the dispensed quantity of cefixime against the theoretical factor for hydrate form. • Firm ha submitted 14 days- in-use stability study report for the reconstituted suspension.

Decision: Registration Baord approved M-Xime 100mg/5ml Dry Suspension & M-Xime Plus 200mg/5ml Dry Suspension.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

112.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Variant pharmaceuticals (Pvt) Ltd, Plot No. 5, M-2, Pharmazone, 26 Km, Lahore Sharikpur Road, Sheikhupura.**
	Name, address of Manufacturing site.	M/s Variant pharmaceuticals (Pvt) Ltd, Plot No. 5, M-2, Pharmazone, 26 Km, Lahore Sharikpur Road, Sheikhupura.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33998 : 29-12-2021
	Details of fee submitted	PKR 30,000/-: 06-12-2021,
	The proposed proprietary name / brand name	**DEXIRANT 30mg Capsules**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Dexlansoprazole (as dual delayed release pellets)……30mg
	Pharmaceutical form of applied drug	Capsules
	Pharmacotherapeutic Group of (API)	Proton pump inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	DEXILANT 30mg Capsule of M/s **TAKEDA PHARMS USA** (USFDA approved)
	For generic drugs (me-too status)	Razodex 30 mg Capsule of M/s GETZ Pharma (Reg # 086976)
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020 General Tablet, General Capsule, General Sachet and General dry powder injectable (pre-lyophilized)
	Name and address of API manufacturer.	M/s Vision pharmaceuticals (pvt) Ltd., Plot no. 22-23, Industrial Triangle, Kahuta Road, Islamabad
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing

		process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API. Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence of test formulation with comparator product DEXILANT 30mg Capsule (B # 511014) of M/s Takeda GmbH, Germany by performing all the quality tests including dissolution in 3 different media (pH 1.2, 5.5 and 7). The results of the tests of both products were found to be within the specifications and are comparable.
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method for the drug substance. Firm has submitted report of validation of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad.		
API Lot No.	**DLP755**		
Description of Pack (Container closure system)	30's blisters packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	VT-001	VT-002	VT-003
Batch Size	1000 caps	1000 caps	1000 caps
Manufacturing Date	05-2021	05-2021	05-2020

Date of Initiation	13-05-2021	14-05-2021	15-05-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any response.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Vision pharma pvt Ltd, Lahore issued by DRAP Lahore. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the purchase of esomeprazole sodium sterile powder (2kg, Batch # DLP755) from M/s vision pharma vide invoice # 703069 dated 19-04-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Observation	Response by the firm
Submission of analytical method verification studies for drug substance performed by drug product manufacturer is required.	Submitted from M/s Variant pharmaceuticals.
Analytical method for routine analysis of drug substance used by the drug product manufacturer is required to be submitted.	Submitted.
Please submit documents confirming the procurement of drug substance for manufacturing of the applied product.	Firm has submitted copy of commetcial invoice for procurement of 2 Kg of Dexlansoprazole DDR pellets 22.5% from /s Vision pharmaceuticals.
In method validation studies for drug product, the exact amount of contents of capsule have not been mention equivalent to 60mg or 30mg dexlansoprazole, please submit complete method for analytical method validation studies including the exact amount of contents of capsule (pellets)taken for preparation of dilutions.	Firm has submitted concentration in terms of mg/ml for performance of each parameter of method validation.
Justification of specification for Dexlasoprazole capsule 30/60mg has not been provided in submitted dossier. However, justification of specification for another dosage form is presented in the	Firm has submitted drug product specification for both 30mg & 60 mg capsule.

dossier, clarify or otherwise submit the required data.	
Please provide complete calculations for potency adjustment of 30/60mg capsule.	Firm has submitted details for weight of pellets per capsule calculated on basis of "As is potency" of Dexlansoprazole pellets.
Since similar batch numbers have been assigned to stability batches of 30mg and 60mg capsules, therefore, the internal SOP/ procedure for assigning the batch numbers is required with the clarification of the same.	Firm has submitted SOP for issuance of BMR".

113.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Variant pharmaceuticals (Pvt) Ltd, Plot No. 5, M-2, Pharmazone, 26 Km, Lahore Sharikpur Road, Sheikhupura.**
	Name, address of Manufacturing site.	M/s Variant pharmaceuticals (Pvt) Ltd, Plot No. 5, M-2, Pharmazone, 26 Km, Lahore Sharikpur Road, Sheikhupura.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33999 : 29-12-2021
	Details of fee submitted	PKR 30,000/-: 06-12-2021,
	The proposed proprietary name / brand name	**DEXIRANT 60mg Capsules**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Dexlansoprazole (as dual delayed release pellets)……60mg
	Pharmaceutical form of applied drug	Capsules
	Pharmacotherapeutic Group of (API)	Proton pump inhibitor
	Reference to Finished product specifications	In-House
	Proposed Pack size	30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	DEXILANT 60mg Capsule of M/s **TAKEDA PHARMS USA** (USFDA approved)
	For generic drugs (me-too status)	Razodex 60 mg Capsule of M/s GETZ Pharma (Reg # 086976)
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020 General Tablet, General Capsule, General Sachet and General dry powder injectable (pre-lyophilized)

	Name and address of API manufacturer.	M/s Vision pharmaceuticals (pvt) Ltd., Plot no. 22-23, Industrial Triangle, Kahuta Road, Islamabad
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API. Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (DLP123T, DLP124T, DLP125T)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence of test formulation with comparator product DEXILANT 60mg Capsule (B # 510902) of M/s Takeda GmbH, Germany by performing all the quality tests including dissolution in 3 different media (pH 1.2, 5.5 and 7). The results of the tests of both products were found to be within the specifications and are comparable.
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method for the drug substance. Firm

		has submitted report of validation of analytical method for the drug product.	
STABILITY STUDY DATA			
Manufacturer of API	M/s Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad.		
API Lot No.	**DLP755**		
Description of Pack (Container closure system)	30's blisters in alu alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	VT-001	VT-002	VT-003
Batch Size	1000 caps	1000 caps	1000 caps
Manufacturing Date	05-2021	05-2021	05-2020
Date of Initiation	13-05-2021	14-05-2021	15-05-2021
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any response.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Vision pharma pvt Ltd, Lahore issued by DRAP Lahore. It is valid till 10-02-2022.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the purchase of esomeprazole sodium sterile powder (2kg, Batch # DLP755) from M/s vision pharma vide invoice # 703069 dated 19-04-2021.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	

Remarks OF Evaluator:

Observation	Response by the firm
Submission of analytical method verification studies for drug substance performed by drug product manufacturer is required.	Submitted from M/s Variant pharmaceuticals.

Analytical method for routine analysis of drug substance used by the drug product manufacturer is required to be submitted.	Submitted.
Please submit documents confirming the procurement of drug substance for manufacturing of the applied product.	Firm has submitted copy of commetcial invoice for procurement of 2 Kg of Dexlansoprazole DDR pellets 22.5% from /s Vision pharmaceuticals.
In method validation studies for drug product, the exact amount of contents of capsule have not been mention equivalent to 60mg or 30mg dexlansoprazole, please submit complete method for analytical method validation studies including the exact amount of contents of capsule (pellets)taken for preparation of dilutions.	Firm has submitted concentration in terms of mg/ml for performance of each parameter of method validation.
Justification of specification for Dexlasoprazole capsule 30/60mg has not been provided in submitted dossier. However, justification of specification for another dosage form is presented in the dossier, clarify or otherwise submit the required data.	Firm has submitted drug product specification for both 30mg & 60 mg capsule.
Please provide complete calculations for potency adjustment of 30/60mg capsule.	Firm has submitted details for weight of pellets per capsule calculated on basis of "As is potency" of Dexlansoprazole pellets.
Since similar batch numbers have been assigned to stability batches of 30mg and 60mg capsules, therefore, the internal SOP/ procedure for assigning the batch numbers is required with the clarification of the same.	Firm has submitted SOP for issuance of BMR".

Decision: Registration Board approved DEXIRANT 30mg Capsules & DEXIRANT 60mg Capsules.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. 04 Registration applications of import cases

a. New cases

Priority Registration Applications

Drug Regulatory Authority of Pakistan in its 129th meeting held on 17th February, 2022 discussed the case regarding **"Priority Consideration of Applications for Registration Submitted After Cancellation of Their Renewal of Registration" vide Agenda Item No.V:.** Wherein, the Authority decided as under;

"The Authority acceded to the request of firms for out-of-queue submission and consideration of registration dossiers on CTD Format (5F) in regard to cancelled products due to late submission of renewals."

Accordingly, M/s Graton Pharma., Suit No.501 and 502 fifth floor plot No. 42C/2lane 8 bukhari commercial DHA phase 6, Karachi-75500, Pakistan. has requested for priority consideration of their following products due to invalid registration status of previously registered product:

114.	Name, address of Applicant / Importer	M/s Graton Pharma., Suit No.501 and 502 fifth floor plot No. 42C/2lane 8 bukhari commercial DHA phase 6, Karachi-75500, Pakistan.
	Details of Drug Sale License of importer	**License No: 160** **Address:** Office No.501 and 502 fifth floor plot No. 42C/2lane 8 Bukhari commercial DHA phase 6, Karachi-75500, Pakistan. **Address of Godown:** -- **Validity:** 21-10-2023. **Status:** License to sell, stock and exhibit for sale, distribute and sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	Beijing Beilu Pharmaceutical Co., Ltd. No. 3 Shuiyuan West Road, Miyun District, Beijing China
	Name, address of manufacturer(s)	Beijing Beilu Pharmaceutical Co., Ltd. Miyun Industrial Development Area., Beijing.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted copy of legalized CoPP certificate (No. Beijing20210129) ***issued by Beijing Municipal Medical Products Administration No. 70 Zaolinqian Street, Xicheng District Bejing*** for Iohexol 50ml: 17.5g (I) Injection. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspections. The name of importing country on CoPP is mentioned as Pakistan. Copy of GMP certificate no. BJ20180345 valid upto 08-08-2023 has been submitted for Beijing Beilu Pharmaceutical Co., Ltd. Miyun Industrial Development Area., Beijing.
	Details of letter of authorization / sole agency agreement	Firm has submitted original product specific authority letter from Beijing Beilu Pharmaceutical Co., Ltd. Address 7th Floor, Block Maples International office, No. 32 Xizhimen North Street, Haidian District, Beijing City, PR. China in the name of M/s Graton Pharma., Suit No.501 and 502 fifth floor plot No. 42C/2lane 8 bukhari commercial DHA phase 6, Karachi-75500, Pakistan. for following products Iohexol Injection 100ml:35g(I) Iohexol Injection 50ml:17.5g(I) Iohexol Injection 50ml:16g(I) This letter of appointment is valid upto 30-04-2026 unless revoked earlier.
	Status of the applicant	☐ Manufacturer ☒ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 808, Date of submission: 13-05-2022
	Details of fee submitted	PKR 75,000/- vide Deposit Slip No:709132227594
	The proposed proprietary name / brand name	MONOPAQUE 50ml injection (Iohexol Injection (50ml: 17.5g (I))
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains 755 mg of Iohexol equivalent to 350mg of Iodine.
	Pharmaceutical form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Medical Imaging drug
	Reference to Finished product specifications	USP
	Proposed Pack size	50ml
	Proposed unit price	***As per SRO***
	The status in reference regulatory authorities	OMNIPAQUE 350 mg iodine/ml (755 mg of iohexol/mL), (50ml=17.5g I), Solution for injection USFDA Approved by M/s Healthcare United States
	For generic drugs (me-too status)	IOBRIX-350 INJECTION 50ml by M/s Hoffmann Human Health Pak Ltd (Reg#032137)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Zhejiang Hichi Pharmaceutical Co., Ltd., Binhai Road, Damaiyu Economic Development Zone, Yuhuan County, Zhejiang China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls of material, control of critical

		steps and intermediates, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturers, manufacturing process and control of critical steps validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, characterization of impurities, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence	Pharmaceutical equivalence performed against reference product having strength 100ml:35g Iohexol injection
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the test of related substances in the applied product since titration method is applied for Assay test.
	Container closure system of the drug product	Medium Borosilicate glass type-I infusion bottles, halogenated butyl rubber stopper (chlorinated) for injections, and aluminum plastic combined caps for infusion bottles
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. The real time stability study data of 2 batches (190907 and 190908) is for 18 months only while the stability study data for 3rd batch (190909) is for 36 months. Batch No. / Mfg. Date 190907 / 10-09-2019 190908 / 10-09-2019 190909 / 11-09-2019

Remarks of Evaluator [XI]:

Section	Observations	Response
1.1	• The applied drug product is a generic drug product and you have submitted fee 75000/- only. Submit differential fee for the applied product	• Firm has submitted differential fee of Rs. 75,000/- vide deposit slip# 12552911.

	• Address of the Product license holder/exporter on authority letter and CoPP are different from each other. Clarification is required.	• Firm has submitted declaration that our manufacturing License address is now described as "No.3 Shuiyuan West Road, Miyun District, Beijing", which refers to the same place that described in the address written in the GMP certificate which is "Miyun Industrial Development Area, Beijing".
1.4.1	• All the information related to type of application mentioned in section 1.4 shall be submitted.	Submitted.
1.5.2	• Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit. Strength of Active ingredient shall be stated clearly. In case API is in the form of salt, specify the equivalent strength of the base e.g., AAA sodium 50 mg (equivalent to AAA) etc.	Submitted.
1.5.10	• You have mentioned the dosage form of applied drug as both injection and oral while the reference product is not available in applied strength in oral dosage form, clarify?	Applied product is Injection dosage form.
3.2.S.4.1-3.2.S.4.3	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	• Submitted
3.2.P.2.2.1	• Pharmaceutical equivalence of the applied drug with reference product in 100ml volume is submitted, while the volume of applied product is 50ml, clarify?	• The iohexol 50 ml and iohexol 100 ml, the two specifications have the same concentrations, only the filling quantity is different.
3.2.P.7	• The innovator product is packed in +PLUSPAK™ (polymer bottle) while you have packed the product in medium borosilicate glass infusion bottles, halogenated butyl rubber stopper (chlorinated) for injections, and aluminum plastic combined caps for infusion bottles clarify?	• Various types of glass used for pharmaceutical packaging as per USP Type I - borosilicate glass our manufacturer packaging is up to mark with USP specification. Study results for the test of leachable have been submitted.

3.2.P.8	• The real time stability study data of Finished Pharmaceutical Product of 2 batches (190907 and 190908) is for 18 months only while the stability study data for 3rd batch (190909) is for 36 months. Submit complete real time stability data till shelf life as per zone IV-A • Moreover, it must be justified that the stability data of 36 months could be performed for batch# R190909 which was manufactured on 11-09-2019 for which 36 months has not been passed yet.	• Firm has submitted data stability reports of accelerated (6months) & long term (36 months) stability studies as per Zone-IV a condition of three new batches i.e., 1506038, 1511019 & T1712008 manufactured in 23-06-2015, 04-11-2015 & 04-12-2017 respectively.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

115.	Name, address of Applicant / Importer	M/s Graton Pharma., Suit No.501 and 502 fifth floor plot No. 42C/2lane 8 bukhari commercial DHA phase 6, Karachi-75500, Pakistan.
	Details of Drug Sale License of importer	**License No: 160** **Address:** Office No.501 and 502 fifth floor plot No. 42C/2lane 8 Bukhari commercial DHA phase 6, Karachi-75500, Pakistan. **Address of Godown:** -- **Validity:** 21-10-2023. **Status:** License to sell, stock and exhibit for sale, distribute and sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	Beijing Beilu Pharmaceutical Co., Ltd. No. 3 Shuiyuan West Road, Miyun District, Beijing China
	Name, address of manufacturer(s)	Beijing Beilu Pharmaceutical Co., Ltd. No. 3 Shuiyuan West Road, Miyun District, Beijing China
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted copy of legalized CoPP certificate (No. Beijing20210128) ***issued by Beijing Municipal Medical Products Administration No. 70 Zaolinqian Street, Xicheng District Bejing*** for Iohexol 100ml: 35g (I) Injection. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspections. The name of importing country on CoPP is mentioned as Pakistan.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of product specific authority letter from Beijing Beilu Pharmaceutical Co., Ltd. Address 7th Floor, Block Maples International office, No. 32 Xizhimen North Street, Haidian District, Beijing City, PR. China in the name of M/s Graton Pharma., Suit No.501 and 502 fifth floor plot No. 42C/2lane 8 bukhari

		commercial DHA phase 6, Karachi-75500, Pakistan. for following products Iohexol Injection 100ml:35g(I) Iohexol Injection 50ml:17.5g(I) Iohexol Injection 50ml:16g(I) This letter of appointment is valid upto 30-04-2026 unless revoked earlier.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 809, Date of submission: 13-05-2022
	Details of fee submitted	PKR 75,000/- vide Deposit Slip No:1467185241
	The proposed proprietary name / brand name	**MONOPAQUE 100ml injection (Iohexol Injection (100ml: 35g (I))**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains 755 mg of Iohexol equivalent to 350mg of Iodine.
	Pharmaceutical form of applied drug	***Injection***
	Pharmacotherapeutic Group of (API)	Medical Imaging drug
	Reference to Finished product specifications	USP
	Proposed Pack size	100ml
	Proposed unit price	***As per SRO***
	The status in reference regulatory authorities	OMNIPAQUE 350 mg iodine/ml (755 mg of iohexol/mL), (100ml=35g I), Solution for injection USFDA Approved by M/s Healthcare United States
	For generic drugs (me-too status)	IOBRIX-350 INJECTION 100ml by M/s Hoffmann Human Health Pak Ltd (Reg#032138)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Zhejiang Starry Pharmaceutical Co., Ltd., No. 1 Sitaili, Modern Industrial Cluster Area, Xianju County Zhejiang Province, China Zhejiang Hichi Pharmaceutical Co., Ltd., Binhai Road, Damaiyu Economic Development Zone, Yuhuan County, Zhejiang China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls of material, control of critical steps and intermediates, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability study conditions of Drug substance by Zhejiang Hichi Pharmaceutical Co., Ltd: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months (Batches: C0042010003, C0042011001, C0042011002) Stability study conditions of Drug substance by Zhejiang Starry Pharmaceutical Co., Ltd: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months (Batches: R190904, R190905, R190906)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturers, manufacturing process and control of critical steps validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, characterization of impurities, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence of applied product manufactured from both API sources performed against reference product having strength 100ml:35g Iohexol injection
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the test of related substances in the applied product since titration method is applied for Assay test.

	Container closure system of the drug product	Medium borosilicate glass infusion bottles, halogenated butyl rubber stopper (chlorinated) for injections, and aluminum plastic combined caps for infusion bottles
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. Batches manufactured from API of Zhejiang Haichang Pharmaceutical Co., Ltd Batch No. / Mfg. Date R190907 / 10-09-2019 R190908 / 10-09-2019 R190909 / 11-09-2019 Batches manufactured from API of Zhejiang Stellite Pharmaceutical Co., Ltd Batch No. / Mfg. Date R190904 / 08-09-2019 R190905 / 09-09-2019 R190906 / 09-09-2019

Remarks of Evaluator [XI]:

Section	Observations	Response
1.1	• The applied drug product is a generic drug product and you have submitted fee 75000/- only. Submit differential fee for the applied product	• Firm has submitted differential fee of Rs. 75,000/- vide deposit slip# 0827443559
	• Address of the Product license holder/exporter on authority letter and CoPP are different from each other. Clarification is required.	• Firm has submitted declaration that our manufacturing License address is now described as "No.3 Shuiyuan West Road, Miyun District, Beijing", which refers to the same place that described in the address written in the GMP certificate which is "Miyun Industrial Development Area, Beijing".
1.4.1	• All the information related to type of application mentioned in section 1.4 shall be submitted.	Submitted
1.5.10	• You have mentioned the dosage form of applied drug as both injection and oral while the reference product is not available in applied strength in oral dosage form, clarify?	Dosage form is injection

3.2.S.4.1-3.2.S.4.3	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	• Submitted
3.2.P.7	• The innovator product is packed in +PLUSPAK™ (polymer bottle) while you have packed the product in medium borosilicate glass infusion bottles, halogenated butyl rubber stopper (chlorinated) for injections, and aluminum plastic combined caps for infusion bottles clarify?	• Various types of glass used for pharmaceutical packaging as per USP Type I - borosilicate glass our manufacturer packaging is up to mark with USP specification. Study results for the test of leachable have been submitted.
3.2.P.8	• The submitted long term stability data of Finished Pharmaceutical Product manufactured from API source of Zhejiang Haichang Pharmaceutical Co., Ltd is of different duration for various batches briefed below. Batch# R190907, …. 6 Months Batch# R190908…..18 Months Batch#R190909……36 Months Clarification is required. • Moreover, it must be justified that the stability data of 36 months could be performed for batch# R190909 which was manufactured on 11-09-2019 for which 36 months has not been passed yet. • The long-term stability data of Finished Pharmaceutical Product manufactured from API source of Zhejiang Stellite Pharmaceutical Co., Ltd has been submitted upto 6 months only. Details of batches: R190904……6 months R190905……6 months R190906……6 months Clarification is required.	Firm has submitted revised data for stability summary, wherein manufacturing dates of previously submitted stability batches has been corrected as 09-2018 along with submission of stability reports of accelerated (6months) & long term (36 months) stability studies as per Zone-IV a condition.
Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.		

b. Routine applications of Import submitted on Form 5F

116.	**Name, address of Applicant / Importer**	**M/s Seatle Private Limited, 45-KM Multan Road, Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-351-0073-029396P **Address:** Seatle Private Limited, 45-KM Multan Road, Lahore. **Address of Godown:** NA **Validity:** 19-03-2022 (Renewal applied) **Status:** License to sell drugs in a Pharmacy **Renewal:** yes
	Name and address of marketing authorization holder (abroad)	LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona - Spain.
	Name, address of manufacturer(s)	**Drug product manufacturer:** LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain. **Water for injection 10ml:** Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France
	Name of exporting country	Spain
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized **copy** of CoPP certificate (No. 2020/01561) dated 20/06/2020 issued by Spanish Agency for Medicines and Health Products, Spain for Fratazid 1g powder and 10ml solvent for solution for injection (IV). The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every 3 years. Submitted COPP does not reflect any detail regarding manufacturer of the accompanying diluent i.e., 10ml WFI. **GMP:** Firm has submitted Legalized "Manufacturing authorization certificate no. 2279E" dated 26-11-2018, issued to LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain., wherein manufacturing facility for sterile products of B-lactam antibiotics" is confirmed. Firm has submitted Legalized "Manufacturing authorization certificate no. M 19/112" dated 13-06-2019, issued to Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France, wherein manufacturing facility for sterile products of Small Volume Parenteral" is confirmed.

		Copy of GMP certificate no. NCF/2024/001/CAT hs also been submitted for LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain valid upto 20-06-2020. Copy of Eudra GMP certificate no. 2020/HPF/FR/081 for Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France, valid upto 13-02-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted original legalized sole agency agreement. The agreement specifies that the manufacturer appoints M/s Seatle Private Ltd. to register their products in Pakistan as sole importer. A manufacturing agreement has also been submitted wherein M/s LDP-LABORATORIOS TORLAN, S.A. has declared Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France as manufacturer of the diluents i.e., Lidocaine HCl 1% ampoule & WFI ampoules for Ceftriaxone formulations to be imported by M/s Seatle.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 17398 dated 22-06-2021
	Details of fee submitted	For Ceftriaxone: PKR 100,000/-: 18-8-2020 For WFI: PKR 100,000/-: 15-06-2020
	The proposed proprietary name / brand name	**FRATAZID INJECTION 1g IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial of powder contains: Ceftriaxone (as Sodium) …….. 1g Each Ampoule contains: Sterile Water for Injection ……10ml

	Pharmaceutical form of applied drug	Powder and solvent for solution for Injection
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	Drug product: USP Diluent WFI: European Pharmacopoeia
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Rocephin Injection 1g **(USFDA** Approved).
	For generic drugs (me-too status)	Oxidil of SAMI Pharma Pvt. Ltd. (Reg # 022422)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Qilu Antibiotics Pharmaceutical Co., Ltd. No. 849 Dongjia Town, Licheng District, Jinan, Shandong Province, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25^{o}C ± 2^{o}C and 60% RH The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence studies have been submitted against the Rocephin 1gm Injection.

	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type II glass vial for Powder Type I glass ampoule for WFI
	Stability study data of drug product, shelf life and storage conditions	**Drug product:** Firm has submitted stability study data of 3 batches of drug powder vial. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. The real time stability study data of all 3 batches is completed till 36 months. **Diluent WFI:** Firm has submitted stability study data of 3 batches of 10ml WFI. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. The real time stability study data of all 3 batches is completed till 60 months.
117.	**Name, address of Applicant / Importer**	**M/s Seatle Private Limited, 45-KM, Multan Road, Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-351-0073-029396P **Address:** Seatle Private Limited, 45-KM, Multan Road, Lahore. **Address of Godown:** NA **Validity:** 19-03-2022 (Renewal applied) **Status:** License to sell drugs in a Pharmacy **Renewal:** Sale License is Valid
	Name and address of marketing authorization holder (abroad)	LDP-LABORATORIOS TORLAN S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona - Spain.
	Name, address of manufacturer(s)	**Drug product manufacturer:** LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain. **Lidocaine HCl 1%w/v:** Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France
	Name of exporting country	Spain
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized **copy** of CoPP certificate (No. 2020/01561) dated 20/06/2020 issued by Spanish Agency for Medicines and Health Products, Spain for Fratazid 1g powder and 10ml solvent for solution for injection (IV). The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every 3 years.

		Submitted COPP does not reflect any detail regarding manufacturer of the accompanying diluent i.e., Lidocaine HCl 1% injection. **GMP:** Firm has submitted Legalized "Manufacturing authorization certificate no. 2279E" dated 26-11-2018, issued to LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain., wherein manufacturing facility for sterile products of B-lactam antibiotics" is confirmed. Firm has submitted Legalized "Manufacturing authorization certificate no. M 19/112" dated 13-06-2019, issued to Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France, wherein manufacturing facility for sterile products of Small Volume Parenteral" is confirmed. Copy of GMP certificate no. NCF/2024/001/CAT hs also been submitted for LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain valid upto 20-06-2020. Copy of Eudra GMP certificate no. 2020/HPF/FR/081 for Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France, valid upto 13-02-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted original sole agency agreement. The agreement specifies that the manufacturer appoints M/s Seatle Private Ltd. to register their products in Pakistan as sole importer.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 17396 dated 22-06-2021

	Details of fee submitted	For Ceftriaxone: PKR 100,000/-: 18-8-2020 For WFI: PKR 100,000/-: 15-06-2020
	The proposed proprietary name / brand name	**FRATAZID INJECTION 500g IM**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial of powder contains: Ceftriaxone (as Sodium) …….. 500mg Each 2ml Ampoule contains: Sterile Lidocaine HCl ……20mg (Ph. Eur specification)
	Pharmaceutical form of applied drug	Powder and solvent for solution for Injection
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	Drug product: USP Diluent Lidocaine HCl injection 2%w/v: European Pharmacopoeia
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Rocephin Injection 500mg **(USFDA** Approved).
	For generic drugs (me-too status)	Oxidil of SAMI Pharma Pvt. Ltd. (Reg # 022422)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	**Ceftriaxone:** Qilu Antibiotics Pharmaceutical Co., Ltd. No. 849 Dongjia Town, Licheng District, Jinan, Shandong Province, China. **Lidocaine:** Haupt Pharma Livron, 1 rue Comte de Sinard, Livron Sur Drome, 26250, France.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time

		conditions. The real time stability data is conducted at 25°C ± 2°C and 60% RH the stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence study has been submitted against Rocephin Injection 500mg.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type II glass vial for Powder Type I glass ampoule for Lidocaine
	Stability study data of drug product, shelf life and storage conditions	**Drug product:** Firm has submitted stability study data of 3 batches of drug powder vial. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. The real time stability study data of all 3 batches is completed till 36 months. **Diluent Lidocaine HCl 1%:** Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. The real time stability study data of all 3 batches is completed till 60 months.
118.	**Name, address of Applicant / Importer**	**M/s Seatle Private Limited, 45-KM, Multan Road, Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-351-0073-029396P **Address:** Seatle Private Limited, 45-KM, Multan Road, Lahore. **Address of Godown:** NA **Validity:** 19-03-2022 (renewal applied) **Status:** License to sell drugs in a Pharmacy **Renewal:** Sale License is Valid
	Name and address of marketing authorization holder (abroad)	LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona - Spain.
	Name, address of manufacturer(s)	**Drug product manufacturer:** LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain.

		Water for injection 5ml: Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France
	Name of exporting country	Spain
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized **copy** of CoPP certificate (No. 2020/01568) dated 20/06/2020 issued by Spanish Agency for Medicines and Health Products, Spain for Fratazid 1g powder and 10ml solvent for solution for injection (IV). The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every 3 years. Submitted COPP does not reflect any detail regarding manufacturer of the accompanying diluent i.e., 10ml WFI. **GMP:** Firm has submitted Legalized "Manufacturing authorization certificate no. 2279E" dated 26-11-2018, issued to LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain., wherein manufacturing facility for sterile products of B-lactam antibiotics" is confirmed. Firm has submitted Legalized "Manufacturing authorization certificate no. M 19/112" dated 13-06-2019, issued to Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France, wherein manufacturing facility for sterile products of Small Volume Parenteral" is confirmed. Copy of GMP certificate no. NCF/2024/001/CAT hs also been submitted for LDP-LABORATORIOS TORLAN, S.A. Ctra. de Barcelona, 135-B 08290 Cerdanyola del Valles Barcelona – Spain valid upto 20-06-2020. Copy of Eudra GMP certificate no. 2020/HPF/FR/081 for Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France, valid upto 13-02-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted original legalized sole agency agreement. The agreement specifies that the manufacturer appoints M/s Seatle Private Ltd. to register their products in Pakistan as sole importer. A manufacturing agreement has also been submitted wherein M/s LDP-LABORATORIOS TORLAN, S.A. has

		declared Haut Pharma Livron SAS, 1 rue Comte de sinard, 26250, Livron sur Drome. France as manufacturer of the diluents i.e., Lidocaine HCl 1% ampoule & WFI ampoules for Ceftriaxone formulations to be imported by M/s Seatle.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 17397 dated 22-06-2021
	Details of fee submitted	For Ceftriaxone: PKR 100,000/-: 18-8-2020 For WFI: PKR 100,000/-: 15-06-2020
	The proposed proprietary name / brand name	**Fratazid 500mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial of powder contains: Ceftriaxone (as Sodium) …….. 500mg Each Ampoule contains: Sterile Water for Injection ……5ml
	Pharmaceutical form of applied drug	Powder and solvent for solution for Injection
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	European Pharmacopoeia
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Rocephin Injection 500mg **(USFDA** Approved).
	For generic drugs (me-too status)	Oxidil of SAMI Pharma Pvt. Ltd. (Reg # 022422)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Name, address of drug substance manufacturer	Qilu Antibiotics Pharmaceutical Co., Ltd. No. 849 Dongjia Town, Licheng District, Jinan, Shandong Province, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25°C ± 2°C and 60% RH The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence study has been submitted against Rocephin Injection 500mg IV
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type II glass vial for Powder Type I glass ampoule for WFI
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of drug powder vial and WFI ampoule. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. The real time stability study data of all 3 batches is completed till 36 months.

Evaluation by PEC:

Section#	Observations	Firm's response
1.3.4	Copy of valid Drug Sale License (DSL) issued by relevant licensing authority shall be submitted. Sole agency agreement / letter of authorization between applicant and	Firm has submitted copy of DSL valid till 19-03-2022 along with receipt of renewal application. Copy of sole agency agreement from M/s LDP-Laboratorios TORLAN,

	marketing authorization holder shall be submitted.	S.A., Ctra Barcelona, Spain in the name of M.s Seatle Provate Ltd., Lahore, Pakistan has been submitted.
1.5.6	The said section declares Pharmacopoeial reference as European Pharmacopoeia specifications, monograph of applied product is not available in European Pharmacopoeia.	Firm has revise specifications to USP , without submission of fee.
2.3	Table for literature references for the drug substance & drug product has not been submitted.	Submitted.
2.3.P.5.1	Assay limits are not as per the Pharmacopoeial monograph.	Revised Specification and Analytical Procedure as per USP is submitted
2.3.R.1.1	Submitted BMR declare the calculation of drug substance fill weight per vial on the basis of "Assay of anhydrous active substance" instead of "Assay of as is active substance"	Firm has submitted revised BMRs.
3.2.S.4.2	• Copy of drug substance specifications and analytical procedure applied by Drug product manufacturer shall be submitted. • The USP monograph of Ceftriaxone sodium, recommends the potency of Ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg) for the calculation of Assay, whereas submitted drug substance analytical procedure applies the potency of Ceftriaxone sodium in %age.	• Revised Specification and Analytical Procedure applied by Drug Product Manufacturer as per USP is submitted
3.2.S.4.3	• Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	• AMV report is submitted form Drug product manufacturer.
3.2.S.4.4	• The specifications for Assay test mentioned in the batch analysis certificate from drug product manufacturer are different from that submitted in section 3.2.S.4.1. • The drug substance COA from the M/s Qilu Pharma is as per USP monograph whereas COA from M/s LDP Laboratories Torlan S.A. is as per the BP monograph. Justification shall be submitted in this regard.	• Revised COA, according to USP monograph and section 3.2.S.4.1 from Drug Product Manufacturer is submitted

3.2.P.2	• A brief information on the pharmaceutical development shall be included. This information specifies the justification of formulation and method of manufacturing. It is also important that critical quality attributes (CQAs) and Critical Process Parameters (CPP) shall be discussed. • Compatibility studies for the applied product shall be performed as per the instructions provided in individual label of the drug product.	• Submitted. • Compatibility study has been submitted for 1gm injection only with water for injection.
3.2. P.5.1	• Submitted drug product specifications does not include Assay limit for the content of dry powder injection i.e., an amount of Ceftriaxone Sodium equivalent to NLT 776 µg/mg of ceftriaxone • Test of crystallinity ha sot been included the drug product specifications.	• Revised Specifications according to USP including the test for crystallinity, are submitted.
3.2.P.5.2	• Sample preparation procedure mentioned in analytical method, does not include sample preparation for "Sample solution 2", as defined in the USP monograph of "Ceftriaxone for injection."	• Firm has submitted revised analytical procedure as per USP monograph
3.2.P.5.4	• Submitted COAs of drug product does not include Assay test for sample solution 2 as recommended by USP monograph of "Ceftriaxone for injection".	• Firm has submitted COA of recent batch of the drug product manufactured in May, 2022 wherein Assay analysis has been performed as per USP monograph.
3.2.P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	• Submitted.
3.2.P.8	• Submitted stability data does not reflect the performance of Assay test for sample solution 2 as recommended by USP monograph of "Ceftriaxone for injection". • Data of stability batches shall be supported by respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	• Please note that the Sample Preparation Method mentioned in Analytical Method does not include sample preparation for "Sample Solution 2" and only the preparation of Sample Solution 1"is included. However, we will include both the preparation of Sample Solution 1 and Sample Solution 2 by revising the specifications and analytical procedures

		according to the USP Monograph. • Submitted.

Decision: Registration Board deferred the applications of FRATAZID INJECTION 1g IV & FRATAZID INJECTION 500g IM for submission of CoPP with details of the composition and manufacturer of accompanying diluent.

119.	**Name, address of Applicant / Importer**	**M/s Himmel Pharmaceuticals (Pvt) Ltd. 793-D, Block ''C'', Faisal Town Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-352-0065-016174-D **Address:** 793-D, Block -C, Faisal Town Lahore **Address of Godown:** NA **Validity:** 06-02-2022 **Status:** License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited Plant address: Kathali Bhaluka Mymensingh Bangladesh Office Address: 9/A Toyenbee Circular Road Motijheel Dhaka Bangladesh
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited Plant address: Kathali Bhaluka Mymensingh Bangladesh Office Address: 9/A Toyenbee Circular Road Motijheel Dhaka Bangladesh
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) Firm has submitted original legalized COPP (DA/6-110/2016/3292) issued on 01-June-2020 Government of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration Oushad Bhaban, Mohkhali Dhaka-1212, Bangladesh. **GMP:** Firm has submitted Legalized GMP certificate (Certificate No. DA/6-110/06/10002) issued by M/s Beacon Pharmaceuticals limited. Also Renewal certificate is submitted.	
	Details of letter of authorization / sole agency agreement • Firm has submitted copy of letter of distribution certificate from Beacon Pharmaceuticals limited. The letter specifies that the manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register their products in Pakistan. The authorization letter is valid till June, 2025.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 7092 dated 03-03-2021
	Details of fee submitted	Rs.50,000/- dated 01-02-2021
	The proposed proprietary name / brand name	**Hernix 40mg tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Neratinib Maleate equivalent to Neratinib ……. 40mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In house
	Proposed Pack size	180's in HDPE bottle
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Nerlynx 40mg (Pierre Fabre Medicament , France)
	For generic drugs (me-too status)	NA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance..
	Name, address of drug substance manufacturer	Beijing Mesochem Technology Co., Ltd. Floor 23, Building 9, Lippo Plaza Economic and Technological Development Zone Beijing
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25±2ºC, 60%±5%RH. The stability study data is till 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical

		development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Comparative analysis Studies against the reference product Nerlynx 40mg (Pierre Fabre Medicament, France) has been submitted
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	HDPE Bottle
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. Accelerated stability studies have been conducted at 40°C±2°C and 75%±5% RH for 6 months. Real time stability studies conducted at 30°C±2°C and 65% ± 5% for 24 months.

Remarks of Evaluator[II]:

Section #.	Deficiencies	Firm's response
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted. • Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studiesjasm, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture	• Drug product manufacturer has submitted, specifications, analytical procedure, analytical method verification studies & COAs for drug substance.
3.2.P.1	• Qualitative composition of applied product is not same as that of the innovator product.	• The excipients used complies with current pharmacopoeial monographs. These excipients are pharmaceutically inert substance and we have used these excipients below the IIG limit of FDA database as well as we have done extensive analysis of the product afer

		formulation and found satisfactory result of assay, dissolution results & impurity profile. Also w have done stability study during developmeht stage and found satisfactory result of the product. So we can conclude that these excipients are not incompatible with the API.
3.2.P.2	Compatibility studies of the Drug Substance(s) with excipients shall be submitted, since the qualitative composition of the formulation is not similar to innovator / reference product.	• The excipients used complies with current pharmacopoeial monographs. These excipients are pharmaceutically inert substance and we have used these excipients below the IIG limit of FDA database as well as we have done extensive analysis of the product afer formulation and found satisfactory result of assay, dissolution results & impurity profile. Also w have done stability study during developmeht stage and found satisfactory result of the product. So we can conclude that these excipients are not incompatible with the API.
3.2.P.5.1	• US FDA review document of the Innovator product i.e., Nerlynx, specifies the dissolution limit as "NLT Q in 30 minutes", whereas submitted specifications declare the dissolution limits as "NLT 75% in 45 minutes". Justify the variation in time point of dissolution. • Submitted specifications does not include test of content uniformity by way of Assay.	• The dissolution time for hernix tablet ha sbeen slected 45 minutes as perthe british Pharmacopeoia guidline, reference chapter monographof the BP in the dissolution tests for tablets & capsules, Appendix XII B1. I nthe reference chapter it I smentioned that , "Unless otherwise indicated in th emongraph, withdraw samples at 45 minutes". Hence, we have selected 45 minutes as a sungle time point.
3.2.P.5.4	• Test of content uniformity by way of Assay has not been performed at the time of batch release.	• Firm has submitted revised finished product specifications including test of content uniformity and committed to provide COA from next commercial batches as per revised specifications.
3.2.P.8	• Following shall be submitted:	• Submitted.

	i. Analytical record for stability studies including raw data sheets, chromatograms etc. ii. Complete batch manufacturing record.	

Decision: Deferred for following:

- **Scientific jusytification for difference in dissolution limits in terms of %age released and time point from that recommended by the US FDA for innovator product along with comparison of disintegration & release profile of the applied product & innovator product.**

120.	**Name, address of Applicant / Importer**	**M/s Himmel Pharmaceuticals (Pvt) Ltd. 793-D, Block ''C'', Faisal Town Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-352-0066-016174-D **Address: 793-D, Block-C, Faisal Town Lahore** **Validity:** 06-02-2022 **Status:** License to sell drugs as a distributor **Address of Godown:** N/A
	Name and address of marketing authorization holder (abroad)	M/s BEACON Pharmaceuticals Limited Plant address:Kathali ,Bhaluka,Mymensingh Bangladesh Office address: 9/B/2, Toynbee Circular RoaD, Motijheel Dhaka, Bangaldesh
	Name, address of manufacturer(s)	M/s BEACON Pharmaceuticals Limited Plant address:Kathali ,Bhaluka,Mymensingh Bangladesh Office address: 9/B/2, Toynbee Circular RoaD, Motijheel Dhaka, Bangaldesh
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) Firm has submitted original legalized COPP (DA/6-110/2016/3296) issued on 01-June-2020 Government of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration Oushad Bhaban, Mohkhali Dhaka-1212, Bangladesh. Firm has submitted Legalized GMP certificate (Certificate No. DA/6-110/06/10002) issued by M/s Beacon Pharmaceuticals limited.	
	Details of letter of authorization / sole agency agreement •	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging

		☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 2037746 Dated 03-03-2020
	Details of fee submitted	Rs.100,000/- Dated 03-03-2020
	The proposed proprietary name / brand name	**Niraparix 100mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains Niraparib Tosylate Monohydrate INN equivalent to Niraparib 100mg
	Pharmaceutical form of applied drug	capsule
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In house
	Proposed Pack size	90's in HDPE bottle
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Zejula 100mg Capsule (GlaxoSmithKline limited, Ireland)
	For generic drugs (me-too status)	NA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	ANQING WORLD CHEMICAL COMPANY LIMITED No.21 Huancheng west road AnQing County, AnHui Province China
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted long term stability study data of 3 batches of drug substance at 25°C ± 2°C / 60 ± 5% RH for 24 months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of

		specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Comparative analysis Studies against the reference product of Zejula 100mg Capsule (GlaxoSmithKline limited) has been submitted has been submitted.
	Analytical method validation/verification of product	Firm has submitted analytical method verification studies of the drug product.
	Container closure system of the drug product	White HDPE bottle
	Stability study data of drug product, shelf life and storage conditions	Firm has submiited stability study data of 3 batches. Accelerated stability studies have been conducted at 40°C±2°C and 75%±5% RH for 6 months. Real time stability studies conducted at 30°C±2°C and 65% ± 5% for 24 months

Remarks of Evaluator[II]:

Section #.	Deficiencies	Firm's response
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted. • Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studiesjasm, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture	Drug product manufacturer has submitted, specifications, analytical procedure, analytical method verification studies & COAs for drug substance.
3.2.P.1	• Qualitative composition of applied product is not same as per that of the innovator product.	• The excipients used complies with current pharmacopoeial monographs. These excipients are pharmaceutically inert substance and we have used these excipients below the IIG limit of FDA database as well as we have done extensive analysis of the product afer formulation and found satisfactory result of assay, dissolution results & impurity profile. Also w have

		done stability study during developmeht stage and found satisfactory result of the product. So we can conclude that these excipients are not incompatible with the API.
3.2.P.2	Compatibility studies of the Drug Substance(s) with excipients shall be submitted, since the qualitative composition of the formulation is not similar to innovator / reference product.	• The excipients used complies with current pharmacopoeial monographs. These excipients are pharmaceutically inert substance and we have used these excipients below the IIG limit of FDA database as well as we have done extensive analysis of the product afer formulation and found satisfactory result of assay, dissolution results & impurity profile. Also w have done stability study during developmeht stage and found satisfactory result of the product. So we can conclude that these excipients are not incompatible with the API.
3.2.P.2.2.1	• Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	• Firm has referred to the Bio equivalence studies of applied prodyuct performed as an open label, balanced, randomized, two-treatment, two sequence, two-period, crossover oral bioequivalence study of single dose of Niraparix capsule against Zejula capsule of m/s tesaro UK ltd.
3.2.P.5.1	• US FDA review document of the Innovator product i.e., Zejula, specifies the dissolution limit as "NLT Q in 45 minutes", whereas submitted specifications declare the dissolution limits as "NLT 70% in 60 minutes". Justify the variation in time point of dissolution.	• For dissolution method, we have used US FD Adatabase for medium, apparatus, volume and time point. However, please note tha, for dissolution time point we slected as 60 minutes. Based n the US FDA databse, dissolution tim endpoint covered 60 minutes in method of analysis.
3.2.P.8	• Accelerated stability studies of batch# 3830004, reflect significant change of in Assay results. • Following shall be submitted:	• Not replied against this point. • Analytical record for stability data not submitted. • BMRs have been submitted.

	i. Analytical record for stability studies including raw data sheets, chromatograms etc. ii. Complete batch manufacturing record. iii. GMP certificate of the drug substance manufacturer issued by the relevant regulatory authority.	• Submitted GMP certificate (No. NP122019) is not verifiable form the NMPA web site.

Decision: Deferred for following:

- **Scientific jusytification for difference in dissolution limits in terms of %age released and time point from that recommended by the US FDA for innovator product along with comparison of disintegration & release profile of the applied product & innovator product.**
- **Submission of valid GMP certificate of the drug substance manufacturer issued by the relevant regulatory authority.**

121.	**Name, address of Applicant / Importer**	**M/s 2 World Traders Pakistan. 55/2, Main Khayaban-e-Hafiz, DHA, Karachi, Pakistan**
	Details of Drug Sale License of importer	**License No:** 316 **Address:** 55/2 Main Khayaban-e-Hafiz Phase-V, DHA Karachi Pakistan **Address of Godown:** NA **Validity:** 15-03-2023 **Status:** Drug License by way of Whole Sale **Renewal:** Valid
	Name and address of marketing authorization holder (abroad) as per COPP	BIOMEDICA FOSCAMA Industria Chimico-Farmaceutica, S.p.A. Via Morolense n.87, 03013 Ferentino (FR) Italy.
	Name, address of manufacturer(s) as per COPP	BIOMEDICA FOSCAMA Industria Chimico-Farmaceutica, S.p.A. Via Morolense n.87, 03013 Ferentino (FR) Italy.
	Name of exporting country	Italy
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized **copy** of CoPP certificate (N^{o}CPP/2021/756) dated 02-04-2021 issued by AIFA (Agenzia Italiana Del Farmaco) for TAD (Glutathione 600mg. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection. **GMP;** Firm has submitted the legalized copy of GMP certificate (No: IT/84/H/2020) which was valid till 31-12-2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted attested copy of Import and Distribution Agreement between Biomedica Foscama and 2 World Traders Pakistan for the applied product.
	Status of the applicant	☐ Manufacturer ☒ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 27041 dated 30-09-2021
	Details of fee submitted	PKR 75,000/-:Slip # 944857553239 10-08-2021
	The proposed proprietary name / brand name	**TAD 600mg dry powder injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Glutathione as sodium …….600mg
	Pharmaceutical form of applied drug	White lyophilized powder packed in moulded clear type-3 vials along with 4ml solvent
	Pharmacotherapeutic Group of (API)	Antidote ATC Code: V03AB32
	Reference to Finished product specifications	European Pharmacopoeia
	Proposed Pack size	10 vials with 10 (4ml) solvent ampoules (WFI)
	Proposed unit price	As per pricing committee.
	The status in reference regulatory authorities	TAD **(AIFA** Approved) complies EU Pharmacopoeia.
	For generic drugs (me-too status)	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	M/s Biomedica Foscama Industria Chimico-Farmaceutica S.P.A (Italy)
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API for accelerated at 40°C ±2°C / 75% ± 5% RH for 6 months as well as Long term testing which is conducted at 25°C ± 2°C / 65% ± 5% RH. The stability study data is till 36 months at ≤ 25°C.
	Module-III Drug Product:	Firm has submitted data of drug product and solvent (WFI) separately, including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not applicable being the innovator product
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	API: Type III glass vials with chlorobutyl stoppers Aluminium oversealed Solvent: Type-I glass ampoules
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The Long-term stability study data is conducted at 25°C ±2°C / 65% ± 5% RH for 36 months. Now the firm has submitted 18 months long term stability studies data as per Zone IVb conditions, detailed as under: **Batch# / Initial date / Duration** 201007 / 07-2020 / 18 months 201008 / 07-2020 / 18 months 201009 / 07-2020 / 18 months Firm has claimed 36 months shelf life on basis of above submitted data.
	Details of diluent:	**Composition:** Water for injection **Container closure:** 4ml Type I glass ampoule. **Manufacturer:** BIOMEDICA FOSCAMA Industria Chimico-Farmaceutica, S.p.A. Via Morolense n.87, 03013 Ferentino (FR) Italy. **Stability data:** Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The Long-term stability study data at 30°C ±2°C / 75% ± 5% RH has been submitted for 9 months only.

Evaluation by PEC^{II}:
Clinical profile of the applied product is as under:

- **Therapeutic indications:**

Prophylaxis of neuropathy following chemotherapy treatment with cisplatin or analogue.

- **Pharmacotherapy category:**

Antidotes, ATC code: V03AB32

- **Dosage:**

The generally recommended daily dose of TAD in patients receiving cisplatin or analogue chemotherapy is 1.5 g / m2 (corresponding to 2.5 g) administered slowly intravenously.

- **Contraindications:**

Hypersensitivity to the active ingredient.

- **Pharmaceutical description:**
  The drug substance is lyophilised in bulk form and then the bulk lyophilised powder is filled in glass vials.

Section#	Observation	Firm's response
1.5.2	Strength per unit is mentioned as Glutathione powder 600mg instead of Glutathione sodium.	Firm has corrected label claim without submission of fee.
1.5.6	Pharmacopoeial reference for applied product is stated as European Pharmacopeia, whereas European monograph is not available for applied product.	Firm has submitted statement from M/s Biomedica Foscama that the TAD 600mg/4ml powder and solvent for infusion state that the product is contained in packaging in compliance with European Pharmacopoeia.
3.2.P.2.6	Compatibility studies shall be performed with the diluent specified in individual label of the drug product.	Firm has submitted stability study of 8hours after reconstitutiton at 25$\pm$2^{o}C.
Diluent		
3.2.P.3.1	Details of the manufacturer of diluent shall be submitted.	
3.2.P.8.3	Long term stability studies data of diluent shall be submitted as per Zone Iva conditions till claimed shelf life i.e., 60 months.	Firm has submitted long term stability studies data of three batches as per Zone IVa for 18 months.

Decision: Deferred for regulatory status of applied formulation in other reference regulatory authorities alongwith its indications, precautions, contra indications etc.

122.	Name, address of Applicant / Importer	M/s Sitech Pharmaceuticals Pvt Ltd. SF 07 and 09 Floor Shahnaz Arcade 158- Main Shaheede Millat Road, BYJCHS, Karachi, Pakistan
	Details of Drug Sale License of importer	License No: 1141 Address: Ground floor House No. 43-2B-1 Waja Abdul Sattar Masti khan Road block-6 P.E.C.H.S Karachi. Address of Godown: SF 07 and 09, 4th Floor Shahnaz Arcade 158- Main Shaheed e Millat Road, BYJCHS, Karachi, Pakistan Validity: 16 November 2023

		Status: License to sell drugs by way of Wholesale. Validity: 01-01-2022.
	Name and address of marketing authorization holder (abroad)	Derma Pharma S.A.R.L. 25, Rue la Boetie, 75008 Paris – France
	Name, address of manufacturer(s)	**Manufacturer:** Laboratorio Farmaceutico S.I.T S.r.l Via Cavour 70, 27035 Mede (PV), Italy **Exporter:** Medexport Italia Via Alcide De Gasperi 35, 00165 Rome (RM), Italy
	Name of exporting country	Italy
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted copy of legalized CoPP certificate (No. 036387) issued by Chamber de Commerce et d Industrie de Region paris Iie-de-France dated 06-August-2020**.** The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspections. The name of importing country on CoPP is mentioned as Pakistan. **Applicant of Certificate:** DB-Pharma -1 Bis, rue du Commandant Riviere-94210 La Varenne Saint -Hilaire.
	Details of letter of authorization / sole agency agreement	Letter of authorization issued by Laboratorio Farmeceutico SIT Specialita Igienico terapeutiche S.r.l Italy in name of M/s Sitech pharmaceuticals for the import of marketing of Dedrogyl 15mg/100mml oral soulton drops in Pakistan, being exported from M/s Consorzio medexport italia.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy.No 7174 dated 04-03-2021
	Details of fee submitted	Rs.100,000/- dated 24-02-2021
	The proposed proprietary name / brand name	**Dedrogyl 10 ml oral drops**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Calcifediol as monohydrate…15mg
	Pharmaceutical form of applied drug	Oral Drops Solution
	Pharmacotherapeutic Group of (API)	Vitamin D
	Reference to Finished product specifications	Eu. Ph. Current Edition
	Proposed Pack size	1's
	Proposed unit price	As per Pricing Policy
	The status in reference regulatory authorities	Approved by ANSM of France
	For generic drugs (me-too status)	--
	Module-II (Quality Overall Summary)	Firm has submitted summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Carbogen Amcis B.V. Nieuweweg 2A, Veenendaal, 3901BE, Netherlands
	Module-III Drug Substance:	Firm has submitted Certificate of Suitability (R1-CEP 1998-059 - Rev 08) issued by EDQM on 07-01-2022.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturers, manufacturing process and control of critical steps validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, characterization of impurities, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not submitted
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Amber glass-type III
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30^{o}C ±2^{o}C / 65% ± 5% RH for 36 months

Evaluation by PEC:
Initially the application was submitted from M/s Sitech Pharmaceuticals Pvt Ltd. dated 04-03-2021, while subsequently M/s Angelini Pharmaceuticals (Pvt) Ltd. has submitted the new Form 5F of same product to be imported from the same principal along with the documents detailed below:

Name, address of Applicant / Importer	M/s Angelini Pharmaceuticals (Pvt) Ltd. 44 Commercial Imperial Block, Paragon City Barki Road, Lahore, Pakistan
Details of Drug Sale License of importer	License No: 05-352-0068-047191D Address: 44 Commercial Imperial Block, Paragon City, Barki Road, Lahore, Pakistan Address of Godown: Same as above Validity: 16 November 2023 Status: License to sell drugs as distributor
Dy. No. and date of submission	Dy.No 31443 dated 15-11-2021
Details of fee submitted	Rs.75,000/- dated 22-10-2021
Details of Letter of Withdrawal from M/s Sitech	Firm has submitted copy of letter from M/s Sitech Pharmaceutical Pvt. Ltd., dated 11-10-2021 stating that "We SiTech Pharmaceuticals (Pvt.) Ltd withdrew from our application of registration of Dedrogyl 10ml oral drops in favor of Angelini Pharmaceuticals (Pvt} Ltd."
Details of NOC from M/s Sitech	Firm has submitted copy of letter from M/s Sitech Pharmaceutical Pvt. Ltd., dated 06-05-2021 stating that "We have submitted our application for registration of drug Dedrogyl 10ml oral drops (Calcifediol l5mg/l00ml) to DRAP Pharma Evaluation Cell on February 24, 2021. Now the exporter and our principal M/s Medexport Italia Rome, Italy has requested to withdraw the application, and instead will be resubmitted by their new distributor/importer M/s. Angelini Pharmaceuticals (Pvt) Ltd. having office at 44 Commercial Imperial Block, Paragon City, Barki Road Lahore. This decision is with our mutual understanding and consent. We have no objection for this and DRAP may process the registration application of drug Dedrogyl 10ml oral drops (Calcifediol 15mg/100ml) submitted by new distributor. We would be grateful, if you please consider & process application of above product submitted by M/s. Angelini Pharmaceuticals (Pvt) Ltd."
Details of letter of authorization / sole agency agreement from Exporter	Letter of authorization issued by Laboratorio Farmeceutico SIT Specialita Igienico terapeuti S.r.l Italy in name of M/s Angelini Pharmaceuticals (Pvt) Ltd. 44 Commercial Imperial Block, Paragon City Barki Road, Lahore, Pakistan for the import of marketing of Dedrogyl 15mg/100mml oral

	soulton drops in Pakistan, being exported from M/s Medexport italia. An authorization letter from M/s Med Export Italia has also been submitted stating as under: "We hereby confirm that our previous authorization to M/s SiTech Pharmaceuticals (Pvt) Ltd. located at SF - 07, 4th Floor, Shahnaz Arcade 158, Shaheed-e-Millat Road, BYJCHS, Karachi Pakistan is no longer valid and now M/s Angelini Pharmaceuticals (Pvt} Ltd. having office at 44 Commercial Imperial Block, Paragon City, Barki Road, Lahore, Pakistan is authorized to import, distribute, market and also handle regulatory matters of this product in the territory of Pakistan."

The letter of authorizations has been issued form the drug product manufacturer i.e., Laboratorio Farmaceutico S.I.T S.r.l Via Cavour 70, 27035 Mede (PV), Italy and Exporter i.e., M/s Medexport Italia Via Alcide De Gasperi 35, 00165 Rome (RM), Italy while submitted COPP mentions Market Authorization holder as Derma Pharma S.A.R.L. 25, Rue la Boetie, 75008 Paris – France.

Decision: Registration Board decided as follows:

a. Acceded the request of M/s Sitech Pharmaceutical Pvt. Ltd. for withdrawal of their submitted application of Dedrogyl 10 ml oral drops dated 04-03-2021 vide Dy. No 7174 and declared it as disposed off.

b. Deferred the application of M/s Angelini Pharmaceuticals (Pvt) Ltd. 44 Commercial Imperial Block, Paragon City Barki Road, Lahore, Pakistan for submission of complete dossier of applied product.

Case no. 05 Registration applications of drugs for which stability study data is submitted

Sr. No.	Name & Address of Manufacturer / Applicant	Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification	Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size	International Availability / Local Availability GMP Inspection Report Date & Remarks
123.	M/s Wilshire Laboratories, 124/A, Kotlakhpat, Indus: Area, Township scheme, Lahore.	Kanlif-M Tablet Each film coated tablet contains: - Canagliflozin …50mg Metforimn HCl …… 500mg (Anti-diabetic)	Form 5-D Diary No. 19627 dated 31-10-2017 Rs. 50,000/- dated 31-10-2017 10's,20's,30's50's ; As per SRO	Invokamet approved by USFDA
	Evaluation by PEC: The firm has submitted stability data along with documents as per checklist approved in 278th meeting of Registration Board.			

	Details of submitted data are as under: (Dy.# 52 dated 01-01-2019)

STABILITY STUDY DATA			
Drug	Kanlif-M Tablet 50/500		
Name of Manufacturer	M/s Wilshire Laboratories, 124/A, Kotlakhpat, Indus: Area, Township scheme, Lahore		
Manufacturer of API	**Canagliflozin hemihydrate:** M/s Nantong Chanyoo Pharmatech Co., Ltd., Jiangsu province, China **Metformin HCl:** M/s Ipca laboratories Ltd., Aurangabad, Maharashtra, India.		
API Lot No.	**Canagliflozin hemihydrate:** RD-CLF (hemihydrate)-201705051 **Metformin HCl:** 6417ML2RMI		
Description of Pack (Container closure system)	Alu-Alu foil		
Stability Storage Condition	Real time : 30˚C ± 2˚C / 75% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3,4,6 months Real Time: 0,3,6 months		
Batch No.	T001	T002	T003
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	02-2018	02-2018	02-2018
Date of Initiation	26-2-2018	26-02-2018	26-02-2018
No. of Batches	03		

Sr. No.	**Name & Address of Manufacturer / Applicant**	**Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification**	**Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size**	**International Availability / Local Availability** **GMP Inspection Report Date & Remarks**
124.	M/s Wilshire Laboratories, 124/A, Kotlakhpat, Indus: Area, Township scheme, Lahore.	Kanlif-M Tablet Each film coated tablet contains:- Canagliflozin …50mg Metforimn HCl…… 1000mg (Anti-diabetic)	Form 5-D Diary No. 19632dated 31-10-2017 Rs. 50,000/- dated 31-10-2017 10's,20's,30's50's ; As per SRO	Invokamet approved by USFDA

STABILITY STUDY DATA	
Drug	Kanlif-M Tablet 50/1000
Name of Manufacturer	M/s Wilshire Laboratories, 124/A, Kotlakhpat, Indus: Area, Township scheme, Lahore
Manufacturer of API	**Canagliflozin hemihydrate:** M/s Nantong Chanyoo Pharmatech Co., Ltd., Jiangsu province, China

	Metformin HCl: M/s Ipca laboratories Ltd., Aurangabad, Maharashtra, India.		
API Lot No.	**Canagliflozin hemihydrate:** RD-CLF (hemihydrate)-201705051 **Metformin HCl:** 6417ML2RMI		
Description of Pack (Container closure system)	Alu-Alu foil		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,3,6 months Real Time: 0,3,6 months		
Batch No.	T001	T002	T003
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	02-2018	02-2018	02-2018
Date of Initiation	26-2-2018	26-02-2018	26-02-2018
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided following documents as per checklist approved by the Registration Board in its 293rd Meeting:

Sr.#	Data requirement	Firm's submission
1.	Reference of previous approval of applications with stability study data of the firm.	Firm has referred to onsite inspection report of their product "Velbuvir 400/100mg Tablet", which was presented in 292nd meeting of Registration Board. Date of inspection: 23-05-2019 According to the report, following points were confirmed: a) Firm has HPLC software 21CFR compliant. b) Audit teai lreports were available. c) Firm's stability chambers were calibrated and equipped with digital data loggers and alarms.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted as per following details: **Canagliflozin hemihydrate:** RD-CLF (hemihydrate)-201705051 **Metformin HCl:** 6417ML2RMI
3.	Method used for analysis of API along with COA.	Analytical method for both APIs have been submitted from relevant API manufacturers as well as from M/s Wilshire Laboratories.
4.	Stability study data of API from API manufacturer	**Canagliflozin hemihydrate:** Firm has submitted both accelerated (40°C ± 2°C & 75± 5%RH) stability studies & long term (30°C ± 2°C & 65%± 5%RH) stability studies reports of three batches. **Metformin HCl:**

<table>
<tr><td></td><td></td><td>Firm has submitted both accelerated (40°C ± 2°C & 75±5%RH) stability studies (6 months) & long term (30°C ± 2°C & 65%±5%RH) stability studies (60 months) reports of three batches.</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Canagliflozin hemihydrate: Manufacturing License (No. Su 20160512) for M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si road, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province, China issued by Jiangsu Food & Drug Administration valid upto 2-12-2025.
Metformin HCl: Copy of GMP certificate (Certificate#. NEW-WHO-GMP/CERT/AD/104179/2021/11/37725) issued by FDA Maharshtra for M/s Ipca Laboratories Ltd., H-4, MIDC, Waluj, Aurangabad, 431136, Mahrashtra, India valid upto 27-10-2024.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>• Canagliflozin hemihydrate: Copy of commercial invoice (Invoice# CYI18153) dated 20-02-2017 has been submitted. (Quantity: 6 Kg)
Copy of Goods declaration has also been submitted.
Metformin HCl: Copy of commercial invoice (Invoice# 21/1212016) attested by AD DRAP I&E dated 02/01/2017. (Quantity: 2000 Kg)</td></tr>
<tr><td>7.</td><td>Authorized Protocols/SOP for the development & stability testing of trial batches.</td><td>Firm has submitted SOP for new product development & stability protocol.</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Drug product analytical method has been submitted.</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Firm has referred to the formulation of innovator product for establishing drug-excipient compatibility.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>Firm has provided Batch Manufacturing Record for all the three batches of both strengths.</td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution studies have been submitted in three physiological buffers i.e., pH 1.2, pH 4.5 & pH 6.8 against the innovator product of Invoka Met, with acceptable values of f_2.
<table>
<tr><th></th><th>Trial Product</th><th>Innovator product</th></tr>
<tr><td>Name</td><td>Kanlif-M 50/500 tablet</td><td>Invoak met 50/500 tablet</td></tr>
<tr><td>Batch #</td><td>T-001</td><td>234751</td></tr>
</table>
<table>
<tr><th></th><th>Trial Product</th><th>Innovator product</th></tr>
<tr><td>Name</td><td>Kanlif-M 50/1000 tablet</td><td>Invoak met 50/1000 tablet</td></tr>
<tr><td>Batch #</td><td>T-001</td><td>264873</td></tr>
</table>
</td></tr>
</table>

12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record for both accelerated & long-term stability studies, including chromatograms, raw data sheets etc..
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Audit trail reports have not been submitted instead a document titled "Declaration of Software Quality" from Agilent technologies has been submitted.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	--

Remarks of Evaluator^{II}:

Sr.#	Observation	Firm's response
1.	Method of dilution preparation for Assay test mentioned in "SOP for New Product Development" is different from that mentioned in "Analytical Test method for Kanlif-M 50/1000 tablets (Document# WS-QC-TM-K-08)".	Revised SOP for product development has been submitted as per the product test method.
2.	Dissolution limits of time of innovator are 20 minutes for metformin while applicant has proposed 30 minutes and 45 minutes for Canagliflozin instead of 30 minutes.	Firm has referred to the 293rd meeting of registration Board while cuggestinig that the appliedproduct falls in the category of immediate relase drugs and now has revised their specifications of dissolution as per innovator's literature.
3.	Complete raw data sheets (including information of sample & standard weights, dilution factors, calculation formulas etc.) for the whole stability studies shall be submitted.	Submitted.
5.	GMP certificate for Metformin HCl has been submitted of M/s Ipca laboratories, Madhya Paradesh, whreas API has been imported form M.s IPCA Labs Aurangabad.	Copy of GMP certificate (Certificate#. NEW-WHO-GMP/CERT/AD/104179/2021/11/37725) issued by FDA Maharshtra for M/s Ipca Laboratories Ltd., H-4, MIDC, Waluj, Aurangabad, 431136, Mahrashtra, India valid upto 27-10-2024.
7.	Submitted batch manufacturing records include dispensing sheets only.	Complet BMRs including details of compression, coating & packaging have been submitted for all three stability batches of both strengths.
8.	Audit trial reports have not been submitted instead a document titled "Declaration of Software Quality" from Agilent technologies has been submitted.	Digital Sytem activity log report has been submitted for the duration of stability studies.
9.	Digital data logger for temperature and humidity monitoring of stability chambers has not been submitted instead manual record of stability chambers has been submitted for both accelerated and long term conditions.	Submitted.

Decision: Registration Board approved Kanlif-M Tablet 50/500mg & Kanlif-M Tablet 50/1000mg with Innovator's specifications.

- **Manufacturer shall submit fee of Rs. 7500/- for each strength for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Furthermore, the Board diretced the firm to adopt dissolution specifications as per innovator for commercial batches.**

125.	M/s Winlet Pharmaceuticals. 30-km, Lahore Sargodha Road, Lahore	Winzole Capsule 30mg Each Delayed Release capsule contains:- Dexlansoprazole (as enteric coated pellets) ….. 30mg	Form-5 Dy.No 39627 dated 03-12-2018 Rs.20,000/- dated 03-12-2018	Dexilant capsule delayed release (30mg, 60mg). USFDA approved. Me-too could not be confirmed.
126.	M/s Winlet Pharmaceuticals. 30-km, Lahore Sargodha Road, Lahore	Winzole Capsule 60mg Each Delayed Release capsule contains:- Dexlansoprazole (as enteric coated pellets) ….. 60mg	Form-5 Dy.No 39627 dated 03-12-2018 Rs.20,000/- dated 03-12-2018	

STABILITY STUDY DATA

Drug	Winzole Capsule 30mg and 60mg		
Name of Manufacturer	M/s Winlet Pharmaceuticals. 30-km, Lahore Sargodha Road, Lahore		
Manufacturer of API	Dexlansoprazole 22.5% DDR pellets: M/s Vision Pharmaceuticals, Islamabad		
API Lot No.	DLP519		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (months) Real Time: 0, 3, 6 (months)		
	For 30mg capsule		
Batch No.	001	002	003
Batch Size	1500	1500	1500
Manufacturing Date	01.2020	01.2020	01.2020
No. of Batches	03		
Time Period	Real time: 6 months Accelerated: 6 months		
	For 60mg capsule		
Batch No.	001	002	003
Batch Size	1500	1500	1500

Manufacturing Date	01.2020	01.2020	01.2020
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	COA of API	Yes
2.	Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	Dexlansoprazole 22.5% DDR pellets: Copy of GMP certificate issued to M/s Vision Pharmaceuticals, Islamabad by DRAP, valid till 10.02.2022.
3.	Protocols followed for conduction of stability study and details of tests.	Yes
4.	Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc.	Yes
5.	Documents confirming import of API etc.	NA
6.	All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Yes
7.	Commitment to continue real time stability study till assigned shelf life of the product.	Yes
8.	Commitment to follow Drug Specification Rules, 1978.	Yes

On-site inspection Report

Name of Manufacturer	M/s Winlet Pharmaceuticals.
Physical Address	30km Lahore Sargodha Road.
Drug Manufacturing License No. and validity	000874 by way of formulation Valid till 20-02-2023.
Date of Inspection.	14-06-2021
Purpose of Inspection	Verification of Authenticity of Stability Data for Purpose of Registration of Drugs with reference to DRAP's letter No. F.1-2/2020-PEC dated 16-03-2021 .
Name of Inspector	1. Mr. Muzammil Waheed. (Director DTL, Faisalabad) 2. Ms. Maham Misbah Assistant Director, DRAP, Lahore.
Name of firm Representatives	1. Mr. Khawaja Shahid Iqbal (CEO) 2. Ms. Misbah Khawaja (Director) 3. Dr. Qamar Soni (Director) 4. Mr. Gulfam Soni (Director) 5. Mr. Kaleem ullah (Production Incharge) 6. Mr. Aslam Hayat (Quality Control Manger)

Sr. No	Question	Observations
1	Whether the firm has documents confirming import of API?	Not Applicable. Firm had locally purchased Dexlansoprazol 22. 5pc DDR pellets from M/s. Vision Pharmaceuticals. (Batc No. DLP519 Manufacturing date 09-19 Expiry date 08-22)
2	What was the rationale behind selecting the particular manufacturer of API?	The rationale behind selecting the manufacturer was the cGM status of M/s Vision Pharmaceuticals, as informed by th management of the firm.
3	Whether documents confirm the import of API reference standard and impurity standards?	Not applicable. Firm had purchased secondary workin standard of API and impurity standards from princip manufacturer.
4	Whether the firm has certificate of Analysis of the API, reference standards and impurity standards from exporter?	Firm had certificates of analysis for the API, working standar and impurity standards.
5	Whether the firm has any approval of API or GMP certificate of API manufacturer issued by regulatory authority of country of origin?	Firm had valid cGMP compliance certificate of M/s Visio Pharmaceuticals issued by DRAP.
6	Whether firm use API manufacturer method of testing?	Yes.
7	Whether firm has stability studies reports on API?	Yes.
8	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	Degradation products had not been quantified.
9	Whether firm has method for quantifying the impurities in the API?	Yes, provided by the vendor.
10	Whether firm has some remaining quantities of the API, its reference standard and impurities standards?	Firm had remaining quantities of API.
11	Whether firm has used pharmaceutical grade excipients?	No excipients used in the process. Firm is only filling the pelle in capsules.
12	Whether firm has documents confirming the import of the used excipients?	Not applicable.
13	Whether firm has test reports and other records on the excipients used?	Not applicable.
14	Whether firm has written and authorized protocols for the development of capsules?	Firm had written protocols for product development. Howeve the protocols required improvement.

15	Whether firm has performed Drug-excipient compatibility studies?	Not applicable.
16	Whether firm has performed comparative dissolution studies?	Firm had not procured innovator's product. Comparative dissolution studies had been performed against Razodex capsules (Getz Pharma)
17	Whether firm has product development (R&D) section?	No. Capsules were filled with pellets using semi-automatic capsule filling machine installed in the commercial production area.
18	Whether firm has necessary equipment available in product development section for development of finished product?	Firm was advised to obtain capsule polishing machine.
19	Are the equipment in product development section qualified?	Equipment of commercial production was used. Installation and Operational qualification had been done for the equipment, as per documents shown to the panel. Performance qualification had not been done.
20	Whether firm has proper maintenance / calibration / re-qualification program for the equipment used in PD section?	Available for major equipment used in product development.
21	Whether firm has qualified staff in product development section with proper knowledge and training in product development?	No. Separate staff for product development was not available.
22	Whether firm has manufactured three stability batches for the stability studies of finished product tablets as required?	Firm had manufactured three stability batches each for the stability studies of finished products Dexlansoprazole 30mg and Dexlansoprazole 60mg. BMRs were shown to the panel. The firm was advised to improve its BMRs.
23	What was the criteria for fixing the batch size of stability batches?	As stated by the firm's management, criteria for fixing batch size of stability batches was the available quantity of API and DRAP guidelines for stability testing.
24	Whether firm has complete record of production of stability batches?	Firm had BMRs of all relevant stability batches.
25	Whether firm has protocols for stability testing of stability batches?	Yes. However, the conformance to protocols required improvement.
26	Whether firm has developed and validated the method for testing of stability batches?	Firm had used the testing method of vendor of pellets. Validation report was shown to the panel.
27	Whether firm has method transfer studies in case when the method of testing being used by your firm is given by any other lab?	No method transfer protocol was followed.
28	Whether firm has documents confirming the qualification of equipments / instruments being	Firm was advised to get testing equipment calibrated from authorized body, without calibration the test results are not acceptable. Further the firm was advised to attach printers with all weighing balances, pH meter and conductivity meter for

	used in the test and analysis of API and the finished drug?	traceability and also advised to conduct daily verification of weighing balances.
29	Whether firm has stability indicating method of analysis?	No.
30	Whether firm has HPLC software 21CFR compliant?	No. (amendments made in the data could not be detected without CFR 21 compliant software). Data used in the stability studies is highly unreliable
31	Whether firm could show you Audit Trail reports ?	Yes, however, time and date could be changed in the HPLC software.
32	Whether firm has some remaining quantities of degradation products and stability batches?	Firm had remaining quantities of stability batches. Degradation products had not been isolated.
33	Whether firm has commitment batches kept on stability testing?	Yes.
34	Whether firm has valid calibration status for the equipment used in production and analysis?	Firm was advised to get testing equipment calibrated from authorized body, further advised to attach printers with all weighing balances, pH meter and conductivity meter and also advised to conduct daily verification of weighing balances.
35	Do proper and continuous monitoring and control are available for stability chamber?	Firm was advised to install proper alarm system in the stability chambers in order to monitor and control excursions. Excursions were seen in the log of data of stability chambers (both real time and accelerated study chambers)
36	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Management of the firm was given several advices related to cGMP. It was advised to: Maintain proper ledgers of packing materials, improve the BMRs and make them more comprehensive, maintain record of deviations, improve testing protocols and SOPs, develop and maintain analyst logbooks for raw data, procure traceable working and impurity standards, impart training of analysts, develop a fully functional QA department, conduct complete testing of primary packing materials, conduct supplier evaluation of vendors of primary packaging materials, procure traceable dead weights for verification of balances, use PDA detector instead of SD-UVA detector.

Remarks:-

With reference to DRAP, Islamabad letter No. F.1-2/2020-PEC dated 16-03-2021 the inspection of M/s Winlet Pharmaceuticals, 30km Lahore-Sargodha Road was conducted by the panel with the remarks that authenticity of the stability data could not be verified without equipment qualification, method transfer protocols and CFR compliant Software. Submitted for further necessary action, please.

Decision of 316th meeting: Registration Board deferred the case for submission of clarification form the firm upon following observations reported by Inspection panel:

- No method transfer protocol was followed for the drug product analytical method.
- Performance qualification had not been done for the manufacturing equipments used in trial batch manufacturing.
- Firm was advised to get testing equipment calibrated from authorized body, without calibration the test results are not acceptable.
- Amendments made in the data could not be detected without CFR 21 compliant software). Data used in the stability studies is highly unreliable
- Authenticity of the stability data could not be verified without equipment qualification, method transfer protocols and CFR compliant Software.

Firm's response:

Observations	Firm's response
No method transfer protocol was followed for the drug product analytical method.	We have already opted comparative analytical testing method for studies of Dexlansorpzole DDR Pellets provided by Manufacturer (Vision Pharma), because the same batch sample was tested in our laboratory as previously tested in manufacturer lab, and the test results of both lab are comparable to satisfactory level (Assay, dissolution & CDP etc). Now we have documented this method transfer studies protocol for commercial scale production of Winzole 30mg & 6mg capsules.
Performance qualification had not been done for the manufacturing equipments used in trial batch manufacturing.	The manufacturing equipments (i.e capsules filling machine, blister machine which are used in trial batch manufacturing are qualified) and the Performance qualification is done and available for all manufacturing equipments and updated it for commercial scale production of Winzole 30mg & 6mg capsules.
Firm was advised to get testing equipment calibrated from authorized body, without calibration the test results are not acceptable.	All the major equipments are now calibrated from authorized bodies and the standard using for calibration are National Institute of Standards and Technology (NIST) traceable.
Amendments made in the data could not be detected without CFR 21 compliant software). Data used in the stability studies is highly unreliable	The HPLC performance of the stability studies was evident from the chromatographic record in the system and was also traceable from the respective equipment log book. Now the HPLC binary gradient system with 21 CFR compliance software has also been installed and now in working condition.
Authenticity of the stability data could not be verified without equipment qualification, method transfer protocols and CFR compliant Software.	It is humbly submitted that the authenticity of the stability data is traceable through the available records in the HPLC system, equipment utility log books, lab note books & other records available at the plant. For the stability studies data (submitted for evaluation) of Winzole 30mg & 60mg capsules, all the data, calculations, are available with date in equipments/machine log books , lab note books and the panel inspection team had checked this data for authenticity in detail. It is also humbly submitted that we have done the qualification of equipments and the record is hereby submitted for ready reference.

Decision of 320th meeting: Registration Board approved Winzole Capsule 30mg & Winzole Capsule 60mg
with Innovator's specifications.

- **Manufacturer shall submit fee of Rs. 7500/- for each strength for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

127.	**Name and address of manufacturer / Applicant**	**M/s Pharmevo Private Limited., Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi**
	Brand Name +Dosage Form + Strength	**IRMAX 100+5MG TABLET**
	Composition	Each film coated tablet contains: Irbesartan…….100mg Amlodipine ...5mg
	Diary No. Date of R& I & fee	Dy. No 1660 dated 29-Aug-2013, Rs.50,000/-
	Pharmacological Group	Antidiabetic
	Type of Form	Form-5D
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	7's, 10's, 14's, 20's, 28's, 30's & As per PRC
	Approval status of product in Reference Regulatory Authorities	AIMIX Approved by JAPAN
	Me-too status (with strength and dosage form)	Not Applicable
	GMP status	GMP inspection dated 23-02-2018 showed that the firm was considered to be operating at an acceptable level of compliance with GMP standards
	Remarks of the Evaluator :	
	Previous decision: The application was initially presented in 260th meeting of Registration Board wherein case was deferred for proof of approval status of same formulation in reference countries and Pakistan. Subsequently firm referred to the Aimix tablet approved by PMDA of Japan and submitted stability studies data against which following observations were communicated to firm: • Valid GMP certificate of M/s Prudence Pharma Chem., Gujarat, India shall be submitted. • Content Uniformity test has not been performed for Amlodipine. Justification shall be submitted. • Justification/Clarification needed as in contrary to Japanese Pharmacopoeia monograph for applied formulation firm has submitted different specifications and parameters for the Assay & Dissolution test. • Firm had submitted revised stability studies data along with documents as per exemption checklist, detailed as below:	

STABILITY STUDY DATA	
Drug	IRMAX 100+5MG TABLET
Name of Manufacturer	M/s Pharmevo Private Limited., Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi.
Manufacturer of API	**Irbesartan:** M/s Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan Duqiao, Linhai, Zhejiang **Amlodipine:**

		M/s Prudence Pharma Chem, Plot No 7407, B/H, Lyka Lab, GIDC. INDIA.		
API Lot No.		Irbesartan: C5055-20-13R Amlodpine: AMB/194/10/20		
Description of Pack (Container closure system)		Alu-Alu Blister		
Stability Storage Condition		Real time : 30°C ± 2° C / 75% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated:0,1,2,3,4,6 (month) Real Time: 0,3,6, (month)		
Batch No.		**21PD-3572-11-T**	**21PD-3575-12-T**	**21PD-3576-13-T**
Batch Size		2500 Tablet	2500 Tablet	2500 Tablet
Manufacturing Date		3-2021	3-2021	3-2021
Date of Initiation		4-2021	4-2021	4-2021
No. of Batches		03		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT				
Documents To Be Provided		**Status**		
1	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product Erli Plus XR Tablet 5/1000mg, 10/1000mg, 12.5/1000mg & 25/1000mg (Empagliflozin + Metformin HCl XR) which was conducted on 05th December, 2019 and were presented in 293rd meeting of Registration Board held on 6th -8th Jan, 2020. According to the report following points were confirmed. • Firm has 21 CFR compliant HPLC software. • Firm has audit trail reports available. • Firm possesses stability chambers with digital data loggers.		
2	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Irbesartan:** M/s Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan Duqiao, Linhai, Zhejiang. API COA & FPP COA Provided **Amlodipine:** M/s Prudence Pharma Chem, Plot No 7407, B/H, Lyka Lab, GIDC. INDIA. API COA & FPP COA Provided		
3	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Submitted.		
4	Stability study data of API from API manufacturer	Irbesartan- LPGA: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 75±5%RH) stability study reports of 03 batches Amlodipine: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches		
5	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Irbesartan: Copy of Drug manufacturing license (License no. ZJ210061) issued by ZHEJIANG MEDICAL PRODUCTS ADMINISTRATION submitted, valid up to 09-May-2024. Amlodipine:		

<table>
<tr><td></td><td></td><td>Copy of Drug manufacturing license (License no. S-GMP/20051984) for Food & Drug Administration Gujrat Estate India, valid upto 18-05-2022</td></tr>
<tr><td>6</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Irbesartan: Copy of form 6, form 7 & Commercial Invoice from M/s Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan Duqiao, Linhai, Zhejiang. is submitted attested by AD(Karachi).
Amlodipine:
Copy of Commercial Invoice from M/s Prudence Pharma Chem, Plot No 7407, B/H, Lyka Lab, GIDC. INDIA.is submitted attested by AD (Karachi).</td></tr>
<tr><td>7</td><td>Protocols followed for conduction of stability study</td><td>Submitted.</td></tr>
<tr><td>8</td><td>Method used for analysis of FPP</td><td>Submitted.</td></tr>
<tr><td>9</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Same excipients used as used by innovator.</td></tr>
<tr><td>10</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted copy of Trial batch manufacturing record. Details are as under:
<table>
<tr><th>Batch no.</th><th>Batch Size</th><th>Mfg. Started</th></tr>
<tr><td>21PD-3572-11-T</td><td>2500</td><td>03-2021</td></tr>
<tr><td>21PD-3572-11-T</td><td>2500</td><td>03-2021</td></tr>
<tr><td>21PD-3572-11-T</td><td>2500</td><td>03-2021</td></tr>
</table></td></tr>
<tr><td>11</td><td>Record of comparative dissolution data (where applicable)</td><td>As per literature of the innovator available with the firm & as per Japanese Pharmacopeia.
The same has been demonstrated by the firm on their product i.e. the product dissolve as per monograph.
Therefore, f2 calculations is not necessary.</td></tr>
<tr><td>12</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted.</td></tr>
<tr><td>13</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Firm has submitted audit trail reports of stability studies of applied formulation.</td></tr>
<tr><td>14</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Submitted.</td></tr>
<tr><td>128.</td><td>Name and address of manufacturer / Applicant</td><td>M/s Pharmevo Private Limited., Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi</td></tr>
<tr><td></td><td>Brand Name +Dosage Form + Strength</td><td>IRMAX 100+10mg TABLET</td></tr>
<tr><td></td><td>Composition</td><td>Each film coated tablet contains:
Irbesartan…….100mg
Amlodipine ...10mg</td></tr>
<tr><td></td><td>Diary No. Date of R& I & fee</td><td>Dy. No 1656 dated 29-Aug-2013, Rs.50,000/-</td></tr>
<tr><td></td><td>Pharmacological Group</td><td>Antidiabetic</td></tr>
<tr><td></td><td>Type of Form</td><td>Form-5D</td></tr>
<tr><td></td><td>Finished product Specifications</td><td>Manufacturer’s specifications</td></tr>
<tr><td></td><td>Pack size & Demanded Price</td><td>7's, 10's, 14's, 20's, 28's, 30's & As per PRC</td></tr>
</table>

	Approval status of product in Reference Regulatory Authorities	AIMIX Approved by JAPAN
	Me-too status (with strength and dosage form)	Not Applicable
	GMP status	GMP inspection dated 23-02-2018 showed that the firm was considered to be operating at an acceptable level of compliance with GMP standards
	Remarks of the Evaluator:	
	Now the firm has submitted stability data detailed as under:	

STABILITY STUDY DATA			
Drug	IRMAX 100+10MG TABLET		
Name of Manufacturer	M/s Pharmevo Private Limited., Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi.		
Manufacturer of API	**Irbesartan:** M/s Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan Duqiao, Linhai, Zhejiang **Amlodipine:** M/s Prudence Pharma Chem, Plot No 7407, B/H, Lyka Lab, GIDC. INDIA.		
API Lot No.	Irbesartan: C5055-20-13R Amlodpine: AMB/194/10/20		
Description of Pack (Container closure system)	Alu-Alu Blister		
Stability Storage Condition	Real time : 30°C ± 2° C / 75% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated:0,1,2,3,4,6 (month) Real Time: 0,3,6, (month)		
Batch No.	**21PD-3573-13-T**	**21PD-3577-14-T**	**21PD-3578-15-T**
Batch Size	2500 Tablet	2500 Tablet	2500 Tablet
Manufacturing Date	3-2021	3-2021	3-2021
Date of Initiation	4-2021	4-2021	4-2021
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
	Documents To Be Provided	**Status**
1	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product Erli Plus XR Tablet 5/1000mg, 10/1000mg, 12.5/1000mg & 25/1000mg (Empagliflozin + Metformin HCl XR) which was conducted on 05th December, 2019 and were presented in 293rd meeting of Registration Board held on 6th -8th Jan, 2020. According to the report following points were confirmed. • Firm has 21 CFR compliant HPLC software. • Firm has audit trail reports available. • Firm possesses stability chambers with digital data loggers.
2	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Irbesartan:** M/s Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan Duqiao, Linhai, Zhejiang. API COA & FPP COA Provided **Amlodipine:** M/s Prudence Pharma Chem, Plot No 7407, B/H, Lyka Lab, GIDC. INDIA.

<table>
<tr><td></td><td></td><td>API COA & FPP COA Provided</td></tr>
<tr><td>3</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Submitted.</td></tr>
<tr><td>4</td><td>Stability study data of API from API manufacturer</td><td>Irbesartan- LPGA: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 75±5%RH) stability study reports of 03 batches
Amlodipine:
The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches</td></tr>
<tr><td>5</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Irbesartan: Copy of Drug manufacturing license (License no. ZJ210061) issued by ZHEJIANG MEDICAL PRODUCTS ADMINISTRATION submitted, valid up to 09-May-2024.
Amlodipine:
Copy of Drug manufacturing license (License no. S-GMP/20051984) for Food & Drug Administration Gujrat Estate India, valid upto 18-05-2022</td></tr>
<tr><td>6</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Irbesartan: Copy of form 6, form 7 & Commercial Invoice from M/s Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan Duqiao, Linhai, Zhejiang. is submitted attested by AD(Karachi).
Amlodipine:
Copy of Commercial Invoice from M/s Prudence Pharma Chem, Plot No 7407, B/H, Lyka Lab, GIDC. INDIA.is submitted attested by AD (Karachi).</td></tr>
<tr><td>7</td><td>Protocols followed for conduction of stability study</td><td>Submitted.</td></tr>
<tr><td>8</td><td>Method used for analysis of FPP</td><td>Submitted.</td></tr>
<tr><td>9</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Same excipients used as used by innovator.</td></tr>
<tr><td>10</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted copy of Trial batch manufacturing record. Details are as under:
<table>
<tr><th>Batch no.</th><th>Batch Size</th><th>Mfg. Started</th></tr>
<tr><td>21PD-3573-13-T</td><td>2500</td><td>3-2021</td></tr>
<tr><td>21PD-3573-13-T</td><td>2500</td><td>3-2021</td></tr>
<tr><td>21PD-3573-13-T</td><td>2500</td><td>3-2021</td></tr>
</table></td></tr>
<tr><td>11</td><td>Record of comparative dissolution data (where applicable)</td><td>As per literature of the innovator available with the firm & as per Japanese Pharmacopeia.
The same has been demonstrated by the firm on their product i.e. the product dissolve as per monograph. Therefore, f2 calculations is not necessary.</td></tr>
<tr><td>12</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted.</td></tr>
<tr><td>13</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Firm has submitted audit trail reports of stability studies of applied formulation.</td></tr>
<tr><td>14</td><td>Record of Digital data logger for temperature and humidity</td><td>Submitted.</td></tr>
</table>

	monitoring of stability chambers (real time and accelerated)	

Remarks by Evaluator[ii]

Firm has not submitted comparative dissolution data for both strengths while referring to the batch release data performed as per JP monograph.

Decision of 317th meeting: Registration Board deferred the applications of IRMAX 100+5mg tablet & IRMAX 100+10mg tablet for submission of Comparative Dissolution Profile data against the relevant strength of Innovator drug product.

Firm's response: Firm ha ssubmitted CDP studies gainst the innovator product of Iluamix tablets manufactured by M/s Sawai Pharmaceutical Co., Ltd., Japan, in three dissolution medium of Physiological pH 1.2, 4.5 & 6.8, with acceptable results for similarity factor f2.

Decision: Registration Board approved Irmax 100+5mg tablet & Irmax 100+10mg tablet with Innovator's specifications.

- **Manufacturer shall submit fee of Rs. 7500/- for each strength for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

129.	**Name and address of manufacture / Applicant**	**M/s Hilton Pharma Pvt Ltd. Plot No. 13-14, Sector 15, Korangi Industrial Area, Karachi, Pakistan**
	Brand Name + Dosage Form and Strength	Agohil 25mg tablets
	Composition	Each Film Coated Tablet Contains: Agomelatine…….25mg
	Dairy No. date of R &I fee	Form-5D Dy.No 217 dated 16-02-2016 Rs.50,000/- Dated 16-02-2016
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of form	Form 5D
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	14's, 28's, 56's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Valdoxan Tablet Approved by EMA
	Me-too-status	Modton 25mg tablet
	GMP Status	Renewla of DML vide letter No. F.2-14/85-Lic(Vol-I) dated 30-06-2020
	Remark of the Evaluator [II]	
	Decision:	

STABILITY STUDY DATA

Drug	Agohil 25mg talet
Name of Manufacturer	M/s Hilton Pharma Pvt Ltd. Plot No. 13-14, Sector 15, Korangi Industrial Area, Karachi, Pakistan
Manufacturer of API	M/s Changzhou Pharmaceutical Factory, Jiangsu Province, China.
API Lot No.	AG191201
Description of Pack (Container closure system)	Alu-Alu foil
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3,4,6 months Real Time: 0,3,6 months		
Batch No.	AGO-418004-3	AGO-418004-4	AGO-418004-5
Batch Size	6666 Tablets	6666 Tablets	6666 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided following documents dated 23-02-2021, as per checklist approved by the Registration Board in its 293rd Meeting:

Sr.#	Data requirement	Firm's submission
1.	Reference of previous approval of applications with stability study data of the firm.	Firm has referred to onsite inspection report of their product **"HILVEL 400mg + 100mg** (Sofosbuvir +Velpatasvir)", which was conducted on 14th December, 2017 and was presented in 277th meeting of Registration Board held on 27-29th December, 2017. Registration Board decided to approve registration of "HILVEL 400mg / 100mg (Sofosbuvir + Velpatasvir" by M/s. Hilton Pharma (Pvt.) Ltd., Karachi. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: i. The HPLC software is 21 CFR compliant. ii. Audit trail on the testing reports of Hilvel Tablets 400mg+100mg is available. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted.
3.	Method used for analysis of API along with COA.	Analytical method for APIs has been submitted from API manufacturer as well as from M/s Highnoon Labs..
4.	Stability study data of API from API manufacturer	Firm has submitted both accelerated (40°C ± 2°C & 75±5%RH) stability studies & long term (25°C ± 2°C & 60%±5%RH) stability studies reports of three batches for 6 & 24 months respectively.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate eissued by Jiangsu Changzhou Drug Administration has been submitted valid upto 20-02-2023
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice (Invoice# CYI19476) attested by AD I&E DRAP, Karachi dated 06-02-2020 has been submitted. (Quantity: 1.5 Kg.)

7.	Authorized Protocols/SOP for the development & stability testing of trial batches.	Firm has submitted SOP for new product development & stability protocol.
8.	Method used for analysis of FPP	Drug product analytical method has been submitted.
9.	Drug-excipients compatibility studies (where applicable)	Firm has referred to the formulation of innovator product for establishing drug-excipient compatibility.
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the three batches of both strengths.
11.	Record of comparative dissolution data (where applicable)	Comparative dissolution studies have been submitted in three physiological buffers i.e., pH 1.2, pH 4.5 & pH 6.8 against the Modton Tablet of M.s Nabiqasim Industries with acceptable values of f_2.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record for both accelerated & long-term stability studies, including chromatograms, raw data sheets etc..
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Audit trail reports have been submitted.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted.

	Trial Product	**Compoarator product**
Name	Agohil tablet 10mg	Modton tablet 25mg
Batch #	AGO-418204-5	MAB002

Remarks of Evaluator[II]:

Sr.#	**Observation**	**Firm's response**
1.	Stability studies of drug substance shall be submitted as per Zone-IVa conditions.	Firm has submitted long term stability studies of three batches from drug substance manufacturer till 24 months as per Zone IVa.
2.	Sample and standard concentration applied for Assay test of drug substance by M/s Hilton is different from that recommended in the analytical method from the drug substance manufacturer for the Assay of Agomelatine.	Assay of Agomelatine has been carried out as per concentration of drug substance manufacturer. Calculation sheet with raw data & revised specification of APl testing are submitted.
3.	Results for CDP studies in pH 6.8 buffer have not been submitted.	Firm has submitted CDP studies in pH 6.8 buffer against the Modton tablet of M/s Nabiqasim with acceptable value of f2 factor.
4.	Justification shall be submitted for not performing CDP studies against the innovator product.	Innovator product is not available in the market. Therefore, generic comparator product Modton Tablets 25mg is being used for CDP studies. This generic product has already been registered from DRAP, registration number 085661

5.	Firm shall submit fee of Rs. 7,500 for pre-approval change in product specifications from that initially submitted in Form 5D dossier, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has submitted fee of Rs. 75,00/- vide deposit slip# 24339917.

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case no. 06 Registration applications for local manufacturing of (Human) drugs on Form 5
Deferred cases

130.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Mox 400mg Tablet
	Composition	"Each Film Coated oral Tablet Contains: Moxifloxacin as HCL…400MG"
	Diary No. Date of R& I & fee	Dy.No 8286 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Fluoroquinolones J01MA14
	Type of Form	Form 5
	Finished product Specification	USP specs
	Pack size & Demanded Price	5's, 10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Moxifloxacin 400mg Tablet by Bayer Health Care USFDA Approved
	Me-too status	074931 Moxpin 400 mg Tablet M/s Winthrox Karachi . .
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	•
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Justification for contract manufacturing as G T Pharma has own tablet section • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General),	

	• Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
131.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave harmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Cip 250mg Tablet
	Composition	"Each Film Coated Tablet Contains: Ciprofloxacin HCL eq to Ciprofloxacin…250mg"
	Diary No. Date of R& I & fee	Dy.No 8284 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Fluoroquinolones
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO
	Approval status of product in Reference Regulatory Authorities.	Cipro® (Ciprofloxacin Hydrochloride) Tablet Approved In USFDA with Box Warning.
	Me-too status	056372 "Ciprowrd 250mg Tablets " Welwrd Pharmaceuticals, Plot No.3, Block No.A, Phase I-II, Industrial Estate,Hattar"
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	

	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
132.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Cip 500mg Tablet
	Composition	"Each Film Coated Tablet Contains: Ciprofloxacin HCL eq to Ciprofloxacin…500mg"
	Diary No. Date of R& I & fee	Dy.No 8285 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Fluoroquinolones
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO
	Approval status of product in Reference Regulatory Authorities.	Cipro® (Ciprofloxacin Hydrochloride) Tablet Approved In USFDA with Box Warning.
	Me-too status	056373 "Ciprowrd 500mg Tablets " Welwrd Pharmaceuticals, Plot No.3, Block No.A, Phase I-II, Industrial Estate,Hattar"
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
133.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave

		Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	G-Mont chewable 5mg Tablet
	Composition	"Each chewable Tablet Contains: Montelukast Sodium eq to Montelukast…5mg"
	Diary No. Date of R& I & fee	Dy.No 8274 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Leukotriene receptor antagonists
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	1x14's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved.
	Me-too status	079342 "NenKast 5 mg Tablets Each Chewable Tablet contains:- " Nenza Pharmaceuticals, 33-A, Hayatabad, Peshawar
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
134.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	G-Mont 10mg Tablet
	Composition	"Each Film Coated Tablet Contains: Montelukast Sodium eq to Montelukast…10mg"
	Diary No. Date of R& I & fee	Dy.No 8275 dated 25-02-2019 Rs.50,000/- 25-02-2019
	Pharmacological Group	Leukotriene receptor antagonists
	Type of Form	Form 5

	Finished product Specification	USP
	Pack size & Demanded Price	1x14's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	MHRA Approved.
	Me-too status	076530 Umcast 10mg Tablet By M/s Umema Pharma Baluchistan.
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
135.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Nestor 8mg Tablet
	Composition	"Each Film Coated Tablet Contains: Ondansetron HCl dihydrate eq to Ondansetron…8mg"
	Diary No. Date of R& I & fee	Dy.No 8288 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Antiemetics And Antinauseants A04AA01 Serotonin (5HT3) antagonists
	Type of Form	Form 5
	Finished product Specification	USP.
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	ZOFRAN Tablets, 8 mg (ondansetron HCl dihydrate equivalent to 8 mg of ondansetron),USFDA Approved.
	Me-too status	081451 Ondonx Tablet ,Genix Pharma Karachi . .
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.

	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
136.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Line 600mg Tablet
	Composition	"Each Film Coated Tablet Contains: Linezolid…600mg"
	Diary No. Date of R& I & fee	Dy.No 8278 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Antibacterial for systemic use. J01XX08
	Type of Form	Form-5
	Finished product Specification	Inhouse Spec.
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	ZYVOX Tablets USFDA Approved.
	Me-too status	055773 Leckzolid 600mg Tablet Medimarker's Pharmaceutical, Hyderabad
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein	

	Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
137.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Mycin 250mg Tablet
	Composition	"Each Film Coated Tablet Contains: Clarithromycin HCl eq to Clarithromycin…250mg"
	Diary No. Date of R& I & fee	Dy.No 8276 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Macrolide
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Biaxin 250mg (Available as only Clarithromycin without HCl) **Federal Register Determination That Product Was Not Discontinued Or Withdrawn For Safety Or Efficacy Reasons** USFDA Approved.
	Me-too status	082036 Claramet -250 Tablets M/s Metro Pharmaceuticals,Plot No.14, Street No.SS-2,National Industrial Zone RCCI,Rawat, Islamabad
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	• Details about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submission of agreement between applicant and manufacturer. • Evidence of approval of applied formulation as "Clarithromycin HCl eq to Clarithromycin…250mg" in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.

	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Submit composition of applied formulation in line with label claim of reference product i.e. "Clarithromycin as HCl 250mg film coated tablet. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
138.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Mycin 500mg Tablet
	Composition	"Each Film Coated Tablet Contains: Clarithromycin HCl eq to Clarithromycin…500mg"
	Diary No. Date of R& I & fee	Dy.No 8277 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Macrolide
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Biaxin 500mg **Federal Register Determination That Product Was Not Discontinued Or Withdrawn For Safety Or Efficacy Reasons** USFDA Approved.
	Me-too status	082037 Claramet -500 Tablets M/s Metro Pharmaceuticals,Plot No.14, Street No.SS-2,National Industrial Zone RCCI,Rawat, Islamabad
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant.	

	• Submit contract manufacturing agreement between applicant and manufacturer. • Submit composition of applied formulation in line with label claim of reference product i.e. "Clarithromycin as HCl 250mg film coated tablet. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
139.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Xime 400mg Capsule
	Composition	"Each Capsule Contains: Cefixime Trihydrate eq to Cefixime…400mg"
	Diary No. Date of R& I & fee	Dy.No 8287 dated 25-02-2019 Rs.50,000/- 25-02-2019
	Pharmacological Group	Third-generation cephalosporins
	Type of Form	Form 5
	Finished product Specification	JP
	Pack size & Demanded Price	1x5's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	SUPRAX® (cefixime) capsules USFDA Approved.
	Me-too status	055093; Vasix 400mg ' By M/s Alfalah Pharma (Pvt.) Ltd.,
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin)	

	• Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
140.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Xime 100mg Dry powder suspension
	Composition	"Each 5ml of reconstituted suspension contains: Cefixime Trihydrate eq to Cefixime…100mg"
	Diary No. Date of R& I & fee	Dy.No 8279 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Third-generation cephalosporin
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	30ml bottle, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved.
	Me-too status	073247 Stlicef Dry Suspension 200mg Treat Pharma A-37, Industrial Estate Kohat Road,Bnnu (contract manufacturing will be conducted by M/s. Shawan Pharmaceuticals, Rawat)"
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	

	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
141.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Xime 200mg Dry powder suspension
	Composition	"Each 5ml of reconstituted suspension contains: Cefixime Trihydrate eq to Cefixime…200mg"
	Diary No. Date of R& I & fee	Dy.No 8280 dated 25-02-2019 Rs.50,000/- 25-02-2019
	Pharmacological Group	Third-generation cephalosporin
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	30ml bottle, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved.
	Me-too status	073248; Stlicef Dry Suspension 200mg Treat Pharma A-37, Industrial Estate Kohat Road,Bnnu (contract manufacturing will be conducted by M/s. Shawan Pharmaceuticals, Rawat)"
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
142.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan

	Brand Name +Dosage Form + Strength	Gt Zone 250mg Injection IV
	Composition	"Each Vial Contains: Ceftriaxone sodium eq to Ceftriaxone…250mg"
	Diary No. Date of R& I & fee	Dy.No 8281 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Third-generation cephalosporins J01DD04
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	1's Type II Vial, as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Rocephin 250 mg Powder for solution for injection. MHRA Approved.
	Me-too status	075935 Breezon Injection 250mg M/s Pliva Balochistan
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Clarification regarding brand name is required whether it is as GT CIP or GT Zone. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
143.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Zone 500mg Injection
	Composition	"Each Vial Contains: Ceftriaxone sodium eq to Ceftriaxone…500mg"
	Diary No. Date of R& I & fee	Dy.No 8282 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Third-generation cephalosporin

	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	1's, Glass III vials, As per SRO
	Approval status of product in Reference Regulatory Authorities.	Rocephin powder for solution for Injection vials by Roche (MHRA Approved)
	Me-too status	062328 "Cefaben 500 mg IV Injection " Imco Pharmaceuticals Laboratories, 73/A.S Industrial Estate, Jamrud Road, Peshawar. (contract manufacturing conducted by M/s. Caraway Pharmaceuticals, Rawat, Islamabad)"
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
144.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Gt Zone 1g Injection
	Composition	"Each Vial Contains: Ceftriaxone as sodium eq to Ceftriaxone…1g"
	Diary No. Date of R& I & fee	Dy.No 8283 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Third-generation cephalosporin
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	Glass II vials, As per SRO
	Approval status of product in Reference Regulatory Authorities.	Rocephin powder for solution for Injection vials by Roche (MHRA Approved)
	Me-too status	070663

		Martixon 1gm I.V Dry powder Injection by Alkemy Hyderabad
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	
145.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	C Pime Injection 500mg
	Composition	"Each Vial Contains: Cefepime HCL…500 mg Arginine…326.5 mg
	Diary No. Date of R& I & fee	Dy.No 8290 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Fourth-generation cephalosporins
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	Type II, 1's Vial, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Maxipime (cefepime hydrochloride) for injection, for intravenous or intramuscular use USFDA Approved
	Me-too status	055465 KC-Pime 500mg Injection M/s Karachi Chemical Industrial
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	•
	Decision of 295th meeting: Deferred for the following: • Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant.	

	• Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. • **Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.** • **Registration Board further directed the firm to revise th label claim for the declaration of content of Arginine, as per innovator product along with submission of full fee that is 75,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
146.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd,23km, Raiwind Road, Lahore contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	C Pime Injection 1000mg
	Composition	"Each Vial Contains: Cefepime as HCL…1000 mg Arginine…725 mg
	Diary No. Date of R& I & fee	Dy.No 8291 dated 25-02-2019 Rs.50,000/- Dated 25-02-2019
	Pharmacological Group	Fourth-generation cephalosporins
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	Type II, 1's Vial, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Maxipime (cefepime hydrochloride) for injection, for intravenous or intramuscular use USFDA Approved
	Me-too status	055466 KC-Pime 1000mg Injection M/s Karachi Chemical Industrial
	GMP status	11-12-2017 & 10-01-2018. GMP Certificate issued on 15-03-2018.
	Remarks of the Evaluator (V)	• Approval of section/manufacturing facility by the Central Licensing Board. However, you may submit panel inspection report for renewal of DML verifying the section/manufacturing facility.
	Decision of 295th meeting: Deferred for the following:	

	• Submit detail about total number of sections & total number of products already approved on contract manufacturing of applicant. • Submit contract manufacturing agreement between applicant and manufacturer. • Capacity assessment of M/s Medisave Pharma	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s. Medisave pharmaceuticals, Lahore presented in 317th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Medisave Pharmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore for following sections: • General Tablet Section (General), • Capsule Section (Cephalosporin) • Dry Powder Suspension Section (Cephalosporin) • Dry Powder Injection Section (Cephalosporin) • Liquid Injection • Infusion (LVP) Section • Liquid Syrup Section Firm has also submitted contract manufacturing agreement with M/s Medisave Pharmaceuticals.	
	Decision of 320th meeting: Approved. • **Registration letter will be issued upon submission of compliance report from the contract manufacturer for further increase in testing capacity especially HPLC, microbiological testing etc. to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.** • **Registration Board further directed the firm to revise the label claim for the declaration of content of Arginine, as per innovator product along with submission of full fee that is 75,000-/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
147.	**Name and address of manufacturer / Applicant**	**"M/s Next Pharmaceutical Products Private Limited. Plot No. 44 A-B, Sundar Industrial Estate, Lahore** Contract manufacturing by **M/s Novamed Pharmaceuticals (Pvt) Ltd. 28-km,Ferozepur Road, Lahore"**
	Brand Name +Dosage Form + Strength	D-Next 5mg/ml IV/IM Injection
	Composition	"Each 1ml Contains: Cholecalciferol (Vitamin D3)…5mg"
	Diary No. Date of R& I & fee	Dy. No 17650 dated 11-05-2018 Rs.20,000/- Dated 11-05-2018 Rs. 30,000/- dated 27-06-2019
	Pharmacological Group	Vitamin
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved by ANSM of France
	Me-too status (with strength and dosage form)	D-Tres 5mg/ml Injection by M/s Sami (Reg#076115)
	GMP status	Last GMP inspection dated 5th & 27th December, 2017 conclusion by Panel ―The firm (M/s NovaMed Pharmaceuticals Pvt. Ltd. Lahore) is compliant to Good cGMP guidelines at the time of inspection.

	Remarks of the Evaluator[II]	Form 5 was initially submitted from the manufacturer i.e. M/s Novamed Pharmaceuticals (Pvt.) Ltd. 28-km, Ferozepur Road, Lahore. Subsequently fresh Form 5 has been submitted by the applicant i.e., M/s Next Pharmaceutical Products Private Limited. Plot No. 44 A-B, Sundar Industrial Estate, Lahore, dated 25-07-2019. • Reference product is available in ampoule whereas firm has applied for vial.
	Decision of 291st meeting: Registration Board decided to defer all applied products of contract manufacturing from M/s Novamed Pharmaceuticals (Pvt) Ltd. 28-km, Ferozepur Road, Lahore, for assessment of manufacturing and quality control capacity of M/s Novamed Pharmaceuticals (Pvt) Ltd. 28-km, Ferozepur Road, Lahore. Moreover, clarification shall be submitted regarding container closure system, since reference product is available in ampoule whereas firm has applied for vial.	
	Firm's response: Firm has referred to the Capacity assessment inspection report of M/s Novamed Pharmaceuticals Pvt Ltd, 28km Ferozepur Road, Lahore presented in 295th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Novamed Pharmaceuticals Pvt Ltd, 28km Ferozepur Road, Lahore for following sections: • Dry Powder Injection (Cephalosporin) Section • Dry Powder Suspension (Cephalosporin) Section • Capsule (Cephalosporin) Section • General Liquid Injection (Ampoule) • General Liquid Injection Vials (SVP)	
	Decision of 320th meeting: Registration Board deferred the applications of contract manufcaturin from M/s Medisave harmaceuticals, Plot 578-579, Sundar Industrial Estate, Lahore, Pakistan for submission of upgradation plan regarding increase in testing capacity especially HPLC, microbilogical testing etc to cater the need of pharmacopeial tesing of already registered drug products, products under development and contract manufactured products as decided in 317th meeting of Registration Board.	

148.	Name and address of Manufacturer/Applicant	"M/s Next Pharmaceutical Products Private Limited. Plot No. 44 A-B, Sundar Industrial Estate, Lahore By M/s Novamed Pharmaceuticals (Pvt) Ltd. 28-km,Ferozepur Road, Lahore"
	Brand Name + Dosage Form + Strength	Cefinext 200mg/5ml Suspension
	Composition	"Each Vial Contains: Cefixime(as trihydrate)…200mg/5ml"
	Diary No. D of R & I & Fee	Dy No. 17661 ; 11-05-18: Rs.20,000
	Pharmacological group	Cephalosporin
	Type of Form	Form 5
	Finished product Specifications	USP Specifications
	Pack Size & demanded price	1's: As per SRO
	Approval status of product in reference regulatory authorities	Approved in USFDA
	Me-too status	Rofil 200mg/5ml suspension of Amrose Pharmaceuticals, Karachi.
	GMP Status	
	Remarks of Evaluator:	

Sr.No.	Queries	Response
1.	Fee for contract manufacturing is 50,000, submit differential fee.	Applicant has submitted Fee Challan of Rs.30,000/- dated 27-006-2019.
2.	Mention type of primary packaging material.	------

Decision of 290th meeting: Deferred for clarification regarding type of primary packaging material for applied formulation and assessment of capacity of M/s Novamed.

Firm's response: Firm has referred to the Capacity assessment inspection report of M/s Novamed Pharmaceuticals Pvt Ltd, 28km Ferozepur Road, Lahore presented in 295th meeting of Registration Board wherein Board decided to allow contract manufacturing from M/s Novamed Pharmaceuticals Pvt Ltd, 28km Ferozepur Road, Lahore for following sections:

- Dry Powder Injection (Cephalosporin) Section
- Dry Powder Suspension (Cephalosporin) Section
- Capsule (Cephalosporin) Section
- General Liquid Injection (Ampoule)
- General Liquid Injection Vials (SVP)

Moreover firm has submitted primary packaging container as "Amber glass bottle" and also requested for change of brand name from "Cefinext 200mg/5ml to Cefinext DS 200mg/5ml"

Decision: Approved.

149.		
	Name and address of manufacturer/ Applicant	M/s Seraph Pharmaceuticals, Plot No. 210, Industrial Triangle, Kahuta Road, Islamabad (Contract giver) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A-159, S.I.T.E Super Highway, Karachi (Contract acceptor) (Ampoule & Vial injection).
	Brand Name + Dosage Form + Strength	Meco 500mcg/ml Injection.
	Composition	Each ml Contains: Mecobalamin ……500mcg
	Diary No. Date of R & I & fee	Dy. No 11930 dated 05-03-2019; Rs. 50,000/- dated 05-03-2019.
	Pharmacological Group	Vitamin B12 (cyanocobalamin and analogues)
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications.
	Pack size & Demanded Price	1ml x 1's, 5's, 10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	Comezengen injection 500 mcg, PMDA Japan Approved.
	Me-too status	Flench injection, Tabros Pharma, Reg. no. 029050.
	GMP status	Same as above.
	Remarks of the Evaluator	• Contract giver has 07 approved sections. • Applicant has submitted that total number of registered products on contract basis are 06. • Firm has provided finished product specifications with submission of 7500/- vide slip No. 641042980 dated 27-08-2021.
	Decision of 312th meeting: Deferred to review and present requirement of JP monograph regarding storage and testing of drug substance and container closure system of drug product.	
	Firm's response: Firm has submitted analytical method for drug substance as per JP specifications along with details of container closure system as amber glass ampoule.	

	• **Decision: Approved with JP specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

150	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Piptam Injection 4.5gm
	Composition	Each Vial Contains: Piperacillin Sodium Eq To Piperacillin…4gm Tazobactam Sodium Eq To Tazobactam…500mg
	Diary No. Date of R& I & fee	Dy. No.12640; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Tanzo Injection of M/s Bosch
	GMP status	Copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
151	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Piptam Injection 2.25gm
	Composition	Each Vial Contains: Piperacillin Sodium Eq To Piperacillin…2gm Tazobactam Sodium Eq To Tazobactam…250mg
	Diary No. Date of R& I & fee	Dy. No.12636; 06-03-2019; Rs.50,000/- 06-03-2019

	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Tanzo Injection of M/s Bosch
	GMP status	Copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
152	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Meren Injection 500mg
	Composition	Each Vial Contains: Meropenem Trihydrate Eq. To Meropenem…500mg
	Diary No. Date of R& I & fee	Dy. No.12642; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Mopen 500mg Injection of M/s Hilton Pharma,Karachi.
	GMP status	Copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications.	

	• **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
153	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Meren Injection 1gm
	Composition	Each Vial Contains: Meropenem Trihydrate Eq. To Meropenem…1Gm
	Diary No. Date of R& I & fee	Dy. No.12641; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Mopen 1gm Injection of M/s Hilton Pharma,Karachi.
	GMP status	Copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
154	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Imicil Injection 500mg/500mg IM/IV
	Composition	Each Vial Contains: Imipenem As Monohydrate…500mg

		Cilastatin As Sodium…500mg
	Diary No. Date of R& I & fee	Dy. No.12649; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Cilapen Injections of M/s Bosch Pharmaceuticals, Karachi.
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
155	**Name and address of manufacturer / Applicant**	**M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi** **By** **M/s Global Pharmaceuticals Pvt Ltd** **Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad**
	Brand Name +Dosage Form + Strength	Imicil Injection 250mg/250mg IM/IV
	Composition	Each Vial Contains: Imipenem As Monohydrate…250mg Cilastatin As Sodium…250mg
	Diary No. Date of R& I & fee	Dy. No.12648; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Cilapen Injections of M/s Bosch Pharmaceuticals, Karachi.
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.

	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Registration Board was apprised that in 313th meeting same products was deferred for submission of product development studies keeping in view the innovator product and product testing and stability studies by complying USP monograph by Global Pharmaceuticals and accordingly the Board deferred instant application and advised to consider alongwith submission of same data. • **Registration Board directed the firm to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
156	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Teinin Injection 400mg
	Composition	Each Vial Contains: Teicoplanin Powder Sterile…400mg
	Diary No. Date of R& I & fee	Dy. No.12651; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by MHRA of UK
	Me-too status	Targocid Injection 200mg of M/s Hoechst Pakistan Ltd, Karachi 019504
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Deferred for: • **Justification of applied dosage form since innovator product is available as lyophilisd vial whereas firm has applied in ready to fill dosage form.** • **Submission of fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
157	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by**

		M/s Vision Pharmaceuticals Pvt Ltd. Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Tigcil Injection 50mg
	Composition	Each Vial Contains: Tigecycline…50mg
	Diary No. Date of R& I & fee	Dy. No.12647; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Tigewel Injection of M/s Welwrd Pharma (Reg.# 082530)
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Deferred for: • **Justification of applied dosage form since innovator product is available as lyophilisd vial whereas firm has applied ready to fill dosage form.** • **Submission of fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
158	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Vision Pharmaceuticals Pvt Ltd. Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	OM-R Injection 40mg
	Composition	Each Vial Contains: Omeprazole As Sodium…40mg
	Diary No. Date of R& I & fee	Dy. No.12652; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	PPI
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Zegrid 40mg injection of M/s Shaigan
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.

	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with Innovators specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
159	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Vision Pharmaceuticals Pvt Ltd. Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Renzole Injection 40mg
	Composition	Each Vial Contains: Esomeprazole As Sodium…40mg
	Diary No. Date of R& I & fee	Dy. No.12653; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	PPI
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Nexium 40mg injection of M/s Getz
	GMP status	--
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with Innovators specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
160	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Vision Pharmaceuticals Pvt Ltd. Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad

	Brand Name +Dosage Form + Strength	Vancoren Injection 500mg
	Composition	Each Vial Contains: Vancomycin As Hcl…500mg
	Diary No. Date of R& I & fee	Dy. No.12654; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by MHRA of UK
	Me-too status	Wangkolin 500mg Injection by M/s Himont (Reg#031032)
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
161	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Ceftam Injection 2gm
	Composition	Each Vial Contains: Cefoperazone Sodium…1000mg Sulbactam Sodium…1000mg
	Diary No. Date of R& I & fee	Dy. No.12656; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved in 03 European countries, i.e., Czech Republic, Poland and Slovakia
	Me-too status	Q- Bact 2gm Injection of High- Q Karachi 061170
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.

	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with JP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
162	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Cepime 1gm Injection
	Composition	Each Vial Contains: Cefepime As Hcl With L-Arginine…1000mg
	Diary No. Date of R& I & fee	Dy. No.12638; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Nuxipim 1g Injection of Bosch
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
163	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by**

		M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Cepime Injection 500mg
	Composition	Each Vial Contains: Cefepime HCl With L Arginine…500mg
	Diary No. Date of R& I & fee	Dy. No.12637; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Nuxipim 1g Injection of Bosch
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with USP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
164	**Name and address of manufacturer / Applicant**	M/s Reign Pharmaceuticals PCSIR-KLC Pvt Ltd. TBIC Building-1, PCSIR Laboratories Complex, Shahrahe Dr. Salim-us-Zaman Siddiqui, Off University Road, Karachi **Contract manufacturing by** M/s Global Pharmaceuticals Pvt Ltd. Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Ceftam Injection 1gm
	Composition	Each Vial Contains: Cefoperazone Sodium…500mg Sulbactam Sodium…500mg
	Diary No. Date of R& I & fee	Dy. No.12639; 06-03-2019; Rs.50,000/- 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by PMDA of Japan
	Me-too status	Ectafin Injection 1gm I/V of M/s Hi-Medic Pharma, Lahore
	GMP status	Firm has submitted copy of GMP certificate of M/s Global Pharmaceuticals dated 24-12-2018 based on the

		inspection dated 24-10-2018. The certificate was valid till 23-10-2021.
	Remarks of the Evaluator.	Registration Board was apprised that in the initial application, the applicant i.e. Reign Pharmaceuticals has not specified any contract manufacturer. Upon the response submitted by the firm they have specified the contract manufacturer i.e. Global Pharmaceuticals.
	Decision: Approved with JP specifications. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.** • **Registration Board further directed the applicant to submit fee of Rs. 75,000/- for change/correction in Form 5 regarding name of the contract manufacturer as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
165	Name and address of manufacturer / Applicant	M/s Medera Pharmaceuticals Pvt. Ltd, Plot 2, Street 4, National Industrial Zone, Rawat
	Brand Name +Dosage Form + Strength	Terbinafine Tablet 250 mg Terbimed, Finomed, Binomed
	Diary No. Date of R& I & fee	Duplicate dossier
	Composition	Each film coated tablet contains: Terbinafine Hydrochloride eq. to Terbinafine ..250mg
	Pharmacological Group	Antifungals for systemic use (D01BA02)
	Type of Form	Form-5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	10's Alu Alu Blister, As per SRO
	Approval status of product in Reference Regulatory Authorities.	Lamisil terbinafine 250mg (as hydrochloride) TGA Approved uncoated.
	Me-too status	081184; Cutis 250mg Tablet M/s Tabros Pharma Karachi.
	GMP status	06-02-2018 Conclusion: Keeping in view of the above facts, overall GMP compliance is found Good as of today.
	Remarks of the Evaluator.	□ Evidence of international availability and me-too as film coated tablet is required. □ Firm has provided evidence of film coated tablets which could not be confirmed. □ Present in USP
	Previous Decision(288): Deferred for following: □ Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm □ Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting □ Confirmation from R&I section for date of submission of original dossier along with details of submitted fee.	
	Evaluation by PEC: Firm has revised their formulation from film coated to uncoated tablet with submission of Rs. 5000/- dated 26-06-2019. Firm has not provided evidence for confirmation from R&I section for date of submission of original dossier along with details of submitted fee.	
	Decision of 291st meeting: The Registration Board deferred the applied formulation for evidence for confirmation from R&I section for date of submission of original dossier along with details of submitted fee.	

	Evaluation by PEC: Firm has submitted copy of R&I receiving dated 17-08-2017, which has been verified from the R&I incharge against the diary no. 12273 dated 17-08-2017.	
	Decision: Approved with USP specifications. • **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

Routine Applications of Locally Manufactured Drugs (Veterinary):

166	Name and address of manufacturer / Applicant	M/s Mallard Pharmaceuticals (Pvt) Ltd., 23-Km Lahore Road, Multan
	Brand Name +Dosage Form + Strength	Florfen Col Liquid
	Composition	Each 100ml liquid contains: Florfenicol…….10g Colistin sulphate…….50 MIU
	Diary No. Date of R& I & fee	11221, 07-08-2017, 20,000/-, 07-08-2017
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished Product Specification	Manufacturer specifications
	Pack size & Demanded Price	50ml, 100ml, 200ml, 400ml, 500ml, 1000ml; Decontrolled
	Me-too status	Florobex C Liquid of M/s Elegance Pharma (Reg#078286)
	GMP status	The firm is granted GMP certificate based on inspection conducted on 13-08-2020.
	Remarks of the Evaluator.	The R&I receipt has been verified from the Incharge R&I against the diary no. mentioned above.
	Decision: Referred to Expert Working Group for review of applied formulation.	
167	Name and address of manufacturer / Applicant	M/s Mallard Pharmaceuticals (Pvt) Ltd., 23-Km Lahore Road, Multan
	Brand Name +Dosage Form + Strength	Feverex Powder
	Composition	Each 100g Powder contains: Paracetamol ……..20g Potassium carbonate.……12.5g Sodium carbonate……..12.5g Vitamin E……..12.5g Vitamin C…….5g
	Diary No. Date of R& I & fee	11222, 07-08-2017, 20,000/-, 07-08-2017
	Pharmacological Group	Anti-inflammatory, Anti-pyretic
	Type of Form	Form-5
	Finished Product Specification	Manufacturer specifications
	Pack size & Demanded Price	50g, 100g, 200g, 400g, 500g, 1000g; Decontrolled
	Me-too status	Paracet WSP of M/s Decent Pharma (Reg#079826)
	GMP status	The firm is granted GMP certificate based on inspection conducted on 13-08-2020.
	Remarks of the Evaluator.	The R&I receipt has been verified from the Incharge R&I against the diary no. mentioned above.
	Decision: Approved with Innovcator's specifications.	
168	Name and address of manufacturer / Applicant	M/s Mallard Pharmaceuticals (Pvt) Ltd., 23-Km Lahore Road, Multan
	Brand Name +Dosage Form + Strength	Vitamall Injection
	Composition	Each ml contains: Vitamin A……80,000 IU Vitamin D3……..40,000 IU

		Vitamin E……20mg
	Diary No. Date of R& I & fee	300, 29-05-2015, 20,000/-, 28-05-2015
	Pharmacological Group	Vitamins
	Type of Form	Form-5
	Finished Product Specification	Manufacturer specifications
	Pack size & Demanded Price	50ml; Decontrolled
	Me-too status	Vitazak Injection of M/s Zakphos Pharma (Reg#052316)
	GMP status	The firm is granted GMP certificate based on inspection conducted on 13-08-2020.
	Remarks of the Evaluator.	The R&I receipt has been verified from the Incharge R&I against the diary no. mentioned above.
	Decision: Approved with Innovcator's specifications.	

Agenda of Evaluator PEC-III

Case No. 01 Registration applications of cases of PINSTECH

DRAP Authority in its **133rd meeting** held on April 13, 2022 while considering the request of PINSTECH for exemption of Form 5F for radiopharmaceuticals decided as under:

I. The Authority decided to grant 06 months relaxation under SRO 713(1)/2018 from Form 5-F (CTD) for following radiopharmaceuticals as CTD is not applicable for radiopharmaceuticals:
   a. DISIDA (Hepatobiliary Agent in Diagnosis of Hepatocellular Carcinoma)
   b. DMSA (Renal Static Imaging Agent: When radiolabeled with Technelium-99m)
   c. PINTHERA (Radiolabeled Somatostatin Receptor analogue for treatment of neuroendocrine Tumors).
   d. HYNIC-TATE (For diagnosis of Neuroendocrine Tumors).
   e. [131 I-MIBG]iobenguane 1131 (Treatment-resistant neuroblastoma (NB), unresectable or metastatic pheochromocytoma (PC) and paraganglioma (PG).

DRAP Authority further in its **134th meeting** held on 29-04-2022 further Advised PE&R Division to process applications of radiopharmaceuticals of M/s PINSTECH on priority / out of queue, wherein relaxation in the Form 5-F was granted by the Authority.

Accordingly, the following applications have been received and evaluated and presented before the Board for consideration.

169.	Name and address of manufacturer / Applicant	M/s Pakistan Institute of Nuclear Science & Technology, Nilore Islamabad.
	Brand Name +Dosage Form + Strength	PINSCAN DISIDA (Freeze dried powder for reconstitution)
	Composition	N-(2,6 Diisopropyl- phenyl carbamoyl methyl iminodiacetic acid)…… 20mg Stannous (II) Chloride Dihydrate……0.24mg
	Diary No. Date of R& I & fee	Dy. No 17772: 17-06-2022 PKR. 75,000/-: 17-06-2022
	Pharmacological Group	Hepatobiliary agent in diagnosis of hepatocellular carcinoma
	Type of Form	Form 5D

	Finished Product Specification	Not submitted
	Pack size & demanded price	Rs. 900 / Vial, 5's
	Approval status of product in Reference Regulatory Authorities.	**TGA Australia** (HEPATOLITE kit for production of Technetium(99mTc) disofenin powder for injection multidose vial) Powder for Injection (White crystalline plug)
	Me-too status	NA
	GMP status	Inspection report of the firm dated 17-05-2017 wherein the panel recommended renewal of DML was presented by the firm.
	Clinical indications of innovator's product	Indicated as an adjunct in the diagnosis of hepatobiliary disease
	Remarks of the Evaluator[3].	• GMP inspection report conducted within a period of last three years. • Provide reference of finished product specification whether pharmacopoeial, in-house or as per innovator's product. Submit copy of official monograph in case of pharmacopoeial specifications. • Revise your label claim as per the innovator's drug product as per follows, since you have mentioned chemical name of Disofenin in the label claim. Each vial contains: Disofenin……. 20 mg Stannous chloride dihydrate……. 0.24 mg
	Decision: Registration Board decided to approve the product with following label claim: **Each vial contains:** **Disofenin……. 20 mg** **Stannous chloride dihydrate……. 0.24 mg** **Firm will submit following documents and the Board Authorized its Chairman for issuance of registration letter.** • **Finished product specification along with applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Revised form 5D along with relvant annexures for the revised label claim.** • **Updated GMP certificate / inspection report of the firm conducted within a period of last three years.**	
170.	Name and address of manufacturer / Applicant	M/s Pakistan Institute of Nuclear Science & Technology, Nilore Islamabad.
	Brand Name +Dosage Form + Strength	PINSCAN DMSA (Freeze dried powder for reconstitution)
	Composition	Meso-2,3-dimercaptosuccinic acid…. 1 mg Stannous chloride dehydrate…….0.4 mg Ascorbic acid……0.7 mg Inositol……50.0 mg
	Diary No. Date of R& I & fee	Dy. No 17771: 17-06-2022 PKR. 75,000/-: 17-06-2022
	Pharmacological Group	Renal static imaging agent
	Type of Form	Form 5D
	Finished Product Specification	Not submitted
	Pack size & demanded price	Rs. 800 / Vial, 5's
	Approval status of product in Reference Regulatory Authorities.	**TGA Australia**

		(RADPHARM DMSA kit for the production of Technetium (99mTc) succimer powder for injection multidose vial) Lyophilised white powder
	Me-too status	NA
	GMP status	Inspection report of the firm dated 17-05-2017 wherein the panel recommended renewal of DML was presented by the firm.
	Clinical indications of innovator's product	Used as a static renal imaging pharmaceutical and is particularly suited for evaluation of renal cortex, deliniation of renal space occupying lesions, determination of intrarenal function, distribution and identification of ectopic renal sites.
	Remarks of the Evaluator[3].	• GMP inspection report conducted within a period of last three years. • Provide reference of finished product specification whether pharmacopoeial, in-house or as per innovator's product. Submit copy of official monograph in case of pharmacopoeial specifications. • Revise your label claim as per the innovator's drug product as per follows: Each vial contains: Succimer…… 1 mg
	Decision: Registration Board decided to approve the product with following label claim: **Each vial contains:** **Succimer…… 1 mg** **Firm will submit following documents and the Board Authorized its Chairman for issuance of registration letter.** • **Finished product specification** • **Revised form 5D along with relvant annexures for the revised formulation along with the submission of applicable fee that is 75,000/- for pre-registration variation for change in composition of the applied product as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Updated GMP certificate / inspection report of the firm conducted within a period of last three years.**	
171.	Name and address of manufacturer / Applicant	M/s Pakistan Institute of Nuclear Science & Technology, Nilore Islamabad.
	Brand Name +Dosage Form + Strength	Iodine-131 Meta-iodobenzylguanidine (Iobenguane I-131) Injectable solution
	Composition	Iobenguane I 131…….. 555 MBq/mL (15 mCi/mL)
	Diary No. Date of R& I & fee	Dy. No 17768: 17-06-2022 PKR. 75,000/-: 17-06-2022
	Pharmacological Group	Neuroectodermal agent in diagnosis of pheochromocytoma
	Type of Form	Form 5D
	Finished Product Specification	Not submitted
	Pack size & demanded price	Rs. 900 / Vial
	Approval status of product in Reference Regulatory Authorities.	**USFDA** AZEDRA (iobenguane I 131) 555 MBq/mL (15 mCi/mL) injection (sterile, clear, colorless to pale yellow injectable solution)
	Me-too status	NA

	GMP status	Inspection report of the firm dated 17-05-2017 wherein the panel recommended renewal of DML was presented by the firm.
	Clinical indications of innovator's product	Radioactive therapeutic agent indicated for the treatment of adult and pediatric patients 12 years and older with iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma who require systemic anticancer therapy
	Remarks of the Evaluator[3].	• GMP inspection report conducted within a period of last three years. • Provide reference of finished product specification whether pharmacopoeial, in-house or as per innovator's product. Submit copy of official monograph in case of pharmacopoeial specifications. • Revise your label claim as per the innovator's drug product as per follows: Each vial contains: Iobenguane I 131…….. 555 MBq/mL (15 mCi/mL)
	Decision: Registration Board decided to approve the product with following label claim: **Each vial contains:** **Iobenguane I 131…….. 555 MBq/mL (15 mCi/mL)** **Firm will submit following documents and the Board Authorized its Chairman for issuance of registration letter.** • **Finished product specification** • **Revised form 5D along with relvant annexures for the revised formulation along with the submission of applicable fee that is 75,000/- for pre-registration variation for change in composition of the applied product as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Updated GMP certificate / inspection report of the firm conducted within a period of last three years.**	
172.	Name and address of manufacturer / Applicant	M/s Pakistan Institute of Nuclear Science & Technology, Nilore Islamabad.
	Brand Name +Dosage Form + Strength	PINTHERA (Freeze dried powder for reconstitution)
	Composition	DOTA-Tyr3-Octreotate, Somatostatin analogue conjugated with metal chelating moiety 1,4,7,10-tetraazacylododecane-1,4,7,10-tetraacetic acid (DOTA)….260ug per vial Lu-177….200mCi
	Diary No. Date of R& I & fee	Dy. No 17770: 17-06-2022 PKR. 75,000/-: 17-06-2022
	Pharmacological Group	Radiolabelled somatostatin receptor analogue for treatment of neuroendocrine tumours.
	Type of Form	Form 5D
	Finished Product Specification	Not submitted
	Pack size & demanded price	Rs. 150,000/ Vial
	Approval status of product in Reference Regulatory Authorities.	**USFDA** (LUTATHERA) Sterile, clear, colorless to slightly yellow solution for intravenous use
	Me-too status	NA

	GMP status	Inspection report of the firm dated 17-05-2017 wherein the panel recommended renewal of DML was presented by the firm.
	Clinical indications of innovator's product	Radiolabelled somatostatin analog indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumours in adults
	Remarks of the Evaluator[3].	• GMP inspection report conducted within a period of last three years. • Provide reference of finished product specification whether pharmacopoeial, in-house or as per innovator's product. Submit copy of official monograph in case of pharmacopoeial specifications. • Revise the applied dosage form from lyophilized powder to injectable solution as per the innovator's drug product along with submission of full fee of registration for pre-registration variation as per SRO No. F.7-11/2012-B&A/DRAP dated 7th May 2021. • Revise your label claim as per the innovator's drug product as per follows: Each vial contains: Lutetium Lu 177 dotatate……370 MBq/mL (10 mCi/mL)
	Decision: Registration Board decided to approve the product with following label claim: **Each vial contains:** **Lutetium Lu 177 dotatate……370 MBq/mL (10 mCi/mL)** **Firm will submit following documents and the Board Authorized its Chairman for issuance of registration letter.** • **Finished product specification** • **Revised form 5D along with relvant annexures for the revised formulation along with the submission of applicable fee that is 75,000/- for pre-registration variation for change in composition of the applied product as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Updated GMP certificate / inspection report of the firm conducted within a period of last three years.**	
173.	Name and address of manufacturer / Applicant	M/s Pakistan Institute of Nuclear Science & Technology, Nilore Islamabad.
	Brand Name +Dosage Form + Strength	PINSCAN (HYNIC-TATAE)
	Composition	HYNIC-[D-Phe1, Tyr3-octreotide] TFA salt 16 mcg EDDA (Ethylenediamine-N,N'-diacetic acid)10 mg
	Diary No. Date of R& I & fee	Dy. No 17769: 17-06-2022 PKR. 75,000/-: 17-06-2022
	Pharmacological Group	Somatostatin receptor analogue for treatment of neuroendocrine tumours.
	Type of Form	Form 5D
	Finished Product Specification	Not submitted
	Pack size & demanded price	Rs. 15,000/ Vial
	Approval status of product in Reference Regulatory Authorities.	**MHRA UK** TEKTROTYD 16 micrograms kit for radiopharmaceutical preparation

		(White or almost white lyophilisates)
	Me-too status	NA
	GMP status	Inspection report of the firm dated 17-05-2017 wherein the panel recommended renewal of DML was presented by the firm.444444443q
	Clinical indications of innovator's product	This medicinal product is for diagnostic use only. 99mTc-EDDA/HYNIC-TOC specifically binds to somatostatin receptors. After radiolabelling with sodium pertechnetate (99mTc) solution, the solution of 99mTcEDDA/HYNIC-TOC obtained is indicated in adult patients with gastro-enteropancreatic neuroendocrine tumours (GEP-NET) for localizing primary tumours and their metastases
	Remarks of the Evaluator[3].	• GMP inspection report conducted within a period of last three years. • Provide reference of finished product specification whether pharmacopoeial, in-house or as per innovator's product. Submit copy of official monograph in case of pharmacopoeial specifications. • Revise the applied formulation from a single vial containing both drug substance to two different vials each containing one drug substance as per the innovator's drug product along with submission of full fee of registration for pre-registration variation as per SRO No. F.7-11/2012-B&A/DRAP dated 7th May 2021. • Revise your label claim as per the innovator's drug product as per follows: Vial I contains: HYNIC-[D-Phe1, Tyr3-octreotide] TFA salt…16 µg Vial II contains: EDDA (Ethylenediamine-N,N'-diacetic acid)…10 mg
	Decision: Registration Board decided to approve the product with following label claim: **Vial I contains:** **HYNIC-[D-Phe1, Tyr3-octreotide] TFA salt……..16 µg** **Vial II contains:** **EDDA (Ethylenediamine-N,N'-diacetic acid)…….10 mg** **Firm will submit following documents and the Board Authorized its Chairman for issuance of registration letter.** • **Finished product specification** • **Revised form 5D along with relvant annexures for the revised formulation along with the submission of applicable fee that is 75,000/- for pre-registration variation for change in composition of the applied product as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Updated GMP certificate / inspection report of the firm conducted within a period of last three years.**	

Case No. 02 Registration applications of New section / New License

Case No. 02: M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi

M/s Biogen Pharmaceuticals, Rawalpindi has been granted new license (DML No. 000911) by way of formulation by Licensing division DRAP dated 13-02-2020. Now the firm has submitted following applications as per the details mentioned in the table below:

Name of Section	Considered till 317th RB meeting		Freshly applied	
	No of molecules	No of products	No of molecules	No of products
Dry Vial section (Cephalosporin)	03	12	-	-
Dry suspension section (Cephalosporin)	01	02	-	-
Capsule section (Cephalosporin)	02	02	-	-
Ampoule Section SVP (General)	05	07	-	-
Capsule section (General)	02	04	01	01
Dry Vial section (General)	03	04	-	-
Soft gel capsule general section	02	03	-	-
Hydrocortisone injection (steroid)	01	03	-	-
Sachet section (General)	01	01	-	-
Dry Vial section (Carbapenem)	02	03	-	-
Cream section (general)	02	02	-	-
Ointment section (General)	01	01	-	-
Lotion section (General)	01	01	-	-
Infusion Section (General)	-	-	02	02

Infusion Section (General): 02 Molecules / 02 Products

174.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Infusion section (General).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1896: 20-01-2022
	Details of fee submitted	PKR 30,000/-: 04-01-2022
	The proposed proprietary name / brand name	**LINZOGEN 600mg/300ml Solution for Infusion**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial of 300ml Contains: Linezolid…..…600mg
	Pharmaceutical form of applied drug	Clear colorless liquid filled in glass vials
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use
	Reference to Finished product specifications	Innovators specs
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zyvox IV **(USFDA** Approved)
	For generic drugs (me-too status)	Nezkil Infusion by Continental pharma
	Name and address of API manufacturer.	Optrix Laboratories Pvt Ltd. Survey No. 145/A & 147, Ramalingampally (V), Bommalaramaram (M), Yadadri-Bhuvanagiri District Telangana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard

		or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Nezkil infusion of S.J & G Fazal Elahi.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Optrix Laboratories Pvt Ltd. Survey No. 145/A & 147, Ramalingampally (V), Bommalaramaram (M), Yadadri-Bhuvanagiri District Telangana India.		
API Lot No.	OT-LIU/06/2008		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	LZN001	LZN002	LZN003
Batch Size	500 Vials	500 Vials	500 Vials
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	15-05-2021	15-05-2021	15-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 68951/TS/2021) issued by Drugs control administration, Government of Telangana dated 20-09-2021. The GMP certificate is valid till 19-09-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 15-04-2020 specifying purchase of 3Kg Linezolid. Firm has submitted copy of DHL invoice number 00206995 dated 29-04-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC system are not 21 CFR compliant.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Specify the exact section in which the applied drug will be manufactured, along with particulars of that section including manufacturing facility whether SVP or LVP and packaging facility whether glass vials or LDPE infusions.	Firm has submitted that they will manufacture the applied product in Infusion section (General). This section has the facility to fill glass vials from 100ml to 300ml.
2.	Submit drug substance specifications in section 3.2.S.4.1 and secion 3.2.S.4.2 from both drug substance manufacturer as well as drug product manufacturer.	Firm has submitted specifications of drug substance from both API manufacturer as well as Biogen Life Sciences.
3.	Submit data of verification of analytical procedure of drug substance	Firm has submitted report of verification studies of analytical procedure of drug substance.
4.	Submit COA of relevant batch of drug substance from API manufacturer as well as drug product manufacturer in section 3.2.S.4.4.	Firm has submitted COA of relevant batch from API manufacturer as well as Biogen Life Sciences.
5.	Justify why the qualitative composition of your formulation is different from that of innovator's product. Provide drug-excipient compatibility studies.	Firm has submitted that their actual composition which is also specified in BMR is as per the innovator's product.
6.	Justify why the pharmaceutical equivalence studies were conducted against the comparator product instead of using innovator / reference product.	Firm has submitted that Nezkil infusion is the commonly used comparator product in Pakistan and they have also performed studies against that product.
7.	Justify why the product is not subjected to terminal sterilization, since this method is recommended by the innovator product.	Firm has submitted copy of BMR which shows terminal sterilization of the product at 121°C for 30 minutes.
8.	You have mentioned innovator's specifications in module-1 and in-house specifications in module-3. Allign your drug product specifications along with submission of requisite fee.	Firm has submitted relevant page of module 1 which now specifies innovator's product. However, the firm has not submitted **fee** for change in specifications in module 1.
9.	Your pH limit is from 4.6 to 5.0, while you have passed the batch number LZN001 having pH value 7.76. Justification is required in this regard.	It was a typo error the actual pH value was 4.76
10.	The container closure system of the innovator is "flexible plastic infusion bags in a foil laminate overwrap" while your prduct is packed in glass vial. Justify how your container	Firm has submitted that their container closure system is glass vial which is exactly simiar to that of comparator product.

	closure system can prevent the product from exposure to the light.	
11.	Submit clear copy of commercial invoice and evidence of import since the submitted invoice is not properly readable. Furthermore, also submit evidence of import of this material.	Firm has submitted copy of commercial invoice dated 15-04-2020 specifying purchase of 3Kg Linezolid. Firm has submitted copy of DHL invoice number 00206995 dated 29-04-2020.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after submission of applicable fee for pre-registration revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

175.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Infusion section (General).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1897: 20-01-2022
	Details of fee submitted	PKR 30,000/-: 30-12-2021
	The proposed proprietary name / brand name	**MOXIGEN 400mg/250ml Solution for Infusion**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial of 250ml Contains: Moxifloxacin (as hydrochloride)……400mg
	Pharmaceutical form of applied drug	Sterile yellow liquid filled in glass vials
	Pharmacotherapeutic Group of (API)	Fluoroquinolone antibiotic
	Reference to Finished product specifications	Innovators specs
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Avelox 400 mg/250 ml solution for infusion **(MHRA** Approved)
	For generic drugs (me-too status)	Avelox Injection by Bayer
	Name and address of API manufacturer.	Shree Je Laboatory Pvt. Ltd. C-24 & 25 RIICO Industrial Area, Sotanala, Behror, District Alwar, Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 12 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Moxiget infusion of Getz Pharma.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
STABILITY STUDY DATA		

Manufacturer of API	Shree Je Laboatory Pvt. Ltd. C-24 & 25 RIICO Industrial Area, Sotanala, Behror, District Alwar, Rajasthan India.		
API Lot No.	MXYUSU001		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	500 Vials	500 Vials	500 Vials
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	29-04-2021	29-04-2021	29-04-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 2019/203) issued by Drugs control Organization, Government of Rajasthan India dated 07-02-2019. The GMP certificate is valid upto three years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 08-03-2021 specifying purchase of 2.5Kg Moxifloxacin.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC system are not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Specify the exact section in which the applied drug will be manufactured, along with particulars of that section including manufacturing facility whether SVP or LVP and packaging	Firm has submitted that they will manufacture the applied product in Infusion section (General). This section has the facility to fill glass vials from 100ml to 300ml.

	facility whether glass vials or LDPE infusions.	
2.	You have submitted label claim "Each vial contains moxifloxacin hydrochloride 400mg/250ml" while the label claim of innovator product is "Each vial of 250ml Contains Moxifloxacin (as hydrochloride) 400mg". Revise your label claim along with submission of fee for revision of label claim.	Firm has submitted revised label claim as follows: Each vial of 250ml Contains: Moxifloxacin (as hydrochloride)……400mg
3.	Submit data of verification of analytical procedure of drug substance	Firm has submitted verification studies of analytical procedure of drug substance.
4.	Submit stability study data of drug substance till claimed shelf life as per zone IV-A conditions, since the submitted stability study data is till 1 year only.	Firm has submitted stability study data as per zone IV-A conditions where the real time data is till 24 months.
5.	Justify why the pharmaceutical equivalence studies were conducted against the comparator product instead of using innovator / reference product.	Due to easy access of comparator product in the market we have used it to perform comparative studies.
6.	Justify why the product is not subjected to terminal sterilization, since this method is recommended by the innovator product.	Firm has submitted copy of BMR which shows terminal sterilization of the product at 121°C for 30 minutes.
7.	You have mentioned innovator's specifications in module-1 and in-house specifications in module-3. Allign your drug product specifications along with submission of requisite fee.	Firm has submitted relevant page of module 1 which now specifies innovator's product. However, the firm has not submitted **fee** for change in specifications in module 1.
8.	The container closure system of the innovator is "Polyolefine bags with polypropylene port sealed in aluminium foil overwrap" while your prduct is packed in glass vial. Justify how your container closure system can prevent the product from exposure to the light.	Firm has submitted that their container closure system is glass vial which is exactly simiar to that of comparator product.
9.	Submit clear copy of commercial invoice and evidence of import since the submitted invoice is not properly readable.	Firm has submitted copy of commercial invoice dated 08-03-2021 specifying purchase of 2.5Kg Moxifloxacin. Firm has also submitted copy of DHL invoice number 270400305DTD.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after submission of pharmaceutical equivalence along with the innovator drug product.**

• **Registration Board further decided that registration letter will be issued after submission of applicable fee for pre-registration revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		
Capsule Section (General): 01 Molecules / 01 Products		
176.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Capsule section (General).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32571: 13-12-2021
	Details of fee submitted	PKR 30,000/-: 07-12-2021
	The proposed proprietary name / brand name	**TAMOGEN 0.4mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule Contains: Tamsulosin hydrochloride (as sustained release pellets)……0.4mg
	Pharmaceutical form of applied drug	White to off white spherical sustained release pellets contained in hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Alpha-adrenoreceptor antagonists
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Contiflo XL 400 micrograms capsules **(MHRA** Approved)
	For generic drugs (me-too status)	Tamsolin Capsule by Getz
	Name and address of API manufacturer.	Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Tamsol 0.4mg Capsule of Global Pharmaceuticals. Firm has submitted results of CDP for their product against Tamsol 0.4mg Capsule of Global Pharmaceuticals.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.
API Lot No.	TMS303
Description of Pack (Container closure system)	Alu-alu blister
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T106	T107	T108
Batch Size	1000 Capsule	1000 Capsule	1000 Capsule
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	20-08-2020	20-08-2020	20-08-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad dated 31-07-2019. The GMP certificate was granted based on inspection dated 11-02-2019. The GMP certificate is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 19-03-2020 specifying purchase of 2Kg Tamsulosin HCL SR pellets.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC system are not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit label claim in line with the innovator product along with submission of fee for revision of label claim.	Firm has submitted following label claim without submission of fee: Each capsule Contains: Tamsulosin hydrochloride (as sustained release pellets)……0.4mg
2.	Submit drug substance specifications in section 3.2.S.4.1 and secion 3.2.S.4.2 from both drug substance manufacturer as well as drug product manufacturer.	Firm has submitted drug substance specifications from both API manufacturer as well as drug product manufacturer.
3.	Submit data of verification of analytical procedure of drug substance	Firm has submitted verification studies of the analytical procedure of drug substance.

4.	Justify why the pharmaceutical equivalence and comparative dissolution profile studies were conducted against the comparator product instead of using innovator / reference product.	Due to easy access of comparator product in the market we have used it to perform comparative studies.
5.	The submitted HPLC chromatograms are not properly readable, resubmit clearly readable copies of the raw data.	Firm has again submitted analytical record with clear readable prints.
6.	Submit batch manufacturing record of three stability batches.	Firm has submitted copy of Batch Manufacturing Record of three stability batches.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after submission of pharmaceutical equivalence and Comparator Dissolution Profile (CDP) along with the reference / comparator drug product.**
- **Registration Board further decided that registration letter will be issued after submission of applicable fee for pre-registration revision of label claim as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

Case No. 02: M/s Nagarsons Pharmaceuticals, Islamabad

Firm has submitted copy of Acknowledgment of receipt of application for grant of DML by way of formulation to M/s Nagarsons Pharmaceuticals dated 19-02-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 278th meeting held on 10th and 11th December 2020 has approved the grant of DML in the name of M/s Nagarsons Pharmaceuticals for following sections:

1. Tablet (General)
2. Tablet (Psychotropic)
3. Capsule (General)
4. Cream /ointment/Lotion/Gel

Now the firm has submitted following applications as per the details mentioned in the table below:

Name of Section	Previously considered		Newly applied		Total	
	No of molecules	No of products	No of molecules	No of products	No of molecules	No of products
Tablet (General)	02	03	02	04	04	07
Tablet (Psychotropic)	-	-	-	-	-	-
Capsule (General)	06	10	-	-	-	-
Cream /ointment/Lotion/Gel	-	-	-	-	-	-

Tablet (General) section: 02 Molecules / 04 Products

177.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of DML number 000927 issued dated 04-06-2021 with effect from 19-02-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML by way of formulation to M/s Nagarsons Pharmaceuticals dated 07-06-2021 for following sections: 1. Tablet (General) 2. Tablet (Psychotropic) 3. Capsule (General) 4. Cream /ointment/Lotion/Gel
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10877: 29-04-2022
	Details of fee submitted	PKR 30,000/-: 11-04-2022
	The proposed proprietary name / brand name	**TERBINAG 125mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Terbinafine (as hydrochloride)……125mg
	Pharmaceutical form of applied drug	white colored round uncoated tablet
	Pharmacotherapeutic Group of (API)	Antifungals for systemic use
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	(**MHRA** Approved)
	For generic drugs (me-too status)	Lamisil Tablet 125mg of M/s Novartis (Reg # 013208)
	Name and address of API manufacturer.	M/s Saptagir Laboratories Pvt Lt. Sy No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill) Chegunta (Mandal), Medak (Dist), Telangana India.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the reference product i.e. Lamisil tablet of M/s Novartis Pakistan. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. Lamisil tablet of M/s Novartis Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	M/s Saptagir Laboratories Pvt Lt. Sy No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill) Chegunta (Mandal), Medak (Dist), Telangana India.		
API Lot No.	TH0180421		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 Tablet	2000 Tablet	2000 Tablet
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	22-09-2021	22-09-2021	22-09-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Nagarsons Pharmaceutical is a new license facility hence no such inspection has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 54991/TS/2021) issued by Drugs Control Administration Government of Telangana. The certificate is valid till 01-03-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying purchase of 25Kg Terbinafine hydrochloride cleared dated 15-09-2021. The invoice is cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with UV spectra, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC systems are not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm

1.	Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications and analytical method from both API manufacturer as well as Nagarsons Pharma.
2.	Submit verification studies of the analytical method of drug substance in section 3.2.S.4.3.	Firm has submitted report of verification studies of the analytical method of drug substance.
3.	Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.	Firm has submitted COA of relevant batch of drug substance from API manufacturer as well as Nagarsons Pharma.
4.	Provide detailed method of analysis by which pharmaceutical equivalence and CDP studies were performed.	Firm has submitted complete method of analysis for CDP and pharmaceutical equivalence which is in line with the drug product specifications of the firm.
5.	Provide valid GMP certificate of the drug substance manufacturer since the submitted GMP certificate was valid till 01-03-2022.	Firm has submitted copy of GMP certificate (No. 54991/TS/2021) issued by Drugs Control Administration Government of Telangana. The certificate is valid till 01-03-2022.
6.	Submit Batch Manufacturing Record of three stability batches.	Firm has submitted copy of Batch Manufacturing Record of three stability batches.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

178.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of DML number 000927 issued dated 04-06-2021 with effect from 19-02-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML by way of formulation to M/s Nagarsons Pharmaceuticals dated 07-06-2021 for following sections: 1. Tablet (General)

		2. Tablet (Psychotropic) 3. Capsule (General) 4. Cream /ointment/Lotion/Gel
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10878: 29-04-2022
	Details of fee submitted	PKR 30,000/-: 11-04-2022
	The proposed proprietary name / brand name	**TERBINAG 250mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Terbinafine (as hydrochloride)……250mg
	Pharmaceutical form of applied drug	white colored round uncoated tablet
	Pharmacotherapeutic Group of (API)	Antifungals for systemic use
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	(**MHRA** Approved)
	For generic drugs (me-too status)	Lamisil Tablet 125mg of M/s Novartis (Reg # 013209)
	Name and address of API manufacturer.	M/s Saptagir Laboratories Pvt Lt. Sy No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill) Chegunta (Mandal), Medak (Dist), Telangana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the reference product i.e. Lamisil tablet of M/s Novartis Pakistan. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. Lamisil tablet of M/s Novartis Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Saptagir Laboratories Pvt Lt. Sy No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill) Chegunta (Mandal), Medak (Dist), Telangana India.		
API Lot No.	TH0180421		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-004	T-005	T-006
Batch Size	2000 Tablet	2000 Tablet	2000 Tablet
Manufacturing Date	09-2021	09-2021	09-2021

Date of Initiation	22-09-2021	22-09-2021	22-09-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Nagarsons Pharmaceutical is a new license facility hence no such inspection has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 54991/TS/2021) issued by Drugs Control Administration Government of Telangana. The certificate is valid till 01-03-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying purchase of 25Kg Terbinafine hydrochloride cleared dated 15-09-2021. The invoice is cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with UV spectra, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC systems are not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications and analytical method from both API manufacturer as well as Nagarsons Pharma.
2.	Submit verification studies of the analytical method of drug substance in section 3.2.S.4.3.	Firm has submitted report of verification studies of the analytical method of drug substance.
3.	Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.	Firm has submitted COA of relevant batch of drug substance from API manufacturer as well as Nagarsons Pharma.
4.	Provide detailed method of analysis by which pharmaceutical equivalence and CDP studies were performed.	Firm has submitted complete method of analysis for CDP and pharmaceutical equivalence which is in line with the drug product specifications of the firm.

5.	Provide valid GMP certificate of the drug substance manufacturer since the submitted GMP certificate was valid till 01-03-2022.	Firm has submitted copy of GMP certificate (No. 54991/TS/2021) issued by Drugs Control Administration Government of Telangana. The certificate is valid till 01-03-2022.
6.	Submit Batch Manufacturing Record of three stability batches.	Firm has submitted copy of Batch Manufacturing Record of three stability batches.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

179.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of DML number 000927 issued dated 04-06-2021 with effect from 19-02-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML by way of formulation to M/s Nagarsons Pharmaceuticals dated 07-06-2021 for following sections: 1. Tablet (General) 2. Tablet (Psychotropic) 3. Capsule (General) 4. Cream /ointment/Lotion/Gel
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7371: 16-03-2022
	Details of fee submitted	PKR 30,000/-: 09-03-2022
	The proposed proprietary name / brand name	**AZONAG 250mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Azithromycin (as dihydrate)……250mg
	Pharmaceutical form of applied drug	Hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Macrolides

	Reference to Finished product specifications	BP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zithromax Capsule of Pfizer (**MHRA** Approved)
	For generic drugs (me-too status)	Zithromax capsule 250mg of M/s Pfizer Pakistan (Reg # 014471)
	Name and address of API manufacturer.	M/s Hebei Guolong Pharmaceutical Co. Ltd No. 9 Xingye Street, Shijiazhuang Economic and Technological Development Zone, Hebei Province China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the reference product i.e. Zetamax 250mg Capsule of M/s Pfizer Pakistan. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. Zetamax 250mg Capsule of M/s Pfizer Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Hebei Guolong Pharmaceutical Co. Ltd No. 9 Xingye Street, Shijiazhuang Economic and Technological Development Zone, Hebei Province China.		
API Lot No.	210507019		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-0022	T-003
Batch Size	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	26-08-2021	26-08-2021	26-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Nagarsons Pharmaceutical is a new license facility hence no such inspection has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of Drug Manufacturing License of Hebei Guolong Pharmaceutical Co. Ltd. (No. JI20150058) issued by Hebei Provincial Drug Administration dated 22-07-2020. The certificate is valid till 21-07-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying purchase of 10Kg Azithromycin dihydrate cleared dated 24-08-2021. The invoice is cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like	Firm has submitted complete record of testing of all batches along with UV spectra,

	chromatograms, Raw data sheets, COA, summary data sheets etc.	raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC systems are not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications and analytical method from both API manufacturer as well as Nagarsons Pharma.
2.	Submit verification studies of the analytical method of drug substance in section 3.2.S.4.3.	Firm has submitted report of verification studies of the analytical method of drug substance.
3.	Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.	Firm has submitted COA of relevant batch of drug substance from API manufacturer as well as Nagarsons Pharma.
4.	Justify why pharmaceutical equivalence and CDP studies are performed against zetamax capsule of Pfizer instead of using the innovator's product.	We use Zetamax Capsule by Pfizer because the innovator product is not available in the market in Pakistan.
5.	Provide raw data sheets for the calculation of results of dissolution test throughout the stability studies.	Firm has submitted raw data sheets for the calculation of results of dissolution test throughout the stability studies using HPLC method.
6.	Submit analytical record for azithromycin capsule since the submitted record contains HPLC chromatograms of azithromycin tablet as well.	Firm has submitted that mistakenly at one time point the data of azithromycin tablet was attached instead of azithromycin capsule. Firm has now submitted analytical record for azithromycin capsule.
7.	Submit Batch Manufacturing Record of three stability batches.	Firm has submitted copy of Batch Manufacturing Record of three stability batches.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

180.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of DML number 000927 issued dated 04-06-2021 with effect from 19-02-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML by way of formulation to M/s Nagarsons Pharmaceuticals dated 07-06-2021 for following sections: 1. Tablet (General) 2. Tablet (Psychotropic) 3. Capsule (General) 4. Cream /ointment/Lotion/Gel
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7370: 16-03-2022
	Details of fee submitted	PKR 30,000/-: 21-02-2022
	The proposed proprietary name / brand name	**AZONAG 250mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Azithromycin (as dihydrate)……250mg
	Pharmaceutical form of applied drug	White to off white film coated tablet
	Pharmacotherapeutic Group of (API)	Macrolides
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	(**USFDA** Approved)
	For generic drugs (me-too status)	Orzit Tablet 250mg of M/s Martin Dow (Reg # 057294)
	Name and address of API manufacturer.	M/s Hebei Guolong Pharmaceutical Co. Ltd No. 9 Xingye Street, Shijiazhuang Economic and Technological Development Zone, Hebei Province China.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the reference product i.e. Zetamax 250mg Tablet of M/s Pfizer Pakistan. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. Zetamax 250mg Tablet of M/s Pfizer Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	M/s Hebei Guolong Pharmaceutical Co. Ltd No. 9 Xingye Street, Shijiazhuang Economic and Technological Development Zone, Hebei Province China.		
API Lot No.	210507019		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-004	T-005	T-006
Batch Size	2500 Tablet	2500 Tablet	2500 Tablet
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	26-08-2021	26-08-2021	26-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Nagarsons Pharmaceutical is a new license facility hence no such inspection has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of Drug Manufacturing License of Hebei Guolong Pharmaceutical Co. Ltd. (No. JI20150058) issued by Hebei Provincial Drug Administration dated 22-07-2020. The certificate is valid till 21-07-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying purchase of 10Kg Azithromycin dihydrate cleared dated 24-08-2021. The invoice is cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with UV spectra, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC systems are not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm

1.	Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications and analytical method from both API manufacturer as well as Nagarsons Pharma.
2.	Submit verification studies of the analytical method of drug substance in section 3.2.S.4.3.	Firm has submitted report of verification studies of the analytical method of drug substance.
3.	Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.	Firm has submitted COA of relevant batch of drug substance from API manufacturer as well as Nagarsons Pharma.
4.	Justify why pharmaceutical equivalence and CDP studies are performed against zetamax tablet of Pfizer instead of using the innovator's product.	We use Zetamax tablet by Pfizer because the innovator product is not available in the market in Pakistan.
5.	Provide raw data sheets for the calculation of results of dissolution test throughout the stability studies.	Firm has submitted raw data sheets for the calculation of results of dissolution test throughout the stability studies using HPLC method.
6.	Provide evidence of column oven which is required to maintain temperature of 50°	Firm has not submitted evidence of HPLC along with column oven.
7.	Submit Batch Manufacturing Record of three stability batches.	Firm has submitted copy of Batch Manufacturing Record of three stability batches.

Decision: Deferred for submission of evidence of HPLC system along with column oven which is required to maintain temperature of 50° for assay testing of drug product as per USP monograph.

181.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of DML number 000927 issued dated 04-06-2021 with effect from 19-02-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML by way of formulation to M/s Nagarsons Pharmaceuticals dated 07-06-2021 for following sections:

		1. Tablet (General) 2. Tablet (Psychotropic) 3. Capsule (General) 4. Cream /ointment/Lotion/Gel
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7372: 16-03-2022
	Details of fee submitted	PKR 30,000/-: 21-02-2022
	The proposed proprietary name / brand name	**AZONAG 500mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Azithromycin (as dihydrate)……500mg
	Pharmaceutical form of applied drug	White to off white film coated tablet
	Pharmacotherapeutic Group of (API)	Macrolides
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	(**USFDA** Approved)
	For generic drugs (me-too status)	Azomax Tablet 500mg of M/s Novartis Pakistan (Reg # 045415)
	Name and address of API manufacturer.	M/s Hebei Guolong Pharmaceutical Co. Ltd No. 9 Xingye Street, Shijiazhuang Economic and Technological Development Zone, Hebei Province China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the reference product i.e. Azomax 500mg Tablet of M/s Novartis Pakistan. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. Azomax 500mg Tablet of M/s Novartis Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Hebei Guolong Pharmaceutical Co. Ltd No. 9 Xingye Street, Shijiazhuang Economic and Technological Development Zone, Hebei Province China.		
API Lot No.	210507019		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH Accelerated: $40^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2500 Tablet	2500 Tablet	2500 Tablet
Manufacturing Date	08-2021	08-2021	08-2021

Date of Initiation	26-08-2021	26-08-2021	26-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Nagarsons Pharmaceutical is a new license facility hence no such inspection has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of Drug Manufacturing License of Hebei Guolong Pharmaceutical Co. Ltd. (No. JI20150058) issued by Hebei Provincial Drug Administration dated 22-07-2020. The certificate is valid till 21-07-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying purchase of 10Kg Azithromycin dihydrate cleared dated 24-08-2021. The invoice is cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with UV spectra, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC systems are not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications and analytical method from both API manufacturer as well as Nagarsons Pharma.
2.	Submit verification studies of the analytical method of drug substance in section 3.2.S.4.3.	Firm has submitted report of verification studies of the analytical method of drug substance.
3.	Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.	Firm has submitted COA of relevant batch of drug substance from API manufacturer as well as Nagarsons Pharma.
4.	Submit stability study data in proper sequence as per the guidelines of registration Board since the	Firm has submitted complete data in section 3.2.P.8.3 as per the guidelines specified in CTD guidance document.

	submitted data is not properly aligned.	
5.	Provide raw data sheets for the calculation of results of dissolution test throughout the stability studies.	Firm has submitted raw data sheets for the calculation of results of dissolution test throughout the stability studies using HPLC method.
6.	Provide evidence of column oven which is required to maintain temperature of 50°	Firm has not submitted evidence of HPLC along with column oven.
7.	Submit Batch Manufacturing Record of three stability batches.	Firm has submitted copy of Batch Manufacturing Record of three stability batches.

Decision: Deferred for submission of evidence of HPLC system along with column oven which is required to maintain temperature of 50° for assay testing of drug product as per USP monograph.

M/s Martin Dow Limited, Plot No. 37, Sector 19, Korangi Industrial Area Karachi.
On the recommendations of panel of experts, the CLB in its 277th meeting held on 15th -16th October has
considered and approved the following one additional section of M/s Martin Dow Limited, Plot No. 37, Sector 19, Korangi Industrial Area, Karachi. The details of the products applied and already considered against new section are as under:

Already considered		Freshly applied	
Molecule	Product	Molecule	Product
03	05	01	01

Dry Powder Inhalers Section (General) (1 molecules / 1 Product)

182.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Limited, Plot No. 37, Sector 19, Korangi Industrial Area Karachi.**
	Name, address of Manufacturing site.	M/s Martin Dow Limited, Plot No. 37, Sector 19, Korangi Industrial Area Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued based on the inspection dated 7th May 2019. Firm has also submitted copy of GMP inspection report dated 20-10-2021 which specifies that the firm is considered to be operating at Good level of compliance with cGMP guidelines.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section dated 27-10-2020 specifying Dry powder Inhaler Capsule (General) - New section.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11212: 10-05-2022
	Details of fee submitted	PKR 75,000/-: 22-03-2022
	The proposed proprietary name / brand name	**INDIBRO-M 150/50/160 mcg DPI Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each DPI Capsule Contains: Indacaterol (as acetate)……150mcg Glycopyrronium (as bromide)…50mcg Mometasone Furoate…160mcg Each delivered dose contains: Indacaterol (as acetate)……114mcg Glycopyrronium (as bromide)…46mcg Mometasone Furoate…136mcg
	Pharmaceutical form of applied drug	Transparent cap and body, Hypromellose capsule size No. 3 containing white to off white powder
	Pharmacotherapeutic Group of (API)	Adrenergics in combination with anticholinergics incl. triple combinations with corticosteroids (ATC code: R03AL12)
	Reference to Finished product specifications	In house
	Proposed Pack size	10's, 30's, 90's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Enerzair Breezhaler 114 micrograms/46 micrograms/136 micrograms inhalation powder, hard capsules of Novartis Europharm Limited (**EMA Approved**)
	For generic drugs (me-too status)	NA
	Name and address of API manufacturer.	**Indacaterol acetate:** Melody Healthcare Pvt. Ltd.Plot No. J-73, M.I.D.C, Tarapur, Boisar, Dist. Palghar 401506, Tal: MIDC Tarapur boisar, Dist: Thane- Zone4. Maharashtra State, India. **Glycopyrronium:** INKE, S.A. C/Argent, 1. Area Industrial del Llobregat 08755 CASTELLBISBAL (BARCELONA). **Mometasone Furoate:** Aarti Industries Limited Plot No E-50, MIDC, Tarapur, Taluka & District-Palghar, 401506 Maharashtra State, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls,

		impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Indacaterol Acetate:** Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ICA/01/21, ICA/02/21, ICA/03/21) **Glycopyrronium Bromide:** Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (P-1M-1, P-2M-1, P-3M-1) **Mometasone Furoate:** Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MF-13013 (JM-01)-001, MF-13014 (JM-01)-001, MF-14305 (JM-01)-001)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence and Invitro Comparative Delivered Dose Uniformity and Aerodynamic Particle Size distribution was performed against Innovator Product Enezair 150/50/160mcg DPI capsule Batch no: BUL36 manufactured by Novartis.

	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Indacaterol acetate:** Melody Healthcare Pvt. Ltd.Plot No. J-73, M.I.D.C, Tarapur, Boisar, Dist. Palghar 401506, Tal: MIDC Tarapur boisar, Dist: Thane- Zone4. Maharashtra State, India. **Glycopyrronium:** INKE, S.A. C/Argent, 1. Area Industrial del Llobregat 08755 CASTELLBISBAL (BARCELONA). **Mometasone Furoate:** Aarti Industries Limited Plot No E-50, MIDC, Tarapur, Taluka & District-Palghar, 401506 Maharashtra State, India.		
API Lot No.	**Indacaterol acetate:** ICA/08/21 **Glycopyrronium:** P-21M **Mometasone Furoate:** MF-20016(JM-01)-001		
Description of Pack (Container closure system)	Alu-alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NPD-C-1736-S	NPD-C-1737-S	NPD-C-1738-S
Batch Size	6000 capsules	6000 capsules	6000 capsules
Manufacturing Date	15-11-2021	15-11-2021	15-11-2021
Date of Initiation	21-12-2021	21-12-2021	21-12-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product "Empator 10mg Tablets" which was presented in 291st meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 6th August, 2019. According to inspection report, following points were confirmed. • The firm has 21CFR compliant HPLC software. • The firm has audit trail reports available.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Indacaterol acetate:** Firm has submitteded copy of GMP certificate (No. 91716/2020/11/31377) of M/s Melody Healthcare Pvt. Ltd.Plot No. J-73, M.I.D.C, Tarapur, Boisar, Dist. Palghar 401506, Thane- Zone4. Maharashtra State, India issued by Food & Drugs Administration (Maharashtra State). The Certificate is valid till 19-03-2023.

		Glycopyrronium: Firm has submitted copy of GMP certificate (No. NCF-II/&1917/001/CAT) of M/s INKE, S.A. C/Argent, 08755 CASTELLBISBAL Spain issued by Competent Regional Authority. Directorate of Regulation, Planning and Sanitary Resources. Health Department. Generalitat of Catalunya. The certificate is present at Eudra GMP database and was issued on the basis of inspection dated 08-04-2019. The certificate is valid till 08-04-2023. **Mometasone Furoate:** Firm has submitted copy of GMP certificate (No. 92338/2020/11/32133) of M/s Aarti Industries Limited Plot No E-50, MIDC, Tarapur, Taluka & District-Palghar, 401506 Maharashtra State, India issued by FDA Mahrashtra. The certificate is valid till 09-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Indacaterol acetate: ICA/08/21:** Firm has submitted copy of commercial invoice cleared dated 30-08-2021 specifying import of 40g Indacaterol acetate. The commercial invoice is attested by AD (I&E) DRAP. **Glycopyrronium: P-21M:** Firm has submitted copy of commercial invoice cleared dated 27-07-2021 specifying import of 0.008Kg Glycopyrronium. The commercial invoice is attested by AD (I&E) DRAP. **Mometasone Furoate: MF-20016(JM-01)-001:** Firm has submitted copy of commercial invoice cleared dated 14-07-2021 specifying import of 0.040Kg mometasone furoate. The commercial invoice is attested by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
Evaluation by PEC:		
Details of DPI device is		

DPI device : **Monodose Inhaler RS01 Mod. 7 (Catalogue Code: "239700001AB")** Manufacturer : **Berry Plastiape S.p.A** Shelf Life: **3 Years**
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration Board further decided that registration letter will be issued after submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **The firm will use DPI device Monodose Inhaler Manufactured by M/s Berry Plastiape S.p.A.**

Case No. 03 Registration applications of CTD cases

a. Routine cases of local manufacturing

183.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Carer Pharmaceuticals Plot # 27, Main Road, Rawat Industrial Estate Rawat.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 01-03-2021 is submitted.
	GMP status of the firm	**Global pharmaceuticals:** 11 & 24-10-2018: On the basis of findings, panel unanimously decided to recommend the issuance of GMP certificate.
	Evidence of approval of manufacturing facility	Not submitted
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23840: 31-08-2021

	Details of fee submitted	PKR 75,000/-: 04-06-2021
	The proposed proprietary name / brand name	**BRIAR 100mg/5ml suspension**

Evaluation by PEC:

The applicant firm (M/s Carer Pharmaceuticals) dated 30-03-2022 (Dy No. 8297) has submitted a new request for registration of their product on contract manufacturing from M/s Seraph Pharmaceuticals along with submission of full fee.
The details of the newly submitted data are as follows:
DY No. 8298: 30-03-2022
New fee: 75,000/-: 07-03-2022

Name, address of Applicant / Marketing Authorization Holder	**M/s Carer Pharmaceuticals Plot # 27, Main Road, Rawat Industrial Estate Rawat.**
Name, address of Manufacturing site.	M/s Seraph Pharmaceuticals Plot # 210, Industrial Triangle Kahuta Road Islamabad.
Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Contract manufacturing agreement between both firms dated 05-01-2022 is provided)
GMP status of the firm	**Seraph Pharmaceuticals:** GMP certificate issued on the basis of inspection conducted on 11/07/2019.
Evidence of approval of manufacturing facility	Firm (M/s Seraph Pharmaceuticals) has submitted copy of Issuance of DML letter dated 12-06-2017 specifying Dry Vial Cephalosporin section.
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
Dy. No. and date of submission	Dy No. 8298: 30-03-2022
Details of fee submitted	Rs. 75,000/-: 07-03-2022
The proposed proprietary name / brand name	**BRIAR 100mg/5ml suspension**
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension contains: Cefixime (as trihydrate)……100mg
Pharmaceutical form of applied drug	Amber colored glass bottle containing white to off white powder for reconstitution volume 30ml (after reconstitution)
Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
Reference to Finished product specifications	USP specs
Proposed Pack size	30ml bottle
Proposed unit price	As per SRO
The status in reference regulatory authorities	**(USFDA** Approved)
For generic drugs (me-too status)	Tripsan 100mg/5ml dry suspension by Seraph Pharmaceuticals

Name and address of API manufacturer.	Saakh Pharma (Pvt) Ltd. C-7/1, North Western Industrial Zone Port Qasim Karachi.
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated and real time conditions. The real time stability data is conducted as per zone IV-A conditions till 12 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted process validation report
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has performed comparative analysis of their developed formulation against the comparator product i.e. "Cefspan Dry powder for suspension 100mg/5ml". Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator product. The analysis of all quality tests were performed according to USP monograph. The results depicts that the developed formulation is comparable to the comparator product. The firm has also performed compatibility studies of the product with diluent i.e. purified (boiled and cooled water). Firm has performed testing of assay pH and other parameters for 7 days at room temperature and 14 days at 2 – 8 ^{o}C and the results after reconstitution were within the acceptable range specified by the firm.
Analytical method validation/verification of product	Firm has submitted report of validation of analytical method for the drug product.

	Firm has submitted report of verification studies of analytical method for the drug substance.		
STABILITY STUDY DATA			
Manufacturer of API	Saakh Pharma (Pvt) Ltd. C-7/1, North Western Industrial Zone Port Qasim Karachi.		
API Lot No.	17CF10172		
Description of Pack (Container closure system)	1's bottle of powder for suspension packed in unit carton		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	10,000 bottles	10,000 bottles	10,000 bottles
Manufacturing Date	01-2018	01-2018	03-2018
Date of Initiation	18-01-2018	19-01-2018	26-03-2018
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to following product specific inspection reports • Dexpro (Dexlansoprazole) 30 and 60mg Capsule. PSI was conducted on 11-09-2018 and the product was approved in 285th meeting of Registration Board. • Neovel 800mg Tablet. Its PSI was conducted on 14-12-2018 and the product was approved in 288th meeting of Registration Board. • Serbica 20mg Capsule. Its PSI was conducted on 29-10-2018 and the product was approved in 290th meeting of Registration Board. Firm has further submitted that their product Neogene 2g Injection was approved in 293th meeting of Registration Board. That product was applied by AGP and contract manufactured by Seraph and was submitted on Form 5F (CTD) along with complete data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML of M/s Saakh Pharma is submitted by the firm. Copy of GMP certificate of M/s Saakh Pharma dated 15-01-2018 issued on the basis of inspection dated 16-10-2017 is submitted by the firm. The certificate is issued by Additional Director DRAP Karachi.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice dated 12-01-2018 specifying purchase of 50Kg cefixime from Saakh Pharma (Pvt) Ltd.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that since the stability study of this product was initiated 2 years ago, at that time our HPLC (Schimadzu) was not 21 CFR compliant. However now we have 21 CFR compliant (Perkin Elmer) HPLC system. We undertake that in future we will use 21 CFR compliant HPLC system for stability testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted that their stability chambers are supplied with uninterrupted power supply and have digital data logger for monitoring temperature and humidity. The digital data logger have been verified by the panel during our onsite inspection as well.

Evaluation by PEC:

- The applied product to be manufactured by M/s Seraph Pharmaceuticals Plot # 210, Industrial Triangle Kahuta Road Islamabad have already been approved by Registration Board in its 297th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 297th meeting are as follows:

Applicant firm	M/s Moringa Pharmaceuticals 35-A, Sunder Industrial Estate, Lahore.
Manufacturer firm	M/s Seraph Pharmaceuticals Plot # 210, Industrial Triangle Kahuta Road Islamabad.
Brand Name	Saf-Xime 100mg/5ml Dry suspension
Batch No. of drug product	001, 002, 003
Case No.	279
BR Meeting	297

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

184.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Akson Pharmaceuticals Pvt Ltd. Plot no.9-B/1 & 2, Sector D-1, Old industrial Estate Mirpur Azad Kashmir**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer

		☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25215: 10-09-2021
	Details of fee submitted	PKR 75,000/-: 05-07-2021
	The proposed proprietary name / brand name	**MERNEM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis

		and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
API Lot No.	MRPS/062/18
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 001	Noopem Injection 001
Batch Size	7,000 Vials	7,000 Vials	7,000 Vials
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	28-06-2019	28-06-2019	28-06-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	820
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

185.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Akson Pharmaceuticals Pvt Ltd. Plot no.9-B/1 & 2, Sector D-1, Old industrial Estate Mirpur Azad Kashmir**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.

	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23056: 24-08-2021
	Details of fee submitted	PKR 75,000/-: 05-07-2021
	The proposed proprietary name / brand name	**MERNEM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities,

		physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10,500 Vials	13,000 Vials	5,500 Vials
Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	30-06-2019	30-09-2019	26-09-2019

No. of Batches	03

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 1g Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001

	Case No.	821
	Registration Board meeting	316th meeting of Registration Board
	Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

186.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Ameer & Adnan Pharmaceutical Pvt Ltd.** **Plot No.47, Sundar Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23054: 24-08-2021
	Details of fee submitted	PKR 75,000/-: 13-07-2021
	The proposed proprietary name / brand name	**MERNEM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The

		accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 001	Noopem Injection 001
Batch Size	7,000 Vials	7,000 Vials	7,000 Vials
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	28-06-2019	28-06-2019	28-06-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar

		Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	820
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61%

•		Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

187.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Ameer & Adnan Pharmaceutical Pvt Ltd.** **Plot No.47, Sundar Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23055: 24-08-2021
	Details of fee submitted	PKR 75,000/-: 13-07-2021
	The proposed proprietary name / brand name	**MERNEM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g

		(blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch

		analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10,500 Vials	13,000 Vials	5,500 Vials
Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	30-06-2019	30-09-2019	26-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 1g Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	821
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

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Decision: Approved. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
188.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23708: 30-08-2021
	Details of fee submitted	PKR 75,000/-: 29-06-2021
	The proposed proprietary name / brand name	**CARBANEM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals

	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
STABILITY STUDY DATA		

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 001	Noopem Injection 001
Batch Size	7,000 Vials	7,000 Vials	7,000 Vials
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	28-06-2019	28-06-2019	28-06-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	820
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

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Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

189.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer

		☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23709: 30-08-2021
	Details of fee submitted	PKR 75,000/-: 29-06-2021
	The proposed proprietary name / brand name	**CARBANEM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis

		and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
API Lot No.	MRPS/062/18
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10,500 Vials	13,000 Vials	5,500 Vials
Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	30-06-2019	30-09-2019	26-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

	Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
	Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Brand Name	MEROCIN 1g Injection
	Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
	Case No.	821
	Registration Board meeting	316th meeting of Registration Board
	Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

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Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

190.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Aulton Pharmaceuticals. Plot No. 84/1, Block A, Phase V, Industrial Estate, Hattar**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020

	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23053: 24-08-2021
	Details of fee submitted	PKR 75,000/-: 29-06-2021
	The proposed proprietary name / brand name	**AROPEN 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis

		and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 001	Noopem Injection 001
Batch Size	7,000 Vials	7,000 Vials	7,000 Vials
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	28-06-2019	28-06-2019	28-06-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	820
Registration Board meeting	316th meeting of Registration Board

•	Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

191.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Aulton Pharmaceuticals. Plot No. 84/1, Block A, Phase V, Industrial Estate, Hattar**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23707: 30-08-2021

	Details of fee submitted	PKR 75,000/-: 29-06-2021
	The proposed proprietary name / brand name	**AROPEN 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10,500 Vials	13,000 Vials	5,500 Vials
Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	30-06-2019	30-09-2019	26-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 1g Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	821
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and

•		advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

192.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Newton Health care Pvt Ltd. Plot No. 8,9. H.I.T.E, Hub Balochistan**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22328: 13-08-2021
	Details of fee submitted	PKR 75,000/-: 08-07-2021
	The proposed proprietary name / brand name	**ENIM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic

	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 001	Noopem Injection 001
Batch Size	7,000 Vials	7,000 Vials	7,000 Vials
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	28-06-2019	28-06-2019	28-06-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.

	chromatograms, Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	820
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.

Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.		
193.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Newton Health care Pvt Ltd. Plot No. 8,9. H.I.T.E, Hub Balochistan**
	Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 26-06-2021 is submitted.
	GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22329: 13-08-2021
	Details of fee submitted	PKR 75,000/-: 08-07-2021
	The proposed proprietary name / brand name	**ENIM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals

	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
STABILITY STUDY DATA		

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10,500 Vials	13,000 Vials	5,500 Vials
Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	30-06-2019	30-09-2019	26-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2022/440) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is also submitted by the firm.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 1g Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	821
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

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Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

194.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Linta Pharmaceuticals (Pvt) Ltd. Plot # 3, Street S-5, National Industrial Zone, Rawat Islamabad.**
	Name, address of Manufacturing site.	M/s Rotex Pharma (Pvt) Ltd, Plot # 206 & 207, Industrial Triangle Kahuta Road Islamabad.

	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Original agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 14-07-2020 is submitted.
	GMP status of the firm	**Linta Pharmaceuticals:** The firm was inspected on 10-07-2019 and conclusion of inspection was: Keeping in view the above it may be concluded that M/s Linta Pharmaceuticals is operating at acceptable level of GMP standard. **Rotex pharma:** GMP certificate issued on the basis of inspection dated 12-08-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000651 of M/s Rotex Pharma Islamabad dated 13-06-2017 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4079: 04-02-2021
	Details of fee submitted	PKR 50,000/-: 15-07-2020
	The proposed proprietary name / brand name	**PENAM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with dark blue flip off seal.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.
STABILITY STUDY DATA		
Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.	

API Lot No.			
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	C160001	C160002	C160003
Batch Size	7042 vials	7042 vials	7042 vials
Manufacturing Date	09-2018	10-2018	03-2019
Date of Initiation	22-09-2018	05-11-2018	29-033-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The status of applicant mentioned in section 1.3.3 of module 1 is "manufacturer" while the application is for contract manufacturing from Rotex Pharma. Clarification is required in this regard.
- Submit module 1 as per the CTD guidance document approved by Registration Board by providing all the information and documents in relevant sections / sub-sections instead of referring to annexures.
- Provide details regarding total number of sections and number of products already registered and applied on contract manufacturing of M/s Linta Pharmaceuticals.
- Submit quality overall summary (QOS) in module 2 as per WHO QOS-PD template or as per the template approved by Registration Board in its 296th meeting and also published in CTD guidance document. The submitted QOS contains extracts from module 3 instead of providing summary of the data as per the requirements of QOS.

- Provide data in section 3.2.S.3.1 as per the guidance document approved by Registration Board which specifies that "Discussion on the potential for isomerism and identification of stereochemistry, studies performed to identify potential polymorphic forms and particle size distribution of the Drug substance shall be submitted, where these parameters may impact the quality, safety or efficacy of the drug product."
- Section 3.2.S.4.1 contains specifications for meropenem trihydrate sterile, sodium carbonate sterile and meropenem for injection. Clarification is required that which particular specifications was used for the testing of drug substance.
- Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."
- Justify the acceptance criteria of assay "NLT 78% as meropenem on dried basis", and also provide scientific justification how it is in line with the USP monograph.
- Specify the relative retention time in terms of quantitative values for the identification of drug substance, since the statement "the retention time of meropenem peak of the sample solution correspond to that of the standard solution obtained in assay" is not scientifically justified without having a relative retention time limit.
- As per the assay method of drug substance, the sample solution is nominally 0.1mg/ml of meropenem in mobile phase. While as per USP monograph the sample solution preparation method is entirely different which involves initial reconstitution with water prior to dilution with mobile phase. Justify how the tests performed by your method can be considered acceptable under the USP monograph.
- Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.
- Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification)".
- Provide COA of reference standard / working standard used in the testing of drug substance.
- Justify how 710mg of meropenem as trihydrate blended with sodium carbonate contains 500mg of meropenem.
- Submit information in section 3.2.P.1 c) Description of accompanying reconstitution diluent(s) as per the guidance document approved by Registration Board which specifies that "Provide information including type of diluent, its composition, quantity or volume, specifications (as applicable) and regulatory status in Pakistan (as applicable) for the diluent which is to be provided along with the applied drug".
- Submit information in section 3.2.P.2 as per the guidance document approved by Registration Board which specifies that "A brief information on the pharmaceutical development shall be included. This information specify the justification of formulation and method of manufacturing. It is also important that critical quality attributes (CQAs) and Critical Process Parameters (CPP) shall be discussed".
- Submit data in section 3.2.P.2.1.1 as per the guidance document approved by Registration Board which specifies that "Discussion shall be provided for the key physicochemical characteristics (e.g. water content, solubility, particle size distribution, polymorphic or

solid state form) of the Drug Substance(s) that can influence the performance of the Drug Product".

- Provide details including batch number, expiry date of the innovator product along with pharmaceutical equivalence was performed.
- You have submitted that 20ml reconstituted volume is available with Meronem 500mg Injection of Pfizer Pakistan, however the meropenem 500mg injection of innovator as well as reference product is reconstituted using 10ml diluent. Clarification is required in this regard.
- Submit data in section 3.2.P.2.6 as per the guidance document approved by Registration Board which specifies that "Compatibility studies for the dry powder for injections and dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product".
- Specify the volume of the vial of the drug product, since 30ml vial was mentioned in section 3.2.P.2 while 20ml vial is mentioned in section 3.2.P.3.
- Specify the colour of seal, since blue colour is mentioned in section 3.2.P.2 while green colour is mentioned in section 3.2.P.3.
- Provide detailed method of sample solution preparation for assay testing of the drug product in section 3.2.P.5.2 specifying the exact volume of water in which reconstitution is carried out.
- Justify why the formula for calculation of assay results of meropenem submitted in section 3.2.P.5.2 is different from that specified in USP monograph.
- Justify why the test of contents of sodium is not included in the specifications of the drug product as per the USP monograph.
- Justify how the 3 batches were released without determining the contents of sodium.
- Submit COA of reference standard / working standard used for the testing of the stability batches in section 3.2.P.6.
- Submit data in section 3.2.P.8.1 as per the guidance document approved by Registration Board which specifies that "Summary of additional stability studies (if applicable) e.g. in-use studies for drug products which are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided".
- Justify why the test of identification, contents of sodium, constituted solution, loss on drying is not performed during the stability studies.
- Justify why test of bacterial endotoxin and sterility was not performed at 6 month time point at accelerated stability studies.
- Justify why only 3 chromatographs of the standard solution was run while USP General chapter <621> recommends that five replicates of standard solution should be used for system suitability studies.
- Submit raw data sheets to support the calculation of results of assay throughout the stability studies.
- Provide analytical record including certificate of analysis at each time point, HPLC chromatograms, raw data sheets using page separators to segregate the data of each time point and each batch, since the submitted data is mixed up and submitted without any sequence.
- Submit stability study data in section 3.2.P.8.3 as per the checklist approved by Registration Board in its 296th meeting and the CTD guidance document, which includes the following:
    - Reference of previous approval of applications with stability study data of the firm (if any)
    - Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.
    - Documents for the procurement of API with approval from DRAP (in case of import).
    - Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.

- Compliance Record of HPLC software 21CFR & audit trail reports on product testing
- Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

- Submit Batch Manufacturing record (BMR) of the three batches for which stability study data is submitted.

Response by the firm:
Firm vide its letter dated 19-08-2021 submitted that they request to change the contract manufacturer to M/s Nicholas Pharmaceuticals, Islamabad. Firm has submitted following documents:

- Complete fee for change of contract manufacturer 75,000/- vide slip number 265253322.
- Complete data in module 1, 2 and 3. The evaluation of the data is placed below

Name, address of Applicant / Marketing Authorization Holder	**M/s Linta Pharmaceuticals (Pvt) Ltd. Plot # 3, Street S-5, National Industrial Zone, Rawat Islamabad.**
Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 25-01-2022 is submitted.
GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
Dy. No. and date of submission	Dy. No. 23504: 19-08-2022
Details of fee submitted	PKR 75,000/-: 19-08-2022
Proposed proprietary name/brand name	**PENAM 500mg Injection**
Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg (blended with sodium carbonate)
Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
Reference to Finished product specifications	USP
Proposed Pack size	1's
Proposed unit price	As per SRO

Status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem500mg Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
API Lot No.	MRPS/062/18
Description of Pack	Glass vial

(Container closure system)			
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	7000 Vials	10700 Vials	7000 Vials
Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	28-06-2019	26-09-2019	28-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2020/214) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2022 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection(Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is as also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 500mg Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001
Case No.	820
Registration Board meeting	316th meeting of Registration Board
Capacity assessmnet	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

195.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Linta Pharmaceuticals (Pvt) Ltd. Plot # 3, Street S-5, National Industrial Zone, Rawat Islamabad.**
	Name, address of Manufacturing site.	M/s Rotex Pharma (Pvt) Ltd, Plot # 206 & 207, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Original agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 14-07-2020 is submitted.
	GMP status of the firm	**Linta Pharmaceuticals:** The firm was inspected on 10-07-2019 and conclusion of

		inspection was: Keeping in view the above it may be concluded that M/s Linta Pharmaceuticals is operating at acceptable level of GMP standard. **Rotex pharma:** GMP certificate issued on the basis of inspection dated 12-08-2020
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000651 of M/s Rotex Pharma Islamabad dated 13-06-2017 specifying dry powder injection (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4078: 04-02-2021
	Details of fee submitted	PKR 50,000/-: 15-07-2020
	The proposed proprietary name / brand name	**PENAM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with dark blue flip off seal
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
API Lot No.	
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	C161001	C161002	C161003
Batch Size	3521 vials	3521 vials	3521 vials
Manufacturing Date	09-2018	10-2018	11-2018
Date of Initiation	19-09-2018	09-11-2018	29-12-2018
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The status of applicant mentioned in section 1.3.3 of module 1 is "manufacturer" while the application is for contract manufacturing from Rotex Pharma. Clarification is required in this regard.
- Submit module 1 as per the CTD guidance document approved by Registration Board by providing all the information and documents in relevant sections / sub-sections instead of referring to annexures.
- Provide details regarding total number of sections and number of products already registered and applied on contract manufacturing of M/s Linta Pharmaceuticals.
- Submit quality overall summary (QOS) in module 2 as per WHO QOS-PD template or as per the template approved by Registration Board in its 296th meeting and also published in CTD guidance document. The submitted QOS contains extracts from module 3 instead of providing summary of the data as per the requirements of QOS.
- Provide data in section 3.2.S.3.1 as per the guidance document approved by Registration Board which specifies that "Discussion on the potential for isomerism and identification of stereochemistry, studies performed to identify potential polymorphic forms and particle size distribution of the Drug substance shall be submitted, where these parameters may impact the quality, safety or efficacy of the drug product."
- Section 3.2.S.4.1 contains specifications for meropenem trihydrate sterile, sodium carbonate sterile and meropenem for injection. Clarification is required that which particular specifications was used for the testing of drug substance.
- Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical

procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."

- Justify the acceptance criteria of assay "NLT 78% as meropenem on dried basis", and also provide scientific justification how it is in line with the USP monograph.
- Specify the relative retention time in terms of quantitative values for the identification of drug substance, since the statement "the retention time of meropenem peak of the sample solution correspond to that of the standard solution obtained in assay" is not scientifically justified without having a relative retention time limit.
- As per the assay method of drug substance, the sample solution is nominally 0.1mg/ml of meropenem in mobile phase. While as per USP monograph the sample solution preparation method is entirely different which involves initial reconstitution with water prior to dilution with mobile phase. Justify how the tests performed by your method can be considered acceptable under the USP monograph.
- Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.
- Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification)".
- Provide COA of reference standard / working standard used in the testing of drug substance.
- Justify how 1420mg of meropenem as trihydrate blended with sodium carbonate contains 1000mg of meropenem.
- Submit information in section 3.2.P.1 c) Description of accompanying reconstitution diluent(s) as per the guidance document approved by Registration Board which specifies that "Provide information including type of diluent, its composition, quantity or volume, specifications (as applicable) and regulatory status in Pakistan (as applicable) for the diluent which is to be provided along with the applied drug".
- Submit information in section 3.2.P.2 as per the guidance document approved by Registration Board which specifies that "A brief information on the pharmaceutical development shall be included. This information specify the justification of formulation and method of manufacturing. It is also important that critical quality attributes (CQAs) and Critical Process Parameters (CPP) shall be discussed".
- Submit data in section 3.2.P.2.1.1 as per the guidance document approved by Registration Board which specifies that "Discussion shall be provided for the key physicochemical characteristics (e.g. water content, solubility, particle size distribution, polymorphic or solid state form) of the Drug Substance(s) that can influence the performance of the Drug Product".
- Provide details including batch number, expiry date of the innovator product along with pharmaceutical equivalence was performed.
- You have submitted that 30ml reconstituted volume is available with Meronem 1g Injection of Pfizer Pakistan, however the meropenem 1g injection of innovator as well as reference product is reconstituted using 20ml diluent. Clarification is required in this regard.
- Submit data in section 3.2.P.2.6 as per the guidance document approved by Registration Board which specifies that "Compatibility studies for the dry powder for injections and

dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product".

- Specify the volume of the vial of the drug product, since 50ml vial was mentioned in section 3.2.P.2 while 30ml vial is mentioned in section 3.2.P.3.
- Specify the colour of seal, since blue colour is mentioned in section 3.2.P.2 while green colour is mentioned in section 3.2.P.3.
- Provide detailed method of sample solution preparation for assay testing of the drug product in section 3.2.P.5.2 specifying the exact volume of water in which reconstitution is carried out.
- Justify why the formula for calculation of assay results of meropenem submitted in section 3.2.P.5.2 is different from that specified in USP monograph.
- Justify why the test of contents of sodium is not included in the specifications of the drug product as per the USP monograph.
- Justify how the 3 batches were released without determining the contents of sodium.
- Submit COA of reference standard / working standard used for the testing of the stability batches in section 3.2.P.6.
- Submit data in section 3.2.P.8.1 as per the guidance document approved by Registration Board which specifies that "Summary of additional stability studies (if applicable) e.g. in-use studies for drug products which are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided".
- Justify why the test of identification, contents of sodium, constituted solution, loss on drying is not performed during the stability studies.
- Justify why test of bacterial endotoxin and sterility was not performed at 6 month time point at accelerated stability studies.
- Justify why only 3 chromatographs of the standard solution was run while USP General chapter <621> recommends that five replicates of standard solution should be used for system suitability studies.
- Submit raw data sheets to support the calculation of results of assay throughout the stability studies.
- Provide analytical record including certificate of analysis at each time point, HPLC chromatograms, raw data sheets using page separators to segregate the data of each time point and each batch, since the submitted data is mixed up and submitted without any sequence.
- Submit stability study data in section 3.2.P.8.3 as per the checklist approved by Registration Board in its 296th meeting and the CTD guidance document, which includes the following:
    - Reference of previous approval of applications with stability study data of the firm (if any)
    - Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.
    - Documents for the procurement of API with approval from DRAP (in case of import).
    - Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
    - Compliance Record of HPLC software 21CFR & audit trail reports on product testing
    - Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)
- Submit Batch Manufacturing record (BMR) of the three batches for which stability study data is submitted.

Response by the firm:
Firm vide its letter dated 19-08-2021 submitted that they request to change the contract manufacturer to M/s Nicholas Pharmaceuticals, Islamabad. Firm has submitted following documents:

• Complete fee for change of contract manufacturer 75,000/- vide slip number 265253322. • Complete data in module 1, 2 and 3. The evaluation of the data is placed below	
Name, address of Applicant / Marketing Authorization Holder	**M/s Linta Pharmaceuticals (Pvt) Ltd. Plot # 3, Street S-5, National Industrial Zone, Rawat Islamabad.**
Name, address of Manufacturing site.	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 25-01-2022 is submitted.
GMP status of the firm	**Nicholas pharma:** Firm has submitted copy of GMP certificate dated 25-02-2020 issued on the basis of inspection dated 28-01-2020
Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML No 000886 of M/s Nicholas Pharma Islamabad dated 29-08-2018 specifying dry powder injection (carbapenem) section.
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
Dy. No. and date of submission	Dy. No. 23503: 19-08-2022
Details of fee submitted	PKR 75,000/-: 19-08-2022
Proposed proprietary name/brand name	**PENAM 1g Injection**
Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g (blended with sodium carbonate)
Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials
Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
Reference to Finished product specifications	USP
Proposed Pack size	1's
Proposed unit price	As per SRO
Status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities,

	physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd manufactured by ACS Dobfar Italy.
Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India.		
API Lot No.	MRPS/062/18		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Noopem Injection 001	Noopem Injection 002	Jeronum Injection 001
Batch Size	10500 Vials	13000 Vials	5500 Vials

Manufacturing Date	06-2019	09-2019	09-2019
Date of Initiation	30-06-2019	30-09-2019	26-09-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area bhiwadi District Alwar Rajasthan, India. (Certificate# DC/A-I/WHO-GMP/2020/214) issued by Drug Control Organization Government of Rajastan valid upto 26-02-2022 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted following: • Copy of Form 5 (License to Import) dated 30-04-2019 • Commercial invoice (invoice# RALIE/19-20/003) Dated: 12-04-2019 cleared by DRAP Islamabad office dated 30-04-2019 specifying import of 20Kg Meropenem Sterile for Injection (Batch# MRPS/062/18).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have performed stability testing as per USP specifications. We have also verified the USP method. The analysis was performed using HPLC system which is 21 CFR compliant. The certificate of compliance is as also submitted by the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s Nicholas Pharmaceuticals have already been approved by Registration Board in its 307th and 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Jinnah Pharmaceutical (Pvt) Ltd. 13-Km, Lahore Road Multan
Manufacturer firm	M/s Nicholas Pharmaceuticals, plot # 34, St # SS-02 National industrial Zone Rawat Islamabad
Brand Name	MEROCIN 1g Injection
Batch No. of drug product	Noopem Injection 001, Noopem Injection 002, Jeronum Injection 001

	Case No.	821
	Registration Board meeting	316th meeting of Registration Board
	Capacity assessment	The capacity assessment was carried on 18-05-2021 and 28-05-2021. Available manufacturing Capacity (Cephalosporin Injection) = 66.78% Available manufacturing Capacity (Carbapenem Injection) = 97.23% Available capacity (HPLC) = 59.61% Available Sterility testing capacity = 77.66% The Board in its 307th meeting decided to allow contract manufacturing from M/s Nicholas Phamrmaceuticals and advised the firm to upgrade their QC and microbiological lab includin gaddition of atleast 2 HPLC systems. The firm vide its letter Dy. No. 5367 dated 08-03-2022 submitted the evidence of purchase of 02 new HPLC systems. The firm also submitted evidence of purchase of atomic absorption spectrophotometer for testing of sodium content vide letter Dy.No. 6363 dated 08-03-2022.
Decision: Approved. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		

196.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt) Ltd. Plot No. 33, Sundar Industrial Estate, Lahore.**
	Name, address of Manufacturing site.	M/s English Pharmaceutical Industries Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 28-05-2021.
	GMP status of the firm	**English Pharmaceutical:** GMP certificate issued based on inspection dated 06-01-2018
	Evidence of approval of manufacturing facility	Firm (M/s English Pharmaceuticals) has submitted copy of renewal of DML letter dated 09-03-2015 specifying Dry powder injectable vial (General) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No 23530 dated 27-08-2021
	Details of fee submitted	Rs. 75,000/- Dated 02-07-2021
	The proposed proprietary name / brand name	**COLIZONE 1MIU Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Colistimethate sodium …… 1MIU
	Pharmacotherapeutic Group of (API)	Antibiotic
	Pharmaceutical form of applied drug	Powder for solution for injection
	Reference to Finished product specifications	USP
	Proposed Pack size	1x1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Colistimethate Sodium 1 Million I.U. Powder for Solution for Injection **MHRA** Approved
	For generic drugs (me-too status)	Colitec 1MIU Injection by Rotex Pharma (Reg # 092316)
	Name and address of API manufacturer.	M/s Hebei Shengxue Dacheng Pharmaceutical Co Ltd. No. 50 Shengxue Road Launcheng District Shijiazhuang Hebei Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability data of 3 batches of API at accelerated and real time conditions**.**
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control,

		process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted pharmaceutical equivalence of their product against the comparator product Colixin Injection of Pharmis Biofamaceutica
	Analytical method validation/verification of product	Firm has submitted analytical method validation study reports for drug substance as well as drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Hebei Shengxue Dacheng Pharmaceutical Co Ltd. No. 50 Shengxue Road Launcheng District Shijiazhuang, Hebei Province, China		
API Lot No.	HN180401		
Description of Pack (Container closure system)	Clear glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 1, 3, 6 (Months)		
Batch No.	CLI-001	CLI-002	CLI-003
Batch Size	46,511 vials	46,511 vials	31,000 vials
Manufacturing Date	02-2019	02-2019	02-2019
Date of Initiation	28-03-2019	28-03-2019	25-03-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous inspection of the firm has been conducted for verification of stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate (No. HE20190058) issued by China Food and Drug Administration valid upto 14-08-2024 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 8Kg Colistimethate sodium. The invoice is attested by AD (I&E) DRAP Lahore dated 19-11-2018 for batch # HN180401
4.	Data of stability batches will be supported by attested respective documents like	Firm has submitted Stability data along-with HPLC chromatograms and raw data sheets.

	chromatograms, Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not available
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied product to be manufactured by M/s English Pharmaceuticals have already been approved by Registration Board in its 296th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 296th meeting are as follows:

Applicant firm	M/s Macter International Limited. F-216, SITE, Karachi.
Manufacturer firm	M/s English Pharmaceutical Industries Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore.
Brand Name	COLMIT 1MIU Injection
Batch No. of drug product	CLI-001, CLI-002, CLI001*
Case No.	2553
Registration Board meeting	296th meeting of Registration Board

* Batch number CLI-001 was a typo mistake in 296th meeting, actually this batch number was CLI-003

Decision: Approved.
Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

197.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Gray's Pharmaceuticals Plot No. 2, Street # N-3, National Industrial Zone Rawat Islamabad.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 12-12-2020 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.

	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7099: 03-03-2021
	Details of fee submitted	PKR 50,000/-: 17-11-2020
	The proposed proprietary name / brand name	**GRAYNEM 500 mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis

		and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH Accelerated: $40^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- Firm has not submitted fee for change of drug substance manufacturer and of change of stability study batches.
- The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies.

Decision: Approved.

- **The Board further decided that the registration letter will be after submission of revised drug product specification as per USP including test for sodium content along with submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility M/s Bio-Next Pharmaceuticals, Rawat.**

198.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Gray's Pharmaceuticals Plot No. 2, Street # N-3, National Industrial Zone Rawat Islamabad.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)

		Contract manufacturing agreement dated 12-12-2020 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7101: 03-03-2021
	Details of fee submitted	PKR 50,000/-: 17-11-2020
	The proposed proprietary name / brand name	**GRAYNEM 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature,

		structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021

Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- Firm has not submitted fee for change of drug substance manufacturer and of change of stability study batches.
- The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies.

Decision: Approved.

- **The Board further decided that the registration letter will be after submission of revised drug product specification as per USP including test for sodium content along with submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility M/s Bio-Next Pharmaceuticals, Rawat.**

199.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Islam Pharmaceuticals, 7-km Pasrur Road Sialkot.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.

	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 15-06-2019 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7105: 03-03-2021
	Details of fee submitted	PKR 50,000/-: 18-01-2021
	The proposed proprietary name / brand name	**MAXLAM 500 mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.
API Lot No.	8MT2103173
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH Accelerated: $40^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- Firm has not submitted fee for change of drug substance manufacturer and of change of stability study batches.
- The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies.

Decision: Approved.

- **The Board further decided that the registration letter will be after submission of revised drug product specification as per USP including test for sodium content along with submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility M/s Bio-Next Pharmaceuticals, Rawat.**

200.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Islam Pharmaceuticals, 7-km Pasrur Road Sialkot.**

	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 15-06-2019 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7095: 03-03-2021
	Details of fee submitted	PKR 50,000/-: 18-01-2021
	The proposed proprietary name / brand name	**MAXLAM 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls,

		impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.
API Lot No.	8MT2103173
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH Accelerated: $40^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- Firm has not submitted fee for change of drug substance manufacturer and of change of stability study batches.
- The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies.

Decision: Approved.

- **The Board further decided that the registration letter will be after submission of revised drug product specification as per USP including test for sodium content along with submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility M/s Bio-Next Pharmaceuticals, Rawat.**

201.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Reliance Pharma. Plot No 8, Street No. S-8, Industrial Estate, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 25-02-2019 is submitted.
	GMP status of the firm	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22750: 20-08-2021
	Details of fee submitted	PKR 50,000/-: 27-04-2021 + PKR 25,000/-: 28-06-2021
	The proposed proprietary name / brand name	**RELEM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with sea green color flip off seal along with 10ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their

		product against Merrem 500mg Injection manufactured by Boehringer Ingelheim.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/BMPM/0990917 S1/BMPM/1031017		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17L078	17L079	17M319
Batch Size	7692 vials	7692 vials	7692 vials
Manufacturing Date	11-2017	11-2017	11-2017
Date of Initiation	04-12-2017	05-12-2017	29-12-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 23-10-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/0990917. The commercial invoice is attested by AD (I&E) DRAP field office. Firm has submitted copy of commercial invoice cleared dated 03-11-2017 specifying

		import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/1031017. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm was informed that
Registration Board in its 316th meeting considered the case of meroepem injection manufactured by Global Pharmaceuticals, Islamabad wherein the Board decided as under:
Registration Board considered the case and noted the fact that the firm has not complied the decision of 313th meeting, wherein Board "advised the manufacturer to perform product development studies keeping in view the innovator product and product testing and stability studies by complying USP monograph and
submit data upon completion of 6 months stability studies", rather firm has submitted stability data of batches manufactured prior to the decision of 313th meeting. Hence Board decided to defer the application for submission of product development & stability studies in compliance with the Innovator product literature and USP monograph. Board also directed the firm to submit relevant sections of Form 5F against the new product development & stability studies data along with submission of full fee of Rs. 75,000/-

Response by the firm:
Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted following documents along with stability study data:
1. Specifications and analytical procedure of drug substance
2. Verification studies of the analytical procedure of drug substance
3. Specifications and analytical procedure of drug product
4. Verification studies of the analytical procedure of drug product
5. Pharmaceutical equivalence studies against Merrem 500mg Injection of Astra Zaneca
5. Process validation report of three commercial batches
6. CoA of working standard
7. Executed BMR of three batches

The details of the newly submitted data is as under:

STABILITY STUDY DATA	
Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.
API Lot No.	682107003

Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A169	22A363	22A364
Batch Size	7418 vials	7418 vials	7418 vials
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	25-01-2022	25-01-2022	25-01-2022
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological

	Development Zone, Hebei Province PR. China. Firm has not submitted any fee for change of source as well as submission of stability study data of new batches.	
Decision: Approved. • **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source as well as submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
202.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Reliance Pharma. Plot No 8, Street No. S-8, Industrial Estate, Rawat, Islamabad**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 25-02-2019 is submitted.
	GMP status of the firm	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 18622: 02-07-2021
	Details of fee submitted	PKR 50,000/-: 27-04-2021 + PKR 50,000/-: 28-06-2021
	The proposed proprietary name / brand name	**RELEM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g

	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with brown color flip off seal along with 20ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures,

		validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Merrem 500mg Injection manufactured by Boehringer Ingelheim.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/MPM/01860817		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17K282	17K283	17K238
Batch Size	3533 vials	3533 vials	3533 vials
Manufacturing Date	10-2017	10-2017	10-2017
Date of Initiation	20-10-2017	25-10-2017	19-10-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 25-09-2017 specifying

		import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/MPM/01860817. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm was informed that
Registration Board in its 316th meeting considered the case of meroepem injection manufactured by Global Pharmaceuticals, Islamabad wherein the Board decided as under:
Registration Board considered the case and noted the fact that the firm has not complied the decision of 313th meeting, wherein Board "advised the manufacturer to perform product development studies keeping in view the innovator product and product testing and stability studies by complying USP monograph and
submit data upon completion of 6 months stability studies", rather firm has submitted stability data of batches manufactured prior to the decision of 313th meeting. Hence Board decided to defer the application for submission of product development & stability studies in compliance with the Innovator product literature and USP monograph. Board also directed the firm to submit relevant sections of Form 5F against the new product development & stability studies data along with submission of full fee of Rs. 75,000/-

Response by the firm:
Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted following documents along with stability study data:
1. Specifications and analytical procedure of drug substance
2. Verification studies of the analytical procedure of drug substance
3. Specifications and analytical procedure of drug product
4. Verification studies of the analytical procedure of drug product
5. Pharmaceutical equivalence studies against Merrem 500mg Injection of Astra Zaneca
5. Process validation report of three commercial batches
6. CoA of working standard
7. Executed BMR of three batches

The details of the newly submitted data is as under:

STABILITY STUDY DATA	
Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.
API Lot No.	682107003

Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A335	21M270	21M271
Batch Size	3709 vials	3709 vials	3709 vials
Manufacturing Date	01-2022	12-2021	12-2021
Date of Initiation	10-01-2022	30-12-2021	30-12-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological

	Development Zone, Hebei Province PR. China. Firm has not submitted any fee for change of source as well as submission of stability study data of new batches.	
Decision: Approved. • **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source as well as submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
203.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Carer Pharmaceuticals Industries, Plot No. 27, Main Road, Rawat Industrial Estate Rawat Islamabad.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10091: 31-03-2021
	Details of fee submitted	PKR 50,000/-: 12-02-2021
	The proposed proprietary name / brand name	**CERONUM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with sea green color flip off seal along with 10ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their

		product against Merrem 500mg Injection manufactured by Boehringer Ingelheim.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/BMPM/0990917 S1/BMPM/1031017		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17L078	17L079	17M319
Batch Size	7692 vials	7692 vials	7692 vials
Manufacturing Date	11-2017	11-2017	11-2017
Date of Initiation	04-12-2017	05-12-2017	29-12-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 23-10-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/0990917. The commercial invoice is attested by AD (I&E) DRAP field office. Firm has submitted copy of commercial invoice cleared dated 03-11-2017 specifying

		import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/1031017. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

The firm was communicated the following decision of 312th meeting of Registration Board.
The product development and stability study data of the contract manufacturer was considered by Registration Board in its 312nd meeting and observed that the contract manufacturer has not performed complete product development studies, the specifications adopted by the manufacturer throughout stability studies were not according to USP and that the stability batches have also expired. Accordingly, the Board deferred for following submissions:

- Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.
- Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,
- Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.
- Scientific justification for having analytical method of drug product without specifying that "*sample should be hold for 1-2 hours at 25± 1°C before testing*" which is recommended in USP monograph.
- Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.
- Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.
- Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.
- Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.
- Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.
- Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.
- Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.
- Scientific justification for not performing compatibility studies of the drug product with the recommended diluent.
- Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.

- Scientific justification for using an entirely different formula for calculation of assay results of commercial batches from that specified in USP monograph.
- Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.
- Scientific justification for the results of assay test of meropenem for the batch No. 17L078 which show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time) keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.
- Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.
- Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.
- Submission of fee for pre-registration changes in the drug product specifications.

Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly.

Response by the firm:

Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted following documents along with stability study data:

1. Specifications and analytical procedure of drug substance
2. Verification studies of the analytical procedure of drug substance
3. Specifications and analytical procedure of drug product
4. Verification studies of the analytical procedure of drug product
5. Pharmaceutical equivalence studies against Merrem 500mg Injection of Astra Zaneca
5. Process validation report of three commercial batches
6. CoA of working standard
7. Executed BMR of three batches

The details of the newly submitted data is as under:

STABILITY STUDY DATA	
Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.
API Lot No.	682107003
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months

	Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A169	22A363	22A364
Batch Size	7418 vials	7418 vials	7418 vials
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	25-01-2022	25-01-2022	25-01-2022
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. Firm has not submitted any fee for change of source as well as submission of stability study data of new batches.

Decision: Approved.

- **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source as well as**

submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. • **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**	

204.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals. Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 01-01-2021 is submitted.
	GMP status of the firm	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7462: 08-03-2021
	Details of fee submitted	PKR 50,000/-: 07-01-2021
	The proposed proprietary name / brand name	**MERONAG 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with sea green color flip off seal along with 10ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their

		product against Merrem 500mg Injection manufactured by Boehringer Ingelheim.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/BMPM/0990917 S1/BMPM/1031017		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17L078	17L079	17M319
Batch Size	7692 vials	7692 vials	7692 vials
Manufacturing Date	11-2017	11-2017	11-2017
Date of Initiation	04-12-2017	05-12-2017	29-12-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 23-10-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/0990917. The commercial invoice is attested by AD (I&E) DRAP field office. Firm has submitted copy of commercial invoice cleared dated 03-11-2017 specifying

		import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/1031017. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

The firm was communicated the following decision of 312th meeting of Registration Board.

The product development and stability study data of the contract manufacturer was considered by Registration Board in its 312nd meeting and observed that the contract manufacturer has not performed complete product development studies, the specifications adopted by the manufacturer throughout stability studies were not according to USP and that the stability batches have also expired. Accordingly, the Board deferred for following submissions:

- Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.
- Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,
- Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.
- Scientific justification for having analytical method of drug product without specifying that "*sample should be hold for 1-2 hours at 25± 1°C before testing*" which is recommended in USP monograph.
- Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.
- Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.
- Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.
- Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.
- Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.
- Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.
- Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.
- Scientific justification for not performing compatibility studies of the drug product with the recommended diluent.
- Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.

- Scientific justification for using an entirely different formula for calculation of assay results of commercial batches from that specified in USP monograph.
- Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.
- Scientific justification for the results of assay test of meropenem for the batch No. 17L078 which show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time) keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.
- Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.
- Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.
- Submission of fee for pre-registration changes in the drug product specifications.

Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly.

Response by the firm:

Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted following documents along with stability study data:

1. Specifications and analytical procedure of drug substance
2. Verification studies of the analytical procedure of drug substance
3. Specifications and analytical procedure of drug product
4. Verification studies of the analytical procedure of drug product
5. Pharmaceutical equivalence studies against Merrem 500mg Injection of Astra Zaneca
5. Process validation report of three commercial batches
6. CoA of working standard
7. Executed BMR of three batches

The details of the newly submitted data is as under:

STABILITY STUDY DATA	
Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.
API Lot No.	682107003
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months

	Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A169	22A363	22A364
Batch Size	7418 vials	7418 vials	7418 vials
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	25-01-2022	25-01-2022	25-01-2022
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. Firm has not submitted any fee for change of source as well as submission of stability study data of new batches.

Decision: Approved.

- **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source as well as**

	submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. • **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**	
205.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals.** **Plot No. 34, St. No. NS-2, National Industrial Zone, Rawat, Islamabad.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 01-01-2021 is submitted.
	GMP status of the firm	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7461: 08-03-2021
	Details of fee submitted	PKR 50,000/-: 07-01-2021
	The proposed proprietary name / brand name	**MERONAG 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with brown color flip off seal along with 20ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their

		product against Merrem 500mg Injection manufactured by Boehringer Ingelheim.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/MPM/01860817		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17K282	17K283	17K238
Batch Size	3533 vials	3533 vials	3533 vials
Manufacturing Date	10-2017	10-2017	10-2017
Date of Initiation	20-10-2017	25-10-2017	19-10-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 25-09-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/MPM/01860817. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like	Firm has submitted complete record of testing of all batches along with

	chromatograms, Raw data sheets, COA, summary data sheets etc.	chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

The firm was communicated the following decision of 312th meeting of Registration Board.

The product development and stability study data of the contract manufacturer was considered by Registration Board in its 312nd meeting and observed that the contract manufacturer has not performed complete product development studies, the specifications adopted by the manufacturer throughout stability studies were not according to USP and that the stability batches have also expired. Accordingly, the Board deferred for following submissions:

- Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.
- Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,
- Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.
- Scientific justification for having analytical method of drug product without specifying that "*sample should be hold for 1-2 hours at 25± 1°C before testing*" which is recommended in USP monograph.
- Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.
- Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.
- Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.
- Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.
- Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.
- Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.
- Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.
- Scientific justification for not performing compatibility studies of the drug product with the recommended diluent.
- Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.
- Scientific justification for using an entirely different formula for calculation of assay results of commercial batches from that specified in USP monograph.
- Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.

- Scientific justification for the results of assay test of meropenem for the batch No. 17L078 which show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time) keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.
- Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.
- Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.
- Submission of fee for pre-registration changes in the drug product specifications.

Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly.

Response by the firm:
Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted following documents along with stability study data:
1. Specifications and analytical procedure of drug substance
2. Verification studies of the analytical procedure of drug substance
3. Specifications and analytical procedure of drug product
4. Verification studies of the analytical procedure of drug product
5. Pharmaceutical equivalence studies against Merrem 500mg Injection of Astra Zaneca
5. Process validation report of three commercial batches
6. CoA of working standard
7. Executed BMR of three batches

The details of the newly submitted data is as under:

STABILITY STUDY DATA

Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.		
API Lot No.	682107003		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A335	21M270	21M271

Batch Size	3709 vials	3709 vials	3709 vials
Manufacturing Date	01-2022	12-2021	12-2021
Date of Initiation	10-01-2022	30-12-2021	30-12-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. Firm has not submitted any fee for change of source as well as submission of stability study data of new batches.

Decision: Approved.

- **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source as well as submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**

206.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26126: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 13-07-2021
	The proposed proprietary name / brand name	LIMAXONE 250mg IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 250mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef Injection of Ceftriaxone Sodium by Pride Pharmaceuticals 025876
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Oxidil 250mg Injection IM.

	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.		0151NJ81HE		
Description of Pack (Container closure system)		Glass vial		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 24 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.		124	125	126
Batch Size		10,000 Vials	12170 Vials	12170 Vials
Manufacturing Date		07-2020	07-2020	07-2020
Date of Initiation		02-7-2020	13-07-2020	29-07-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		
Evaluation by PEC:				
• The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May				

2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin injection 250mg IM
Batch No. of drug product	124, 125, 126
Case No.	6
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

207.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26947: dated 29-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-06-2021

	The proposed proprietary name / brand name	ROCEXON 250mg IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 250mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef Injection of Ceftriaxone Sodium by Pride Pharmaceuticals 025876
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of

		manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40 ^{O} ± 2 ^{O} C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2 ^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Oxidil 250mg Injection IM.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	124	125	126
Batch Size	10,000 Vials	12170 Vials	12170 Vials
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	02-7-2020	13-07-2020	29-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin injection 250mg IM
Batch No. of drug product	124, 125, 126
Case No.	6
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration

	Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.	
Decision: Approved. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**		
208.	Name, address of Applicant / Marketing Authorization Holder	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26948: dated 29-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-06-2021
	The proposed proprietary name / brand name	ROCEXON 250mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 250mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef Injection of Ceftriaxone Sodium by Pride Pharmaceuticals 025876
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Oxidil 250mg Injection IV.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	103	115	120
Batch Size	5,000 packs	5,000 packs	5,000 packs
Manufacturing Date	10-2019	05-2020	06-2020
Date of Initiation	09-10-2019	05-05-2020	04-06-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin injection 250mg IV
Batch No. of drug product	103, 115, 120
Case No.	7
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

209.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26127: dated 21-9-2021

	Details of fee submitted	PKR 75,000/-: dated 13-07-2021
	The proposed proprietary name / brand name	LIMAXONE 500mg IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 500mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef 500mg Injection of M/s. Pride Pharmaceuticals 025878
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C))
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Rocephin Pharmaceuticals 500mg IM.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE (RM 4987)		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	109	114	119
Batch Size	6,000 packs	14000 packs	15000 packs

Manufacturing Date	02-2020	05-2020	06-2020
Date of Initiation	08-04-2020	03-05-2020	16-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin Injection 500mg IM
Batch No. of drug product	109, 114, 119
Case No.	4
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus

	authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection. • After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.	
Decision: Approved. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**		
210.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26132: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-06-2021
	The proposed proprietary name / brand name	ROCEXON 500mg IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 500mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef 500mg Injection of M/s. Pride Pharmaceuticals 025878

	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C))

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Rocephin Pharmaceuticals 500mg IM.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE (RM 4987)		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	109	114	119
Batch Size	6,000 packs	14000 packs	15000 packs
Manufacturing Date	02-2020	05-2020	06-2020
Date of Initiation	08-04-2020	03-05-2020	16-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin Injection 500mg IM
Batch No. of drug product	109, 114, 119
Case No.	4
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

211.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**

	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26128: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 13-07-2021
	The proposed proprietary name / brand name	LIMAXONE 500mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 500mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef Injection of Ceftriaxone Sodium by Pride Pharmaceuticals 025877
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized

		information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C))
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Rocephin 500 mg IV.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	109	114	119
Batch Size	6,000 packs	14000 packs	15000 packs
Manufacturing Date	02-2020	05-2020	06-2020
Date of Initiation	08-04-2020	03-05-2020	16-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin Injection 500mg IV
Batch No. of drug product	109, 114, 119
Case No.	5
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

212.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26133: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-06-2021
	The proposed proprietary name / brand name	ROCEXON 500mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 500mg

	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef Injection of Ceftriaxone Sodium by Pride Pharmaceuticals 025877
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C))
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Rocephin 500 mg IV.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	109	114	119
Batch Size	6,000 packs	14000 packs	15000 packs
Manufacturing Date	02-2020	05-2020	06-2020
Date of Initiation	08-04-2020	03-05-2020	16-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin Injection 500mg IV
Batch No. of drug product	109, 114, 119
Case No.	5
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson

	Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.	
Decision: Approved. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**		
213.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26949: dated 29-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-6-2021
	The proposed proprietary name / brand name	ROCEXON 1gm IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone sodium eq. to Ceftriaxone 1gm
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Topcef 1g Injection of M/s. Pride Pharmaceuticals 025878
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template.

		Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months. (Batch No. 60155GJ81H-C, 60156GJ81H-C, 6015GJ81H-C))
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Rocephin Injection 1g IM.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0151NJ81HE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	124	125	126
Batch Size	10,000 Vials	12170 Vials	12170 Vials
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	28-08-2020	28-08-2020	28-08-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Trophin Injection 1 gm IV/IM later approved as Trophin Injection 1 gm IV
Batch No. of drug product	124, 125, 126
Case No.	3
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.
- **Firm has applied for both IV/IM injection however the data of contract manufacturer i.e. M/s Gray's Pharmaceuticals already considered and approved in 316th meeting was for 1gm IV Injection.**

Decision: Approved as IV Injection.
Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.

214.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Iceberg Pharmaceuticals Pvt Ltd. Plot # 144, Nowshera Indsutrial Estate, Risalpur**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26124: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 30-06-2021
	The proposed proprietary name / brand name	CEFTIME 500mg IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefotaxime sodium eq. to Cefotaxime… 500mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA approved
	For generic drugs (me-too status)	Cefotaxime 500mg Injection of M/s. Friends Pharma
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or

		materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40 ^{O} ± 2 ^{O} C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2 ^{O} C / 65% ± 5% RH for 36 months. Batch numbers: (3079GL81F, 3078GL81F, 3080GL81F)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Claforan Injection 500mg.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
API Lot No.	0089L81F
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	TDI001	TDI002	TDI003
Batch Size	2000 Vials	2000 Vials	2000 Vials
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	27-02-2021	27-02-2021	27-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Onexin Injection 500mg
Batch No. of drug product	TDI001, TDI002, TDI003
Case No.	12

Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

215.	Name, address of Applicant / Marketing Authorization Holder	**M/s Iceberg Pharmaceuticals Pvt Ltd. Plot # 144, Nowshera Indsutrial Estate, Risalpur**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26936 dated 29-9-2021
	Details of fee submitted	PKR 75,000/-: dated 30-06-2021
	The proposed proprietary name / brand name	CEFTIME 1g IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefotaxime sodium eq. to Cefotaxime 1gm
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	USFDA approved
	For generic drugs (me-too status)	Cefotaxime 1g Injection of M/s. Friends Pharma
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is

		conducted at 30^{O}C ± 2 ^{O} C / 65% ± 5% RH for 36 months. Batch numbers: (3079GL81F, 3078GL81F, 3080GL81F)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Claforan Injection 1g.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	0089L81F		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	TDI001	TDI002	TDI003
Batch Size	2000 Vials	2000 Vials	2000 Vials
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	27-02-2021	27-02-2021	27-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Kerazon Plus Injection 1g
Batch No. of drug product	TDI001, TDI002, TDI003
Case No.	12
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

216.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26130: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-06-2021
	The proposed proprietary name / brand name	CEPTAM 1g IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefoperazone (as sodium)……..500mg Sulbactam (as sodium)……500mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	Innovator
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Firm has provided reference from EMA website where this combination is registered as Sulperazone 1 & 2 gm Injection by Pfizer in following countries: • Poland • Slovakia • Lithuania • Czech Republic • Italy • Bulgaria
	For generic drugs (me-too status)	Adzone 1g Injection of M/s. Farm Aid group
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.

	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months (Batches: 9001HK81NG; 9002HK81NG; 9003HK81NG)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at

		acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Sulzone Injection 1g.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy & recovery, method precision, specificity bearing document number GP/QC-SAP-052 effective date 5-6-2018.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	101AJ81NE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	TDI001	TDI002	TDI003
Batch Size	2000 Vials	2000 Vials	2000 Vials
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	25-02-2021	25-02-2021	25-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Kerazon Plus Injection 1g
Batch No. of drug product	TDI001, TDI002, TDI003
Case No.	14
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved with JP Specifications.

- **Registration Board decided that registration letter will be issued after submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

217.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Iceberg Pharmaceuticals Pvt Ltd. Plot # 144, Nowshera Indsutrial Estate, Risalpur**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3,

		National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26939: dated 29-9-2021
	Details of fee submitted	PKR 75,000/-: dated 30-06-2021
	The proposed proprietary name / brand name	ASOFEN 1gm IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefoperazone (as sodium)……..500mg Sulbactam (as sodium)……500mg
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	Innovator
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Firm has provided reference from EMA website where this combination is registered as Sulperazone 1 & 2 gm Injection by Pfizer in following countries: • Poland • Slovakia • Lithuania • Czech Republic • Italy • Bulgaria
	For generic drugs (me-too status)	Adzone 1g Injection of M/s. Farm Aid group
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months (Batches: 9001HK81NG; 9002HK81NG; 9003HK81NG)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Sulzone Injection 1g.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy & recovery, method precision, specificity bearing document number GP/QC-SAP-052 effective date 5-6-2018.

STABILITY STUDY DATA

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	101AJ81NE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	TDI001	TDI002	TDI003
Batch Size	2000 Vials	2000 Vials	2000 Vials
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	25-02-2021	25-02-2021	25-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of	Firm has submitted record of data logger for temperature and humidity monitoring of

	stability chambers (real time and accelerated)	real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Kerazon Plus Injection 1g
Batch No. of drug product	TDI001, TDI002, TDI003
Case No.	14
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved with JP Specifications.

- **Registration Board decided that registration letter will be issued after submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

218.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26131: dated 21-9-2021
	Details of fee submitted	PKR 75,000/-: dated 29-6-2021
	The proposed proprietary name / brand name	CEPTAM 2g IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefoperazone (as Sodium)……..1g Sulbactam (as sodium)……1g
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	Innovator
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Firm has provided reference from EMA website where this combination is registered as Sulperazone 1 & 2 gm Injection by Pfizer in following countries: • Poland • Slovakia • Lithuania • Czech Republic • Italy • Bulgaria
	For generic drugs (me-too status)	Adzone 1g Injection of M/s. Farm Aid group
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard,

		container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months (9001HK81NG; 9002HK81NG; 9003HK81NG)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the Firm has performed pharmaceutical equivalence against the product Sulzone Injection2 g.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy & recovery, method precision,

		specificity bearing document number GP/QC-SAP-052 effective date 5-6-2018.		
STABILITY STUDY DATA				
Manufacturer of API		M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.		101AJ81NE		
Description of Pack (Container closure system)		Glass vial		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 24 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.		TDI001	TDI002	TDI003
Batch Size		2000 Vials	2000 Vials	2000 Vials
Manufacturing Date		02-2021	02-2021	02-2021
Date of Initiation		25-02-2021	25-02-2021	25-02-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		
Evaluation by PEC:				
• The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May				

2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Kerazon Plus Injection 2g
Batch No. of drug product	TDI001, TDI002, TDI003
Case No.	15
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved with JP Specifications.

- **Registration Board decided that registration letter will be issued after submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

219.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Iceberg Pharmaceuticals Pvt Ltd. Plot # 144, Nowshera Indsutrial Estate, Risalpur**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 26940: dated 29-9-2021
	Details of fee submitted	PKR 75,000/-: dated 30-6-2021
	The proposed proprietary name / brand name	ASOFEN 2gm IV/IM Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefoperazone (as Sodium)……..1g Sulbactam (as sodium)……1g
	Pharmaceutical form of applied drug	Almost white to off white colored powder filled in glass vial.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	Innovator
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Firm has provided reference from EMA website where this combination is registered as Sulperazone 1 & 2 gm Injection by Pfizer in following countries: • Poland • Slovakia • Lithuania • Czech Republic • Italy • Bulgaria
	For generic drugs (me-too status)	Adzone 1g Injection of M/s. Farm Aid group
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 5-5-17, valid upto 4-5-18.
	Name and address of API manufacturer.	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture,

		manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months (9001HK81NG; 9002HK81NG; 9003HK81NG)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the Firm has performed pharmaceutical equivalence against the product Sulzone Injection2 g.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy & recovery, method precision, specificity bearing document number GP/QC-SAP-052 effective date 5-6-2018.
STABILITY STUDY DATA		

Manufacturer of API	M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China.		
API Lot No.	101AJ81NE		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	TDI001	TDI002	TDI003
Batch Size	2000 Vials	2000 Vials	2000 Vials
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	25-02-2021	25-02-2021	25-02-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Qilu Antibiotics Pharmaceutical CO. Ltd. No. 849 Dongjia Town Licheng District Jinan City China. issued by State food and drug administration china, valid Up to 5-6-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice#JTRF210117-MQ)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Kerazon Plus Injection 2g
Batch No. of drug product	TDI001, TDI002, TDI003
Case No.	15
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved with JP Specifications.

- **Registration Board decided that registration letter will be issued after submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

220.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26931 dated 29/09/2021
	Details of fee submitted	PKR 75,000/-: dated 13/07/2021
	The proposed proprietary name / brand name	LEXIME 100mg/5ml Suspension

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml Dry Suspension contains: Cefixime as trihydrate……. 100mg
	Pharmaceutical form of applied drug	Dry Suspension
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	USP
	Proposed Pack size	1×30ml's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Suprex 100mg /5ml Dry Suspension by M/s Lupin Pharma, USFDA Approved.
	For generic drugs (me-too status)	Cefspan 100mg /5ml Dry Suspension by M/s Barrett Hodgson, Reg. No. 010429
	GMP status of the Finished product manufacturer	New license granted on 22/06/2016 (Cephalosporin Antibiotic) section approved.
	Name and address of API manufacturer.	M/s CITI Pharmacueticals (PVT.) LTD. 588-Q, Johar Town, Lahore – 53100, Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefixime as Trihydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CFM1602001,CFM1602002, CFM1602003)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Cefspan 100mg /5ml Dry Suspension by M/s Barrett Hodgson.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s CITI Pharmacueticals (PVT.) LTD. 588-Q, Johar Town, Lahore – 53100, Pakistan		
API Lot No.	CFM2101001		
Description of Pack (Container closure system)	PET Bottle packed in unit carton (1×30ml's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T007	T008	T009
Batch Size	1500 Bottles	1500 Bottles	1500 Bottles
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	03.02.2021	03-02-2021	03.02.2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	N/A

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	AKSOXIME 100mg/5ml Dry Suspension
Batch No. of drug product	T-007, T-008, T-009
Case No.	9
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

221.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**

	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26930 dated 29/09/2021
	Details of fee submitted	PKR 75,000/-: dated 13/07/2021
	The proposed proprietary name / brand name	LEXIME 200mg/5ml Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml Dry Suspension contains: Cefixime as trihydrate ……. 200mg
	Pharmaceutical form of applied drug	Dry Suspension
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	USP
	Proposed Pack size	1×30ml's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Suprex 200mg /5ml Dry Suspension by M/s Lupin Pharma, USFDA Approved.
	For generic drugs (me-too status)	Cefspan 200mg /5ml Dry Suspension by M/s Barrett Hodgson, Reg. No. 024634
	GMP status of the Finished product manufacturer	New license granted on 22/06/2016 (Cephalosporin Antibiotic) section approved.
	Name and address of API manufacturer.	M/s CITI Pharmacueticals (PVT.) LTD. 588-Q, Johar Town, Lahore – 53100, Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

	Module III (Drug Substance)	Official monograph of Cefixime as Trihydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CFM1602001,CFM1602002, CFM1602003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Cefspan 200mg /5ml Dry Suspension by M/s Barrett Hodgson, by performing quality tests (Identification, Assay, and Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s CITI Pharmacueticals (PVT.) LTD. 588-Q, Johar Town, Lahore – 53100, Pakistan
API Lot No.	CFM2101001
Description of Pack (Container closure system)	PET Bottle packed in unit carton (1×30ml's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	T004	T005	T006
Batch Size	1500 Bottles	1500 Bottles	1500 Bottles
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	28-01-2021	29-01-2021	30-01-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	N/A
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	AKSOXIME 200mg/5ml Dry Suspension
Batch No. of drug product	T-004, T-005, T-006
Case No.	10
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus

authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.

- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

222.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Leama Chemi Pharma Pvt Ltd. 37-A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26932 dated 29/09/2021
	Details of fee submitted	PKR 75,000/-: dated 13/07/2021
	The proposed proprietary name / brand name	LEXIME 400mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Cefixime as trihydrate……. 400 mg
	Pharmaceutical form of applied drug	Hard Gelatin Capsule
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	JP
	Proposed Pack size	1×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Suprex 400mg Capsule by M/s Lupin Pharma, USFDA Approved.
	For generic drugs (me-too status)	Cefspan 400mg capsule by M/s Barrett Hodgson, Reg. No. 013860
	GMP status of the Finished product manufacturer	New license granted on 22/06/2016

		(Cephalosporin Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Citi Pharma (Pvt.) Ltd. 3 Kilometer, Head Balloki Road, Phool Nagar, Kasur -55050 Punjab, Pakistan. Tel: +92 49 4510192, 510189 Fax: +92 49 4510191 Website: www.citipharma.com Email ID: info@citipharma.com
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefixime is present in JP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CFM1602001, CFM1602002, CFM1602003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is

		Cefspan 400mg capsule by M/s Barrett Hodgson, CDP has been performed against the same brand that is Cefspan 400mg capsule by M/s Barrett Hodgson, in A , Acetate Buffer (pH 4.5) , Phosphate Buffer (pH 6.8) & Kcl Buffer (pH 1.2). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Citi Pharma (Pvt.) Ltd. 3 Kilometer, Head Balloki Road, Phool Nagar, Kasur -55050 Punjab, Pakistan. Tel: +92 49 4510192, 510189 Fax: +92 49 4510191 Website: www.citipharma.com Email ID: info@citipharma.com		
API Lot No.	CFM1602001		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×5's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 Capsules	2000 Capsules	2000 Capsules
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	08-12-2020	09-12-2020	10-12-2020
No. of Batches	03		

Administrative Portion

7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
9.	Documents for the procurement of API with approval from DRAP (in case of import).	N/A
10.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	AKSOXIME 400mg capsule
Batch No. of drug product	T-001, T-002, T-003
Case No.	11
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved with Manufacturer's Specifications as approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022.

- **Registration Board decided that registration letter will be issued after submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

223.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Iceberg Pharmaceuticals Pvt Ltd. Plot # 144, Nowshera Indsutrial Estate, Risalpur**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26937 dated 29.09.2021
	Details of fee submitted	PKR 75000/-: dated 30.06.2021
	The proposed proprietary name / brand name	**CEF-ICE 500mg IV/IM Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Cefepime (as hydrochloride)……500mg (with L-arginine)
	Pharmaceutical form of applied drug	Powder For Solution For Injection Or Infusion
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Renapime 500mg Powder for solution for injection/infusion Manufacturer: Renascience Pharma Ltd (MHRA approved)
	For generic drugs (me-too status)	Maxipime 1g Injection by M/s Novartis
	GMP status of the Finished product manufacturer	Tablet (General), Capsule (General), Dry Suspension (Ceph), Capsule (Ceph), Dry powder injection (Ceph), cream & Ointment and ampule section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of

		manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefepime HCl is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-034, T-035, T-036)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Maxipime 1g Injection by M/s Novartis
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China
API Lot No.	0022CJ66DB
Description of Pack (Container closure system)	USP type III glass vial. Packed in a unit carton with leaflet
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-034	T-035	T-036
Batch Size	1500 Vials	1500 Vials	1500 Vials
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	02-03-2021	02-03-2021	03-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20160497 issued by China food and Drug administration valid till 25/08/2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Commercial invoice and ADC clearance of the same batch of API as used in the stability studies.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Endopime 500mg powder for solution for injection or infusion

Batch No. of drug product	T-034, T-035, T-036
Case No.	8
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

224.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar.**
	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26945 dated 29.09.2021
	Details of fee submitted	PKR 75000/-: dated 29.06.2021
	The proposed proprietary name / brand name	**EPIME 500mg IV/IM Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Cefepime (as hydrochloride)……500mg (with L-arginine)
	Pharmaceutical form of applied drug	Powder For Solution For Injection Or Infusion
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	USP

	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Renapime 500mg Powder for solution for injection/infusion Manufacturer: Renascience Pharma Ltd (MHRA approved)
	For generic drugs (me-too status)	Maxipime 1g Injection by M/s Novartis
	GMP status of the Finished product manufacturer	Tablet (General), Capsule (General), Dry Suspension (Ceph), Capsule (Ceph), Dry powder injection (Ceph), cream & Ointment and ampule section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefepime HCl is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-034, T-035, T-036)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and

		justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Maxipime 1g Injection by M/s Novartis
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China		
API Lot No.	0022CJ66DB		
Description of Pack (Container closure system)	USP type III glass vial. Packed in a unit carton with leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-034	T-035	T-036
Batch Size	1500 Vials	1500 Vials	1500 Vials
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	02-03-2021	02-03-2021	03-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20160497 issued by China food and Drug administration valid till 25/08/2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Commercial invoice and ADC clearance of the same batch of API as used in the stability studies.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Endopime 500mg powder for solution for injection or infusion
Batch No. of drug product	T-034, T-035, T-036
Case No.	8
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

225.	Name, address of Applicant / Marketing Authorization Holder	M/s Iceberg Pharmaceuticals Pvt Ltd. Plot # 144, Nowshera Indsutrial Estate, Risalpur
	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26938 dated 29.09.2021
	Details of fee submitted	PKR 75000/-: dated 30.06.2021
	The proposed proprietary name / brand name	**CEF-ICE 1gm IV/IM Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Cefepime (as hydrochloride)……1g (with L-arginine)
	Pharmaceutical form of applied drug	Powder For Solution For Injection Or Infusion
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Renapime 1g Powder for solution for injection/infusion Manufacturer: Renascience Pharma Ltd (MHRA approved)
	For generic drugs (me-too status)	Maxipime 1g Injection by M/s Novartis
	GMP status of the Finished product manufacturer	Tablet (General), Capsule (General), Dry Suspension (Ceph), Capsule (Ceph), Dry powder injection (Ceph), cream & Ointment and ampule section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefepime HCl is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-037, T-038, T-039)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Maxipime 1g Injection by M/s Novartis
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China		
API Lot No.	0022CJ66DB		
Description of Pack (Container closure system)	USP type III glass vial. Packed in a unit carton with leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-037	T-038	T-039
Batch Size	1500 Vials	1500 Vials	1500 Vials
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	04-03-2021	04-03-2021	05-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20160497 issued by China Food and Drug Administration valid till 25/08/2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Commercial invoice and ADC clearance of the same batch of API as used in the stability studies.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Endopime 1g powder for solution for injection or infusion
Batch No. of drug product	T-037, T-038, T-039
Case No.	2
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved. • **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**		
226.	Name, address of Applicant / Marketing Authorization Holder	Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar
	Name, address of Manufacturing site.	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26946 dated 29.09.2021
	Details of fee submitted	PKR 75000/-: dated 29.06.2021
	The proposed proprietary name / brand name	**EPIME 1gm IV/IM Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Cefepime (as hydrochloride)……1g (with L-arginine)
	Pharmaceutical form of applied drug	Powder For Solution For Injection Or Infusion
	Pharmacotherapeutic Group of (API)	Anti-Biotic (Cephalosporin)
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Renapime 1g Powder for solution for injection/infusion Manufacturer: Renascience Pharma Ltd (MHRA approved)
	For generic drugs (me-too status)	Maxipime 1g Injection by M/s Novartis
	GMP status of the Finished product manufacturer	Tablet (General), Capsule (General), Dry Suspension (Ceph), Capsule (Ceph), Dry powder injection (Ceph), cream & Ointment and ampule section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and

		controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefepime HCl is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-037, T-038, T-039)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Maxipime 1g Injection by M/s Novartis
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. No.849 Dongjia Town, Licheng District, Jinan, Shandong Province, China
API Lot No.	0022CJ66DB
Description of Pack (Container closure system)	USP type III glass vial. Packed in a unit carton with leaflet
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 2, 4, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	T-037	T-038	T-039
Batch Size	1500 Vials	1500 Vials	1500 Vials
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	04-03-2021	04-03-2021	05-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20160497 issued by China Food and Drug Administration valid till 25/08/2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Commercial invoice and ADC clearance of the same batch of API as used in the stability studies.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Evaluation by PEC:

- The applied formulation to be manufactured by M/s Gray's Pharmaceuticals, Rawat have already been granted approval vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022. The case of the applied formulation of M/s Gray's Pharmaceuticals, Rawat was considered by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already considered product in 316th meeting are as follows:

Applicant firm	M/s Akson Pharmaceuticals, Plot No.9-B/ 1& 2, Old, Industrial Estate New Mirpur City, Azad Jammu and Kashmir
Manufacturer firm	M/s Gray's Pharmaceuticals, Plot #2, Street # N-3, National Industrial Zone, Rawat-Pakistan
Brand Name	Endopime 1g powder for solution for injection or infusion
Batch No. of drug product	T-037, T-038, T-039
Case No.	2
Registration Board meeting	316th meeting of Registration Board

- The case was discussed in 316th meeting wherein Registration Board deliberated that as case pertains to contract manufacturing of already registered drug products thus authorized its Chairman for approval of contract manufacturing permission after rectification of identified shortcomings and product specific inspection.
- After 316th meeting of Registration Board the case was considered in light of rectifications of identified shortcomings (as identified in minutes of 316th meeting) and product inspection report, and accordingly after approval by Chairman Registration Board, letter for approval for the grant of contract manufacturing permission vide letter No.F.316-RB/2022 (PR-II) dated 26th May 2022 was issued to M/s Akson Pharmaceuticals was issued wherein the contract manufacturer was M/s Gray's Pharmaceuticals, Rawat.

Decision: Approved.

- **Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Gray's Pharmaceutical Plot # 2, Street # N-3, National Industrial Zone, Rawat Islamabad.**

227.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt) Ltd. Plot No. 145, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of GMP certificate of M/s Bio-Labs dated 21-05-2019 based on the inspection dated 23-04-2019. The certificate is valid till 22-04-2022. The GMP certificate specifies Lyophilized vial (General) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of GMP certificate of M/s Bio-Labs dated 21-05-2019 based on the inspection dated 23-04-2019. The certificate is valid till 22-04-2022. The GMP certificate specifies Lyophilized vial (General) section. Firm has also submitted copy of letter for grant of additional section dated 23-07-2012 specifying Lyophilized vial (General) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25416: 13-09-2021
	Details of fee submitted	PKR 50,000/-: 07-04-2021
	The proposed proprietary name / brand name	**ALLOZOLE Injection 40mg**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Esomeprazole (as sodium)……40mg
	Pharmaceutical form of applied drug	Almost white coloured lyophilized hygroscopic powder contained in glass vial
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	In house
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexium IV Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Nexum injection by Getz Pharma
	Name and address of API manufacturer.	Sterile India Pvt Ltd. Plot No. 100, Sec-56 Phase-4, Kundli Sonipat (Haryana) India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch

		analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against the comparator i.e. Nexum 40mg Injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Sterile India Pvt Ltd. Plot No. 100, Sec-56 Phase-4, Kundli Sonipat (Haryana) India.		
API Lot No.	SI/BEPZ/00061019		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	L-315	L-287	L-283
Batch Size	5,000 vials	5,000 vials	5,000 vials
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	26-02-2020	22-02-2020	28-02-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has refered to their previous inspection conducted for Empaglif 10mg Tablet (Empagliflozin) & Empaglif 25mg Tablet which was considered by the Board in its 296th meeting and the product was approved based on the inspection report. Following points were noted during the inspection: • All the stability study of EMPAGLIF (10mg & 25mg) Tablets has been conduct on Shimadzu HPLC (Model SPD-20) operated via LABSOLUTION software version 6.5 (complying FDA 21 CFR part 11) • Audit trail reports for Testing of Empaglif 10mg & 25mg Tablets are available. • Proper and continuous monitoring record for stability chamber is available, along with 5KV backup generator with ATS.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 5Kg Esomeprazole sodium sterile powder dated 02-12-2019. The invoice is cleared by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has not submitted audit trail reports for the product testing
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.
- Manufacturer has changed specifications of the drug product without submission of fee.
- The applied product to be manufactured by M/s Bio-Labs (Pvt) Ltd. Plot No. 145, Industrial Triangle Kahuta Road Islamabadhave already been approved by Registration Board in its 316th meeting based on the data of same batches of drug product as submitted in the instant case. The details of the already approved product in 316th meeting are as follows:

Applicant firm	M/s Gray's Pharmaceuticals. Plot No. 2, Street No. N-3, RCCI Rawat Rawalpindi.
Manufacturer firm	M/s Bio-Labs (Pvt) Ltd. Plot No. 145, Industrial Triangle Kahuta Road Islamabad
Brand Name	ESOMEP Injection 40mg
Batch No. of drug product	L-315, L-287, L-283
Case No.	787
Registration Board meeting	316th meeting of Registration Board

Decision: Approved.

- **Firm shall submit differential fee of Rs. 25,000/- for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.**
- **Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
228.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Swiss Pharmaceuticals Pvt Ltd A/159, SITE-II Super Highway Karachi.**
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-05-2020 is submitted.
	GMP status of the firm	Firm has submitted copy of GMP certificate of M/s Vision Pharmaceuticals dated 25-03-2022 based on inspection dated 11-02-2019. As per the certificate, it was valid till 09-05-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of DML of M/s Vision Pharmaceuticals DML No 000517 dated 07-06-2021 specifying sterile dry powder injectable vial (General) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 20655: 29-07-2021
	Details of fee submitted	PKR 50,000/-: 22-12-2020
	The proposed proprietary name / brand name	**PTONIX 40mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Pantoprazole (as sodium)……40mg
	Pharmaceutical form of applied drug	White or almost white colored lyophilized powder
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	BP specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Protonix IV 40mg **(USFDA** Approved)
	For generic drugs (me-too status)	Zopent Injection by Hilton

	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for their product against Protonix IV Injection of Pfizer Pharmaceutical
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.
API Lot No.	2008902

Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	2009714	2009715	2009716
Batch Size	16,800 Vials	16,800 Vials	16,800 Vials
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	08-10-2020	08-10-2020	08-10-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate dated 31-07-2019 of M/s Vision Pharmaceuticals (DML No. 000806 semi basic) issued based on inspection dated 11-02-2019
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted inventory transfer note from SAP of the firm dated 08-10-2020 for the same batch.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

The application of the firm for contract manufacturing from M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad was not submitted as per the guidance document approved by Registration Board. The submitted application was in variation to the guidance document for various modules, sections and sub sections majorly including complete module 1, section 3.2.S.4.1, 3.2.S.4.2, 3.2.S.4.3, 3.2.S.4.4, 3.2.S.5, 3.2.P.2.2.1, 3.2.P.2.6, 3.2.P.3.5, 3.2.P.5.1, 3.2.P.5.2, 3.2.P.5.3, 3.2.P.5.4, 3.2.P.6 and 3.2.P.8. Furthermore, it is also pertinent to mention that the drug product manufacturer has submitted COA of drug substance which is released on 26-02-2018 and provided batch release certificates of 3 batches of drug product released on 09-2017 instead of submitting data of same batches as per the guidance document. Therefore, the firm was advised to resubmit the application compiled in the light of the guidance document approved by Registration Board so that further evaluation of your application could be carried out.

In response, the firm has changed drug product specifications from in house to BP without submission of fee. Firm has also changed the drug substanbce source from Everest Organics Limited Aroor Village Sadasivapet Mandal Sangareddy District Aroor (V), Sadasivpet(M), Sangareddy District Telangana India to M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.

The response was also evaluated, and the found deficient for various points. The following points were communicated to the firm.

Sr. No	Shortcomings communicated	Response by the firm
1.	Submit label claim of the applied product in line with innovator product / reference product along with submission of requisite fee.	Firm has submitted following label claim without submission of fee. Each vial Contains: Pantoprazole (as sodium)……40mg
2.	In your initial submission, you have mentioned in house specifications for the drug product, while in the later submission you have mentioned BP specifications. Justification is required in this regard along with evidence when you have changed the specifications of your already registered product.	In our previous submission the testing for 3 batches was done on UV, but parallel we change our Standard Analytical Procedure and shift our testing method to HPLC. Firm has submitted Revised testing method which was signed and issued on 31-12-2021. This method contains HPLC test for assay of drug product, however, for bulk stage the assay method was based on UV. **As per Documents, firm has changed assay to HPLC method on 31-12-2021 while the stability data was initiated on October 2020. Furthermore, firm could not provide any evidence of intimation to DRAP regarding revision of the specifications of their already registered product from in house to BP specs.**
3.	In your initial application you have specified that the source of drug substance is Everest Organics Limited Aroor Village Sadasivapet Mandal Sangareddy District Aroor (V), Sadasivpet(M), Sangareddy District Telangana India, while in new submission you have changed the source to M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad. Justification is required in this regard along with submission of requisite fee.	As we have two DMLs one for finished drugs and secod for semi basic dosage forms. The lyophilized pantoprazole is always procured from M/s Vision Pharmaceuticals but the powder pantoprazole for lyophilization is procured from Everest organics limited.
4.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient	Firm has submitted standard testing method of pantoprazole sodium sesquihydrate drug substance from Vision Pharmaceuticals dated 29-12-2021. **The submitted document does not specify whether it is of semi basic DML or of DML issued by way of formulation. Moreover the specifications are issued on**

	by both Drug substance & Drug Product manufacturer is required."	**December 2021 while stability batches were manufactured in October 2020.**
5.	Submit data in section 3.2.S.4.3 as per the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted".	Firm has submitted verification studies dated 05-09-2020 based on HPLC method, **while as per the submitted specifications of the drug substance, the assay method is based on potentiometric titration.**
6.	The COA of drug substance manufacturer specifies that the material was released on 31-09-2020 while the drug product manufacturer has sampled the product on 02-09-2020 and released on 16-09-2020. Justification is required in this regard.	Firm submitted that it was a typo error. Firm has submitted another copy of COA of the same batch. In the newly submitted COA from Vision Pharmaceuticals (Semi-Basic DML) the batch was released on 31-08-2020 as per In-house specification and assay on UV method. While as per the raw material analysis report from Vision Pharmaceuticals (Formulation DML), the batch was released on 16-09-2020 as per Innovator's specification and assay on UV method. **The drug substance specifications, BP monograph and submitted COA are contradictory.**
7.	Justify the use of 10ml water for injection as diluent since the innovator product recommends that the product should be reconstituted with 10ml 0.9% sodium chloride solution.	Firm has submitted that they are using 10ml of 0.9% sodium chloride solution as diluent. **However previously the firm has specified water for injection as the diluent.**
8.	Submit results of compatibility studies in section 3.2.P.2.6.	Firm has not submitted compatabiity study report instead only submitted a batch release report.
9.	The analytical method and specifications of the drug product has been generated and signed on 31-12-2021 with a dsscription "this is a new document on this subject" while the stability batches were manufactured in September 2020. Justify how the submitted specifications could be considered applicable for testing of these batches.	The provided analytical method and specifications of drug product has been submitted is the updated one, replacing the old version. **As per Documents, firm has changed assay to HPLC method on 31-12-2021 while the stability data was initiated on October 2020. Furthermore, firm could not provide any evidence of intimation to DRAP regarding revision of the specifications of their already registered product from in house to BP specs.**
10.	Analytical method alidation studies of the drug product were developed in 2017 wherein the specifications and analytical method of BP 2020 were claimed. Justify how validation	**Firm has once again submitted same old verification studies of 2017 in which the assay method was different from that specified in the latest specifications of the firm as well as BP monograph.**

	of analytical method of 2020 can be performed in 2017.	
11.	Justify how three batches of drug product with BP specs were released on 05-10-2020 while the drug specifications are different from that specified in BP monograph and are exactly same as that submitted in initial application as in-house specifications.	**It was a typo error, updated range was according to BP.**
12.	Submit evidence of procurement of the drug substance.	Firm has submitted inventory transfer note from SAP of the firm dated 08-10-2020 for the same batch. **However, the document does not specify any quantity. Moreover, the document for transfer of inventory is of 08-10-2020, while as per the raw material analysis report from Vision Pharmaceuticals (Formulation DML), the batch was released on 16-09-2020.**
13.	Justify how the manufacturing of commercial batches were carried out from 17-09-2020 while the drug substance used in those batches was released on 31-09-2020.	The drug substance was released on 07-09-2020. However as per invoice the material was transferred o 08-10-2020, and as per raw material analysis report the material was released on 16-09-2020.

Decision: Deferred for following:

- **Submission of applicable fee for revision of source of drug substance, revision of specifications and label claim as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Scientific justification how a revised HPLC method dated 31-12-2021 can represent the results of the stability studies which were initiated in October 2020.**
- **Approval of DRAP for change in specifications of the registered product for which stability data is submitted.**
- **Scientific justification for performing verification studies of analytical method of drug substance dated 05-09-2020 based on HPLC method, while as per the submitted specifications of the drug substance, the assay method is based on potentiometric titration.**
- **Scientific justification for having drug substance specifications which are different from the specifications of drug substance manufacturer as well as BP monograph.**
- **Clarification about the use of 10ml water for injection as diluent for the applied product since the innovator product recommends different diluent.**
- **Verification studies of the analytical method of drug product.**
- **Evidence of procurement of the drug substance.**
- **Scientific justification for manufacturing and testing commercial batches of a registered drug product on non-pharmacopoeial specifications while BP monograph was already available for the drug product.**

229.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Limited, Plot No. 37, Sector 19, Korangi Industrial Area, Karachi.**
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer

		☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 02-08-2021 is submitted.
	GMP status of the firm	Firm has submitted copy of GMP certificate of M/s Vision Pharmaceuticals dated 25-03-2022 based on inspection dated 11-02-2019. As per the certificate, it was valid till 09-05-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of DML of M/s Vision Pharmaceuticals DML No 000517 dated 07-06-2021. Firm has also submitted copy of letter dated 09-12-2021 which specifies that CLB in its 283rd meeting held on 28th October 2021 also approved renewal of DML for Liquid Injectable (LVP) General Section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23864: 31-08-2021
	Details of fee submitted	PKR 75,000/-: 06-08-2021
	The proposed proprietary name / brand name	**JYTHON 600mg/300ml Infusion**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial of 300ml Contains: Linezolid…..…600mg
	Pharmaceutical form of applied drug	Liquid infusion
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use
	Reference to Finished product specifications	In-house specs
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zyvox IV **(USFDA** Approved)
	For generic drugs (me-too status)	Nezkil Infusion by Continental pharma
	Name and address of API manufacturer.	Optrix Laboratories Pvt Ltd. Survey No. 145/A & 147, Ramalingampally (V), Bommalaramaram (M), Yadadri-Bhuvanagiri District Telangana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for their product against Nezkil infusion of Continental Pharma.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Optrix Laboratories Pvt Ltd. Survey No. 145/A & 147, Ramalingampally (V), Bommalaramaram (M), Yadadri-Bhuvanagiri District Telangana India.
API Lot No.	OP-LID/10/17/107
Description of Pack (Container closure system)	Glass vials
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	1217901	1217902	1217904
Batch Size	1000 Vials	1000 Vials	1000 Vials
Manufacturing Date	12-2017	12-2017	12-2017
Date of Initiation	27-12-2017	29-12-2017	29-12-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 68951/TS/2021) issued by Drugs control administration, Government of Telangana dated 20-09-2021. The GMP certificate is valid till 19-09-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 08-11-2017 specifying import of 50Kg Linezolid. The invoice is cleared by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC system are not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	Justify the manufacturing of 300ml glass vial (linezolid 600mg/300ml Infusion), while your approved manufacturing facility is "Liquid Injectable Vial SVP (General) section".	Firm has also submitted copy of letter dated 09-12-2021 which specifies that CLB in its 283rd meeting held on 28th October 2021 also approved renewal of DML for Liquid Injectable (LVP) General Section.
2.	The drug substance manufacturer has specified HPLC test for assay of drug substance while the drug product manufacturer has specified UV method for assay of drug substance. Justify how drug product	The drug substance testing was done by UV method at that time, but currently we are using HPLC method for both API and product.

	manufacturer can adopt different test for assay method from that recommended by the drug substance manufacturer.	
3.	Submit COA of relevant batch of API used in the manufacturing of batches for which stability study data is submitted in section 3.2.P.8.3 from both drug substance manufacturer as well as drug product manufacturer in section 3.2.S.4.4, since you have submitted COA of batch number OP-LID/10/17/107 (Mfg date: 09-2017), while as per the submitted import documents the lot number of the API is OP-LID/07/18/077 (Mfg date: 05-2018) and the three stability batches are manufactured in 12-2017.	Firm has submitted ADC attested commercial invoice for lot number OP-LID/10/17/107.
4.	Innovator drug product is using sodium hydroxide and/or hydrochloric acid for ataining the pH within a narrow range of 4.4-5.2 while your master formulation does not specify the use of any such ingredient. Justification is required in this regard.	For pH adjustment we had mentioned HCL and sodium hydroxide in BMR. As our formulation is stable and upon manufacturing the pH comes in limit as defined, and we do not require HCl or Sodium hydroxide for pH adjustment.
5.	Justify why the pharmaceutical equivalence studies were conducted against the comparator product instead of using innovator / reference product. Further justify why pharmaceutical equivalence does not include all quality tests.	Pharmaceutical equivalence study was done against Nezkil of continental pharma as mentioned in DRAP 293rd meeting we can use Reference or comparator product for comparison and comparator product is among brand leaders in Pakistan.
6.	The pH of the product mentioned in section 3.2.P.2.6 is 6.12 with a range of 5.0 to 7.0 which is contrary to the limit defined in your speifications. Justification is required in this regard.	It was a typo error. Actual pH range is 4.4 to 5.5 and our results fall in it.
7.	Justify why terminal sterilization is not performed for the said product although being the method of choice for sterilization.	Firm has submitted that they have performed terminal sterilization and have also submitted copy of BMR.
8.	Justify why the test for filled volume is not specified in the specifications of the drug product although this test is recommended in general monograph of official pharmacopoeia.	Filled volume test reports are now provided by the firm.
9.	Justify the pH of the drug product from 4.4 to 5.5 since the pH range recommended by the innovator's product is 4.4-5.2.	Linezolid infusion batches kept on stability have pH almost in the range of 4.4 to 4.8, and this is in limit of 4.4 to 5.2, However we will revise the pH limit as according to innovator specs and will revise the testing SOP.

10.	Justify the analytical method for assay testing of the drug product which is based on UV method since the innovator's product as well as the drug substance manufacturer specify HPLC method for assay test.	Firm has submitted revised analytical procedures of the drug product dated 13-09-2021. As per the method, buk product is tested by UV method while filled vial are tested using HPLC method. **The revised method is signed on 13-09-2021 while the stability studies were initiated on December 2017.**
11.	The container closure system of the innovator is "flexible plastic infusion bags in a foil laminate overwrap" while your prduct is packed in glass vial. Justify how your container closure system can prevent the product from exposure to the light.	Stability is done in glass vial and it is stable. Also our glass vials are wrapped in laminated foil.
12.	Justify why the test of pH is not performed during stability studies.	pH is not included in stability summary sheets, however all testing is performed and mentioned in analysis certificates. pH results added in stability summary sheet.

Decision: Deferred for following:

- **Scientific justification for revised analytical procedures of the drug product dated 13-09-2021 in which buk product is tested by UV method while filled vial are tested using HPLC method.**
- **Scientific justification how a revised method dated 13-09-2021 can represent the results of the stability studies which were initiated in December 2017.**

230.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Genetics Pharmaceuticals (Pvt) Ltd. 539-A, Sundar Industrial Estate, Raiwind Road Lahore.**
	Name, address of Manufacturing site.	M/s Cunningham Pharmaceuticals (Pvt) Ltd. Plot No. 81, Sunder Industrial Estate, Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 29-03-2021.
	GMP status of the firm	Firm has submitted copy of GMP certificate of M/s Cunningham Pharmaceuticals (Pvt) Ltd dated 19-04-2019 based on the inspection dated 01-04-2019. The GMP certificate specifies Dry powder suspension (cephalosporin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter for issuance of DML of M/s Cunningham Pharmaceuticals (Pvt) Ltd dated 13-06-2016 specifying Dry powder suspension (cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 16132: 10-06-2021
	Details of fee submitted	PKR 50,000/-: 19-05-2021 + PKR 25,000/-: 26-05-2021
	The proposed proprietary name / brand name	**GENFIXIM 100mg/5ml Dry Suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension Contains: Cefixime as trihydrate……100mg
	Pharmaceutical form of applied drug	White to light yellow powder filled in amber colored glass bottle
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	30 ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefixime suspension **(USFDA** Approved)
	For generic drugs (me-too status)	Cefim suspension by Hilton
	Name and address of API manufacturer.	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability

		data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Cebosh dry suspension of Bosch pharmaceuticals.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.		
API Lot No.	00243/342/2017		
Description of Pack (Container closure system)	Amber color glass bottle		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	180012	180013	180015
Batch Size	5,000 bottles	5,000 bottles	5,000 bottles
Manufacturing Date	02-2018	02-2018	04-2018
Date of Initiation	22-03-2018	19-03-2018	19-04-2018
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous PSI has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 09-02-2018 specifying purchase of 25Kg Cefixime (micronized).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with raw data sheets, HPLC chromatograms, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings Communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from API manufacturer as well as Cunningham pharmaceuticals dated February 2021. **The specifications of Cunningham pharma are different from API manufacturer as well as BP monograph. Further the API specs are of February 2021 while stability testing was initiated in March 2018.**
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board and in line with ICH guidelines specifying the exact concentration of each solution and the detailed procedure for each test.	Firm has submitted verification studies of analytical method of drug substance. The analytical method mentioned in verification studies is different from the analytical procedure submitted in section 3.2.S.4.2. Furthermore the method specifies HPLC technique while the calculation method specifies UV absorbance values.
3.	Submit COA of reference standard actually used in the analysis of drug substance and drug product.	Firm has submitted COA of working standard from Pharmagen Limited.
4.	Submit stability study data of the drug substance (cefixime trihydrate in micronized form) from the drug substance manufacturer as per zone IV-A conditions.	Firm has again submitted the same stability data without clarification whether the cefixime was compacted or micronized.
5.	Provide complete master formulation for each bottle in section 3.2.P.1.	Firm has submitted master formulation per bottle.
6.	Provide details of reconstitution solvent / diluent along with its exact volume which is to be used for reconstitution of the drug product.	Water for injection 20ml is the diluent for reconstitution.

7.	Justify why the pharmaceutical equivalence studies are not performed against the innovator / reference product.	No response submitted by the firm, firm has again submitted the same pharmaceutical equivalence report. **Firm has not performed preservative effectiveness studies.**
8.	Justify why comparative dissolution profile / drug release studies are not performed for your product since USFDA has recommended such studies for cefixime suspension.	Firm has submitted that test for CDP is not mentioned in USP monograph.
9.	Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.	Firm has submitted results of compatibility studies.
10.	Justify why the test for deliverable volume is not added in drug product specification as recommended in USP monograph. Revise your product specifications in line with USP monograph along with submission of fee for revision of specifications.	Firm has submitted revised specifications in which test of deliverable volume is also added. Firm has not submitted any fee for change of specifications.
11.	Provide details about the standard solution preparation instead of just using the general statement "0.2mg/ml of USP cefixime RS in solution C" as mentioned in USP monograph.	Firm has submitted revised specifications in which detailed method of standard solution preparation is mentioned.
12.	Submit exact details of the assay preparation since the words "*Reconstitute sample as directed n the labelling"* should not be used in the method adopted by a firm. Instead provide details about the exact diluent along with volume in which reconstitution is to be carried out.	Firm has submitted revised specifications in which detailed method of sample solution preparation is mentioned.
13.	Justify the alternate method for assay testing of the drug product which is based on UV analysis.	Firm has submitted that UV method is only for final mix stage in order to save time during the process.
14.	The concentration of standard solution is 0.2mg/ml while your linearity studies are conducted between 0.008mg/ml to 0.02mg/ml in which does not include the concentration of standard solution. Justify your results.	Method verification of finished product has been revised as per ICH guidelines. **Firm has not justified previous verification studies.**
15.	The repeatability, reproducibility and accuracy studies are reported without specifying the exact concentration of each solution which is tested. Provide results of your verification studies in the light of ICH guidelines.	Method verification of finished product has been revised as per ICH guidelines. **Firm has not justified previous verification studies.**
16.	Justify how same verification studies are used for the analytical method of cefixime capsule, and suspension as well.	Method verification of finished product has been revised as per ICH guidelines. **Firm has not justified previous verification studies.**
17.	For Batch No. 180012, the results of batch analysis (performed on 19-02-2018) was 109.86% while the results in	It was a typographical error.

	initial stability studies at accelerated (performed on 22-03-2018) was 102.65% while the results in initial stability studies at real time (performed on 22-03-2018) was 104.71%. Justify how such significant difference in assay value exists and further justify how the results of initial stability is different for accelerated and real time studies.	
18.	For Batch No. 180013, the results of batch analysis (performed on 22-02-2018) was 104.71% while the results in initial stability studies at accelerated (performed on 19-03-2018) was 101.23% while the results in initial stability studies at real time (performed on 19-03-2018) was 104.62%. Justify how such significant difference in assay value exists and further justify how the results of initial stability is different for accelerated and real time studies.	It was a typographical error.
19.	Specify the date of initiation of stability studies for the batch number 180015.	19-04-2018

Decision: Deferred for following:

- **Scientific justification for having different specifications of the drug substance from that of API manufacturer as well as BP monograph.**
- **Scientific justification how a revised method of February 2021 can represent the results of the stability studies which were initiated in March 2018.**
- **Scientific justification for performing verification studies of the analytical method of drug substance using a different analytical method from that specified in section 3.2.S.4.2.**
- **Submission of stability study data of three batches of cefixime trihydrate (micronized) from the API manufacturer as per zone IV-A conditions.**
- **Submission of pharmaceutical equivalence and Comparative Dissolution Profile (CDP) against the innovator's product.**
- **Submission of preservative effectiveness studies.**
- **Submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Scientific justification how the results of at zero month time point can be different for accelerated and real time conditions.**

231.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Genetics Pharmaceuticals (Pvt) Ltd. 539-A, Sundar Industrial Estate, Raiwind Road Lahore.**
	Name, address of Manufacturing site.	M/s Cunningham Pharmaceuticals (Pvt) Ltd. Plot No. 81, Sunder Industrial Estate, Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 29-03-2021.

	GMP status of the firm	Firm has submitted copy of GMP certificate of M/s Cunningham Pharmaceuticals (Pvt) Ltd dated 19-04-2019 based on the inspection dated 01-04-2019. The GMP certificate specifies Dry powder suspension (cephalosporin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter for issuance of DML of M/s Cunningham Pharmaceuticals (Pvt) Ltd dated 13-06-2016 specifying Dry powder suspension (cephalosporin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 16133: 10-06-2021
	Details of fee submitted	PKR 50,000/-: 19-05-2021 + PKR 25,000/-: 26-05-2021
	The proposed proprietary name / brand name	**GENFIXIM 200mg/5ml Dry Suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension Contains: Cefixime as trihydrate……200mg
	Pharmaceutical form of applied drug	White to light yellow powder filled in amber colored glass bottle
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	30 ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefixime suspension **(USFDA** Approved)
	For generic drugs (me-too status)	Cefim suspension by Hilton
	Name and address of API manufacturer.	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature,

		structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Cebosh dry suspension of Bosch pharmaceuticals.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.		
API Lot No.	00243/342/2017		
Description of Pack (Container closure system)	Amber color glass bottle		
Stability Storage Condition	Real time : 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	180011	180016	180048
Batch Size	5,000 bottles	5,000 bottles	5,000 bottles
Manufacturing Date	02-2018	04-2018	08-2018
Date of Initiation	19-03-2018	~~22-03-2018~~	~~22-03-2018~~

No. of Batches	03

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous PSI has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 09-02-2018 specifying purchase of 25Kg Cefixime (micronized).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with raw data sheets, HPLC chromatograms, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings Communicated	Response by the firm
1.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance specifications from API manufacturer as well as Cunningham pharmaceuticals dated February 2021. **The specifications of Cunningham pharma are different from API manufacturer as well as BP monograph. Further the API specs are of February 2021 while stability testing was initiated in March 2018.**
2.	Submit data of verification of analytical procedure of drug substance in section 3.2.S.4.3 as per the guidance document approved by Registration Board and in line with ICH guidelines specifying the exact concentration of each solution and the detailed procedure for each test.	Firm has submitted verification studies of analytical method of drug substance. The analytical method mentioned in verification studies is different from the analytical procedure submitted in section 3.2.S.4.2. Furthermore the method specifies HPLC technique while the calculation method specifies UV absorbance values.
3.	Submit COA of reference standard actually used in the analysis of drug substance and drug product.	Firm has submitted COA of working standard from Pharmagen Limited.

4.	Submit stability study data of the drug substance (cefixime trihydrate in micronized form) from the drug substance manufacturer as per zone IV-A conditions.	Firm has again submitted the same stability data without clarification whether the cefixime was compacted or micronized.
5.	Provide complete master formulation for each bottle in section 3.2.P.1.	Firm has submitted master formulation per bottle.
6.	Provide details of reconstitution solvent / diluent along with its exact volume which is to be used for reconstitution of the drug product.	Water for injection 20ml is the diluent for reconstitution.
7.	Justify why the pharmaceutical equivalence studies are not performed against the innovator / reference product.	As innovator product is not available in Pakistan therefore we performed testing against Cebosh suspension. **Firm has not performed preservative effectiveness studies.**
8.	Justify why comparative dissolution profile / drug release studies are not performed for your product since USFDA has recommended such studies for cefixime suspension.	Firm has submitted that test for CDP is not mentioned in USP monograph.
9.	Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.	Firm has submitted results of compatibility studies.
10.	Justify why the test for deliverable volume is not added in drug product specification as recommended in USP monograph. Revise your product specifications in line with USP monograph along with submission of fee for revision of specifications.	Firm has submitted revised specifications in which test of deliverable volume is also added. Firm has not submitted any fee for change of specifications.
11.	Provide details about the standard solution preparation instead of just using the general statement "0.2mg/ml of USP cefixime RS in solution C" as mentioned in USP monograph.	Firm has submitted revised specifications in which detailed method of standard solution preparation is mentioned.
12.	Submit exact details of the assay preparation since the words "*Reconstitute sample as directed n the labelling"* should not be used in the method adopted by a firm. Instead provide details about the exact diluent along with volume in which reconstitution is to be carried out.	Firm has submitted revised specifications in which detailed method of sample solution preparation is mentioned.
13.	Justify the alternate method for assay testing of the drug product which is based on UV analysis.	Firm has submitted that UV method is only for final mix stage in order to save time during the process.
14.	The concentration of standard solution is 0.2mg/ml while your linearity studies are conducted between 0.008mg/ml to 0.02mg/ml in which does not include the concentration of standard solution. Justify your results.	Method verification of finished product has been revised as per ICH guidelines. **Firm has not justified previous verification studies.**
15.	The repeatability, reproducibility and accuracy studies are reported without	Method verification of finished product has been revised as per ICH guidelines.

	specifying the exact concentration of each solution which is tested. Provide results of your verification studies in the light of ICH guidelines.	**Firm has not justified previous verification studies.**
16.	Justify how same verification studies are used for the analytical method of cefixime capsule, and suspension as well.	Method verification of finished product has been revised as per ICH guidelines. **Firm has not justified previous verification studies.**
17.	Justify how the results of initial stability is different for accelerated and real time studies.	Results of initial stability study are not different from accelerated and real time time studies. However, it was a typographical error. Results of Batch 180016 and Batch 180048 after correction are attached.
18.	Justify why the results of real time stability studies for batch 180016 and 180048 are exactly same.	It was a typographical error. Results of Batch 180016 and Batch 180048 after correction are attached.

Decision: Deferred for following:

- **Scientific justification for having different specifications of the drug substance from that of API manufacturer as well as BP monograph.**
- **Scientific justification how a revised method of February 2021 can represent the results of the stability studies which were initiated in March 2018.**
- **Scientific justification for performing verification studies of the analytical method of drug substance using a different analytical method from that specified in section 3.2.S.4.2.**
- **Submission of stability study data of three batches of cefixime trihydrate (micronized) from the API manufacturer as per zone IV-A conditions.**
- **Submission of pharmaceutical equivalence and Comparative dissolution profile (CDP) against the innovator's product.**
- **Submission of preservative effectiveness studies.**
- **Submission of applicable fee for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Scientific justification how the results of initial stability can be different for accelerated and real time conditions.**

232.	**Name, address of Applicant / Mar keting Authorization Holder**	**M/s Islam Pharmaceuticals. 7 km, Pasrur Road, Sialkot**
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt) Ltd. Plot No. 145, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 15-06-2019.
	GMP status of the firm	Firm has submitted copy of GMP certificate of M/s Bio-Labs dated 21-05-2019 based on the inspection dated 23-04-2019. The certificate is valid till 22-04-2022. The GMP certificate specifies dry powder injection (cephalosporin) section.

	Evidence of approval of manufacturing facility	Firm has submitted copy of GMP certificate of M/s Bio-Labs dated 21-05-2019 based on the inspection dated 23-04-2019. The certificate is valid till 22-04-2022. The GMP certificate specifies dry powder injection (cephalosporin) section. Firm has also submitted copy of letter for grant of additional section dated 27-02-2011 specifying dry powder injection (cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17789: 25-06-2021
	Details of fee submitted	PKR 50,000/-: 15-03-2021
	The proposed proprietary name / brand name	**TYRONE 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Cefotaxime (as sodium)……500mg
	Pharmaceutical form of applied drug	Sterile white to off white powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefotaxime sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Claforan injection by Sanofi Aventis
	Name and address of API manufacturer.	Qilu Antibiotics Pharmaceutical Co. Ltd. 849 Dongjia Town, Licheng District Jinan City PR China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications,

		analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against the comparator i.e. Claforan 500mg Injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Qilu Antibiotics Pharmaceutical Co. Ltd. 849 Dongjia Town, Licheng District Jinan City PR China.		
API Lot No.	0046L81F		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	VP-01712	VP-1511	VP-1626
Batch Size	16,000 vials	4000 vials	3100 vials
Manufacturing Date	10-2018	03-2018	07-2018
Date of Initiation	05-11-2018	07-05-2018	06-08-2018
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has refered to their previous inspection conducted for Empaglif 10mg Tablet (Empagliflozin) & Empaglif 25mg Tablet which was considered by the Board in its 296th meeting and the product was approved based on the inspection report. Following points were noted during the inspection: • All the stability study of EMPAGLIF (10mg & 25mg) Tablets has been conduct on Shimadzu HPLC (Model SPD-20) operated via LABSOLUTION software version 6.5 (complying FDA 21 CFR part 11) • Audit trail reports for Testing of Empaglif 10mg & 25mg Tablets are available. Proper and continuous monitoring record for stability chamber is available, along with 5KV backup generator with ATS.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. SD20170590) issued by CFDA China dated 31-07-2017. The GMP certificate is valid till 30-07-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted drug substance data of Qilu Antibiotics Pharmaceutical Co. Ltd. China, later on the firm revised API source to Nectar life sciences. Firm has not submitted any justification or fee for revision of source of API.

Sr. No	Shortcomings Communicated	Response by the firm
1.	Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.	Firm has submitted fee 25,000 vide slip number 44849567547 dated 21-02-2022.
2.	You have submitted Innovator's specification in module 1 while the product monograph is available in USP, revise the specifications along with submission of requisite fee.	Innovator's specs was written mistakenly in Form 5-F. Rest of the dossier is of USP specs. **Firm has not submitted any fee for correction in Specs**

3.	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has not submitted any justification.
4.	Justify how you have used drug substance to manufacture cefotaxime injection with USP specifications in which the drug substance is being tested using different mobile phase as that recommended in USP.	Firm has not submitted any justification.
5.	Submit data in section 3.2.S.4.3 as per the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted". Further justify how the analysis of drug substance was conducted without performing verification studies of the analytical method of drug substance.	**Run time 9 min against USP which say 56 mins**
6.	Justify how the drug product manufacturer i.e. M/s Bio labs released drug substance (lot No. 0046L81F) on 08-03-2021 without the test for sterility and bacterial endotoxin, since all of these tests are mentioned in drug substance specifications as well as in the COA of drug substance manufacturer.	Sterility and bacterial endotoxin was performed at the material testing time but mistakenly not mentioned in COA. Now we are submitting COA of lot number which was actually used in drug product.
7.	Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture, since the submitted COA of API are of 2021 while the drug product batches were manufactured in 2018.	We didn't cross check and submit same batches COA earlier. Now are providing relevant batches COAs **The new COA are from different source**
8.	The acceptance criteria for assay test in the drug substance specifications (3.2.S.4.1) is 96 – 102% while the acceptance criteria in COA is 91.6 – 96.4%.	Firm has not submitted any justification.

<table>
<tr><td>9.</td><td>Provide COA of reference standard which is actually used in the analysis of drug substance in section 3.2.S.5.</td><td>Firm has submitted their own in house generated COA for working standard taken from commercial lot.</td></tr>
<tr><td>10.</td><td>Submit master formulation including theoretical fill weight per vial in section 3.2.P.1.</td><td>Firm has submitted theoretical fill weight per vial</td></tr>
<tr><td>11.</td><td>Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator product as per USP specifications. Justify how only pH and assay test can demonstrate pharmaceutical equivalence.</td><td>Firm has not submitted any justification.</td></tr>
<tr><td>12.</td><td>Justify your process validation protocols and report without any process for optimization of sterilization process and sealing of vials etc.</td><td>Firm has not submitted any justification.</td></tr>
<tr><td>13.</td><td>Justify why the specifications of the drug product (section 3.2.P.5.1) does not contain complete tests as recommended by USP.</td><td>Firm has not submitted any justification.</td></tr>
<tr><td>14.</td><td>Provide detailed testing method for the applied drug product instead of submitting copy of USP monograph.</td><td>Still not complete, formula is diff</td></tr>
<tr><td>15.</td><td>Specify the exact details of the accuracy and recovery test including the details of exact concertation of 50%, 100% and 150% solutions.</td><td>Firm has submitted concentrations for each percentage used in accuracy studies.</td></tr>
<tr><td>16.</td><td>Justify the verification studies in which the chromatogram run is till 10 minutes since the gradient HPLC testing till 56 minutes is recommended in USP monograph.</td><td>We have followed USP criteria and on this criteria peak arises at about 5.2 minutes. So the routine adjusted around 10 minutes to safe the time upto 56 minutes.
USP recommends the mobile phase as under:
<table>
<tr><td>Time</td><td>Solution A (%)</td><td>Solution B (%)</td></tr>
<tr><td>0</td><td>100</td><td>0</td></tr>
<tr><td>7</td><td>100</td><td>0</td></tr>
<tr><td>9</td><td>80</td><td>20</td></tr>
<tr><td>16</td><td>80</td><td>20</td></tr>
<tr><td>46</td><td>0</td><td>100</td></tr>
<tr><td>51</td><td>0</td><td>100</td></tr>
<tr><td>56</td><td>100</td><td>0</td></tr>
</table></td></tr>
<tr><td>17.</td><td>Submit the results of verification studies of analytical method of drug product in the light of ICH guidelines, since the submitted studies are not exactly as per ICH guidelines.</td><td>Firm has again submitted verification studies results.</td></tr>
<tr><td>18.</td><td>Justify how three commercial batches were released for commercial use without performing complete tests as specified in USP monograph.</td><td>Complete testing was performed as per USP monograph although COA that provided does not include all performed test parameter. Now COA is revised according to specifications</td></tr>
</table>

19.	Provide COA of reference standard actually used in the analysis of drug product in section 3.2.P.6.	Firm has submitted their own in house generated COA for working standard taken from commercial lot.
20.	Justify why the stability study data of three different batches is submitted from those for which batch analysis is provided in section 3.2.P.5.4.	We didn't cross check and submit same batches COA earlier. Now are providing relevant batches COAs
21.	Specify the exact API lot number and source of API used in the manufacturing of each batch of drug product.	Drug substance B#CFT101029217N COA is attached **The drug substance manufacturer is changed.**
22.	Justify the difference in batch size ranging from 3100 vials to 16000 vials.	**Firm has not submitted any justification.**
23.	Justify why in-use stability study is not performed.	**Firm has not submitted any justification.**
24.	Justify why the test for water contents, constituted solution etc is not performed during stability studies since these tests are very critical and are required to make assessment of the stability profile and shelf life.	Test for water content and constituted solution is performed at stability testing. test was missing in report.
25.	Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch.	**The submitted stability data is performed using analytical method which is not as per USP monograph.**
26.	Justify how assay testing was conducted using only 3 analysis of standard solution.	By considering this deficiency, it is noted that 3 standards are performed in assay. The reason by using 3 standard are considering with the USP monograph 621 which states that RSD will be with in range i.e; NMT 2%.
27.	How you have performed assay testing throughout the stability studies in which the chromatogram run is till 10 minutes since the gradient HPLC testing till 56 minutes is recommended in USP monograph.	We have followed USP criteria and on this criteria peak arises at about 5.2 minutes. So the routine adjusted around 10 minutes to safe the time upto 56 minutes.

Decision: Deferred for following:

- **Submission of applicable fee for revision of source of drug substance and revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Submission of copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer.**
- **Scientific justification for having drug substance specification which is different from USP monograph in terms of mobile phase.**
- **Scientific justification for verification studies of analytical procedure of drug substance in which the HPLC run time is 9 minutes while USP monograph recommends run time for 56 minutes.**
- **Submission of results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.**
- **Scientific justification for having acceptance criteria for assay test in the drug substance specifications (3.2.S.4.1) is 96 – 102% while the acceptance criteria in COA is 91.6 – 96.4%.**

- **Scientific justification why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator product as per USP specifications.**
- **Scientific justification for process validation protocols and report without any process for optimization of sterilization process and sealing of vials etc.**
- **Scientific justification why the specifications of the drug product (section 3.2.P.5.1) does not contain complete tests as recommended by USP. Further justify why the calculation formula for assay testing is different from that recommended in USP.**
- **Scientific justification for verification studies of the drug product in which HPLC run time is for 10 minutes while USP recommends run time for 56 minutes.**
- **Scientific justification for having batch size of commercial product ranging from 3100 vials to 16000 vials.**
- **Scientific justification why in-use stability study of the drug product is not performed.**
- **Scientific justification for testing commercial batches of registered product using the analytical procedure which is different from USP monograph in terms of mobile phase, run time and calculation formula.**

233.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Valor Pharmaceuticals. 124/A Industrial Triangle, Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Dry Vial section (Cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 16395: 14-06-2021
	Details of fee submitted	PKR 75,000/-: 31-05-2021
	The proposed proprietary name / brand name	**ROVITROX 250mg Injection IM**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……250mg
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. 1% lignocaine hydrochloride injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e.

		Rocephin 250mg Injection of M/s Roche Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/002/2019		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	400 vials	400 vials	400 vials
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	20-02-2020	20-02-2020	20-02-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm was asked to submit the following:

- Submit valid contract manufacturing agreement between the contract giver and contract acceptor.
- Submit product development and stability study data of commercial batches manufactured by the drug product manufacturer, since the submitted data are of trial batches.

Response by the firm:
The firm submitted its response (Dy No. 6985) dated 14-03-2022 submitted the following data:

STABILITY STUDY DATA

Manufacturer of API	Sinopharm Weiqida Pharmaceutical Co. Ltd. First Medical Zone, Economic and Technological Development Zone, Datong Shanxi. China.		
API Lot No.	Q012105004		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21H015	21H019	21H037
Batch Size	10,000 vials	10,000 vials	10,000 vials
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	16-08-2021	24-08-2021	29-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. SX20180229) issued by CFDA China dated 06-06-2018. The GMP certificate is valid till 05-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 28-06-2021 specifying import of 150Kg Ceftriaxone sodium (sterile). The invoice was cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance from Pharmagen limited to Sinopharm Weiqida.
- Firm has submitted copy of BMR of commercial batches.
- Firm has not submitted fee for change of API source and stability study data.

Decision: Approved.

- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after submission of applicable fee for change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

234.	**Name, address of Applicant / Mar keting Authorization Holder**	**M/s Valor Pharmaceuticals. 124/A Industrial Triangle, Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Dry Vial section (Cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 16106: 10-06-2021
	Details of fee submitted	PKR 75,000/-: 31-05-2021
	The proposed proprietary name / brand name	**ROVITROX 500mg Injection IM**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……500mg
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. 1% lignocaine hydrochloride injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Rocephin 500mg Injection of M/s Roche Pakistan.

	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/002/2019		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	400 vials	400 vials	400 vials
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	20-02-2020	20-02-2020	20-02-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm was asked to submit the following documents:

- Submit valid contract manufacturing agreement between the contract giver and contract acceptor.
- Submit product development and stability study data of commercial batches manufactured by the drug product manufacturer, since the submitted data are of trial batches.

Response by the firm:
The firm submitted its response (Dy No. 6984) dated 14-03-2022 submitted the following data:

STABILITY STUDY DATA

Manufacturer of API	Sinopharm Weiqida Pharmaceutical Co. Ltd. First Medical Zone, Economic and Technological Development Zone, Datong Shanxi. China.		
API Lot No.	Q012105004		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21H016	21H017	21H038
Batch Size	11750 vials	16750 vials	11750 vials
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	30-08-2021	31-08-2021	12-09-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. SX20180229) issued by CFDA China dated 06-06-2018. The GMP certificate is valid till 05-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 28-06-2021 specifying import of 150Kg Ceftriaxone sodium (sterile). The invoice was cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

	stability chambers (real time and accelerated)	

Evaluation by PEC:

- Firm has changed the source of drug substance from Pharmagen limited to Sinopharm Weiqida.
- Firm has submitted copy of BMR of commercial batches.
- Firm has not submitted fee for change of API source and stability study data.

Decision: Approved.

- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

235.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Valor Pharmaceuticals. 124/A Industrial Triangle, Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 17-12-2020.
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Dry Vial section (Cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19890: 15-07-2021
	Details of fee submitted	PKR 75,000/-: 31-05-2021
	The proposed proprietary name / brand name	**ROVITROX 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……1g
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. water for injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Rocephin 1g Injection of M/s Roche Pakistan.

	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/002/2019		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	400 vials	400 vials	400 vials
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	20-02-2020	20-02-2020	20-02-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm was asked to submit product development and stability study data of commercial batches manufactured by the drug product manufacturer as per the decision of 312nd meeting of Registration Board, since the submitted data was of trial batches.

Response by the firm:
The firm submitted its response (Dy No. 6981) dated 14-03-2022 submitted the following data:

STABILITY STUDY DATA

Manufacturer of API	Sinopharm Weiqida Pharmaceutical Co. Ltd. First Medical Zone, Economic and Technological Development Zone, Datong Shanxi. China.		
API Lot No.	Q012105004		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21H020	21H022	21H023
Batch Size	5875 vials	8375 vials	8375 vials
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	07-09-2021	08-09-2021	08-09-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. SX20180229) issued by CFDA China dated 06-06-2018. The GMP certificate is valid till 05-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 28-06-2021 specifying import of 150Kg Ceftriaxone sodium (sterile). The invoice was cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:		
• Firm has changed the source of drug substance from Pharmagen limited to Sinopharm Weiqida. • Firm has submitted copy of BMR of commercial batches. • Firm has not submitted fee for change of API source and stability study data.		
Decision: Approved. • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration Board further decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		
236.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Valor Pharmaceuticals. 124/A Industrial Triangle, Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 25-03-2021.
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Dry Vial section (Cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19891: 15-07-2021
	Details of fee submitted	PKR 50,000/-: 27-04-2021
	The proposed proprietary name / brand name	**ROVITROX 2g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ceftriaxone (as sodium)……2g
	Pharmaceutical form of applied drug	Sterile white to off white / yellowish crystalline powder filled in transparent glass vials
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Ceftriaxone sodium Injection **(MHRA** Approved)
	For generic drugs (me-too status)	Rocephin injection by Roche.
	Name and address of API manufacturer.	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability. Firm has also submitted compatibility studies of the drug product along with the recommended diluent i.e. water for injection.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in USP for their product against the comparator i.e. Rocephin 2g Injection of M/s Roche Pakistan.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance.

		Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Ltd. Kot Nabi Buksh Wala 34-Km, Ferozepur Road, Lahore.		
API Lot No.	00421/002/2019		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	400 vials	400 vials	400 vials
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	20-02-2020	20-02-2020	20-02-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying import of 10Kg Ceftriaxone sodium (sterile) dated 19-02-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm was asked to submit the following:

- Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.

- Submit product development and stability study data of commercial batches manufactured by the drug product manufacturer as per the decision of 312nd meeting of Registration Board, since the submitted data are of trial batches.

Response by the firm:
The firm submitted its response (Dy No. 6979) dated 14-03-2022 submitted the following data:

STABILITY STUDY DATA

Manufacturer of API	Sinopharm Weiqida Pharmaceutical Co. Ltd. First Medical Zone, Economic and Technological Development Zone, Datong Shanxi. China.		
API Lot No.	Q012105004		
Description of Pack (Container closure system)	Glass vials		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21H043	21H044	21H045
Batch Size	10,000 vials	10,000 vials	10,000 vials
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	16-08-2021	16-08-2021	16-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. SX20180229) issued by CFDA China dated 06-06-2018. The GMP certificate is valid till 05-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 28-06-2021 specifying import of 150Kg Ceftriaxone sodium (sterile). The invoice was cleared by AD (I&E).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that their HPLC system is not 21 CFR compliant.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:		
• Firm has changed the source of drug substance from Pharmagen limited to Sinopharm Weiqida. • Firm has submitted copy of BMR of commercial batches. • Firm has not submitted fee for change of API source and stability study data.		
Decision: Deferred for clarification for performing pharmaceutical equivalence studies against Rocephin Injection 2g since this product is not registered in Pakistan.		
237.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Capsule section (Cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8315: 15-03-2021
	Details of fee submitted	PKR 20,000/-: 09-03-2021
	The proposed proprietary name / brand name	**GEN-ONE 250mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule Contains: Cephradine as monohydrate……250mg
	Pharmaceutical form of applied drug	White to yellowish powder filled in purple/purple hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cephradine capsule **(MHRA** Approved)
	For generic drugs (me-too status)	Velosef capsule by GSK
	Name and address of API manufacturer.	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information

		related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Velosef capsule. Firm has submitted results of CDP for their product against Velosef capsule. Firm has tested CDP in three dissolution medium and the results of f2 factor are within the acceptable limit.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
API Lot No.	00204/164/2020
Description of Pack (Container closure system)	Alu-alu blister

Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-046	T-047	T-048
Batch Size	1000 capsule	1000 capsule	1000 capsule
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	20-06-2020	20-06-2020	20-06-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 07-04-2020 specifying purchase of 5Kg Cephradine (compacted).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	The method of analysis of the drug substance of Pharmagen Limited submitted in section 3.2.S.4.2 is different from BP as well as USP monograph. Justification is required in this regard.	Firm has submitted method of analysis of the drug substance of Pharmagen Limited submitted in section 3.2.S.4.2 as per USP monograph.
2.	Submit specifications as well as analytical method of the drug substance from the drug product manufacturer in section 3.2.S.4.1 and 3.2.S.4.2.	Firm has submitted specifications as well as analytical method of the drug substance from the drug product manufacturer in section 3.2.S.4.1 and 3.2.S.4.2.
3.	Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board	Firm has submitted verification studies of analytical method of drug substance in section 3.2.S.4.3.

4.	Submit COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.	Firm has submitted COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.
5.	Justify how the batch No 0023/163/2019 was tested by Biogen Pharma and declared pass without testing the cephalexin contents. Further justify how the assay limit used by drug product manufacturer is different from BP as well as of drug substance manufacturer.	Firm has submitted COA of the batch number 00204/164/2020 which was actually used for the manufacturing of three batches. The newly submitted COA contains cephalexin contents test.
6.	Justify the submission of reference standard or material in section 3.2.S.5 in which USP reference standard is used against a drug substance which complies BP specifications.	Firm has submitted copy of COA of working standard from API manufacturer based on USP standard.
7.	Submit COA of cephalexin reference standard which is also required in the analysis of drug substance.	Firm has submitted COA of cephalexin reference standard.
8.	Justify the selection of excipients in the master formulation, since your qualitative composition is different from that of reference product.	Firm has submitted that the formulation was as per the reference product.
9.	Justify why drug-excipient compatibility studies is not performed while the formulation is qualitatively different from that of reference product.	Firm has submitted that the formulation was as per the reference product.
10.	Specify the details regarding Batch number, manufacturing date and expiry date of the product against which pharmaceutical equivalence and CDP is not performed.	Velosef 250mg Capsule by GSK (Batch number UD2P)
11.	Submit evidence of procurement of drug substance from Pharmagen Limited.	Firm has submitted copy of commercial invoice dated 07-04-2020 specifying purchase of 5Kg Cephradine (compacted).

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit fee for change of title of the firm from Biogen Pharmaceuticals to Biogen Life Sciences.**

238.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi**
	Name, address of Manufacturing site.	M/s Biogen Pharmaceuticals 8Km, Chakbeli Road Rawat, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	GMP status of the firm	Firm has been granted new license (DML No. 000911) by way of formulation dated 13-02-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 14-02-2020 which specifies Capsule section (Cephalosporin).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8316: 15-03-2021
	Details of fee submitted	PKR 20,000/-: 09-03-2021
	The proposed proprietary name / brand name	**GEN-ONE 500mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule Contains: Cephradine as monohydrate……500mg
	Pharmaceutical form of applied drug	White to yellowish powder filled in purple/purple hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cephradine capsule **(MHRA** Approved)
	For generic drugs (me-too status)	Velosef capsule by GSK
	Name and address of API manufacturer.	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Velosef capsule. Firm has submitted results of CDP for their product against Velosef capsule. Firm has tested CDP in three dissolution medium and the results of f2 factor are within the acceptable limit.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.		
API Lot No.	00204/164/2020		
Description of Pack (Container closure system)	Alu-alu blister		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-049	T-050	T-051
Batch Size	1000 capsule	1000 capsule	1000 capsule
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	20-06-2020	20-06-2020	20-06-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Biogen Pharmaceutical is a new License facility hence no such inspection has been conducted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Additional Director DRAP, Lahore dated 11-01-2019. The GMP certificate was granted based on inspection dated 08-01-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 19-02-2020 specifying purchase of 2Kg Cefixime (compacted).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. No	Shortcomings communicated	Response by the firm
1.	The method of analysis of the drug substance of Pharmagen Limited submitted in section 3.2.S.4.2 is different from BP as well as USP monograph. Justification is required in this regard.	Firm has submitted method of analysis of the drug substance of Pharmagen Limited submitted in section 3.2.S.4.2 as per USP monograph.
2.	Submit specifications as well as analytical method of the drug substance from the drug product manufacturer in section 3.2.S.4.1 and 3.2.S.4.2.	Firm has submitted specifications as well as analytical method of the drug substance from the drug product manufacturer in section 3.2.S.4.1 and 3.2.S.4.2.
3.	Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board	Firm has submitted verification studies of analytical method of drug substance in section 3.2.S.4.3.
4.	Submit COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.	Firm has submitted COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.
5.	Justify how the batch No 0023/163/2019 was tested by Biogen Pharma and declared pass without testing the cephalexin contents. Further justify how the assay limit used by drug product manufacturer is different from BP as well as of drug substance manufacturer.	Firm has submitted COA of the batch number 00204/164/2020 which was actually used for the manufacturing of three batches. The newly submitted COA contains cephalexin contents test.
6.	Justify the submission of reference standard or material in section 3.2.S.5 in which USP reference standard is used against a drug substance which complies BP specifications.	Firm has submitted copy of COA of working standard from API manufacturer based on USP standard.

7.	Submit COA of cephalexin reference standard which is also required in the analysis of drug substance.	Firm has submitted COA of cephalexin reference standard.
8.	Justify the selection of excipients in the master formulation, since your qualitative composition is different from that of reference product.	Firm has submitted that the formulation was as per the reference product.
9.	Justify why drug-excipient compatibility studies is not performed while the formulation is qualitatively different from that of reference product.	Firm has submitted that the formulation was as per the reference product.
10.	Specify the details regarding Batch number, manufacturing date and expiry date of the product against which pharmaceutical equivalence and CDP is not performed.	Velosef 500mg Capsule by GSK (Batch number UC2P)
11.	Submit evidence of procurement of drug substance from Pharmagen Limited.	Firm has submitted copy of commercial invoice dated 07-04-2020 specifying purchase of 5Kg Cephradine (compacted).

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit fee for change of title of the firm from Biogen Pharmaceuticals to Biogen Life Sciences.**

b) Deferred cases

239.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Benson Pharmaceuticals Plot # 3 Main Road National Industrial Zone RCCI Rawat Rawalpindi.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 12-12-2020 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7459: 08-03-2021
	Details of fee submitted	PKR 50,000/-: 01-03-2021
	The proposed proprietary name / brand name	**MEROBEN 500 mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ±

		5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-001	MR-002	MR-003
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization, Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 21-05-2021.
- Stability study data of the following batches

21E001	21E002	21E005
14598 vials	14598 vials	14598 vials
05-2021	05-2021	05-2021
07-05-2021	08-05-2021	21-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh Submission by the firm

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.
API Lot No.	8MT2103173
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH

	Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3. Firm has submitted fee 75,000/- (Slip number 506116296955) dated 09-06-2022 for change of drug substance manufacturer and of change of stability study batches.

- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

• **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**		
240.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Benson Pharmaceuticals Plot # 3 Main Road National Industrial Zone RCCI Rawat Rawalpindi.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 12-12-2020 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7460: 08-03-2021
	Details of fee submitted	PKR 50,000/-: 01-03-2021
	The proposed proprietary name / brand name	**MEROBEN 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
API Lot No.	UIMRPS19021
Description of Pack (Container closure system)	Glass vial

Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-004	MR-005	MR-006
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 26-05-2021.
- Stability study data of the following batches

21E008	21E009	21E010
10948 vials	10948 vials	10948 vials
05-2021	05-2021	05-2021
24-05-2021	25-05-2021	26-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh submission by the firm:

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.

Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3. Firm has submitted fee 75,000/- (Slip number 1377263792) dated 09-06-2022 for change of drug substance manufacturer and of change of stability study batches.

- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

241.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Cherwel Pharmaceuticals (Pvt) Ltd. Plot # 20, Phase 4, Hattar Industrial Estate Hattar.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 21-04-2017 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7214: 04-03-2021

	Details of fee submitted	PKR 50,000/-: 24-02-2021
	The proposed proprietary name / brand name	**MEROFACT 500 mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture,

		manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-001	MR-002	MR-003
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization, Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E)

		DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 21-05-2021.
- Stability study data of the following batches

21E001	21E002	21E005
14598 vials	14598 vials	14598 vials
05-2021	05-2021	05-2021
07-05-2021	08-05-2021	21-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh Submission by the firm

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China

Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40ºC ± 2ºC / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30ºC ± 2ºC / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.
API Lot No.	8MT2103173
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3. Firm has submitted fee 75,000/- (Slip number 13096519180) dated 20-07-2022 for change of drug substance manufacturer and of change of stability study batches.

- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

242.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Cherwel Pharmaceuticals (Pvt) Ltd. Plot # 20, Phase 4, Hattar Industrial Estate Hattar.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 21-04-2017 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7215: 04-03-2021
	Details of fee submitted	PKR 50,000/-: 24-02-2021
	The proposed proprietary name / brand name	**MEROFACT 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing

		process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
API Lot No.	UIMRPS19021
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-004	MR-005	MR-006
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report

- Process validation report dated 26-05-2021.
- Stability study data of the following batches

21E008	21E009	21E010
10948 vials	10948 vials	10948 vials
05-2021	05-2021	05-2021
24-05-2021	25-05-2021	26-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh submission by the firm:

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product,

	specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3. Firm has submitted fee 75,000/- (Slip number 54968138208) dated 20-07-2022 for change of drug substance manufacturer and of change of stability study batches.

- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

243.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma, Plot # 25, S6, National Industrial Zone, Rawat, Islamabad.**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 01-04-2021 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12552: 28-04-2021
	Details of fee submitted	PKR 50,000/-: 02-04-2021
	The proposed proprietary name / brand name	**JUPENEM 500 mg Injection IV**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation

		of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-001	MR-002	MR-003
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization, Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg

		meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 21-05-2021.
- Stability study data of the following batches

21E001	21E002	21E005
14598 vials	14598 vials	14598 vials
05-2021	05-2021	05-2021
07-05-2021	08-05-2021	21-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh Submission by the firm

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers,

	description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005

Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- **Firm has not submitted fee for change of drug substance manufacturer and of change of stability study batches.**
- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

244.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jupiter Pharma, Plot # 25, S6, National Industrial Zone, Rawat, Islamabad..**

	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 01-04-2021 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12553: 28-04-2021
	Details of fee submitted	PKR 50,000/-: 02-04-2021
	The proposed proprietary name / brand name	**JUPENEM 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch

		analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
API Lot No.	UIMRPS19021
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	MR-004	MR-005	MR-006
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 26-05-2021.
- Stability study data of the following batches

21E008	21E009	21E010

10948 vials	10948 vials	10948 vials
05-2021	05-2021	05-2021
24-05-2021	25-05-2021	26-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh submission by the firm:

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- **Firm has not submitted differential fee and fee for change of drug substance manufacturer and of change of stability study batches.**
- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

245.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 01-04-2021 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13168: 06-05-2021
	Details of fee submitted	PKR 50,000/-: 07-04-2021
	The proposed proprietary name / brand name	**ALLONEM 500 mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)

	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard

		or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-001	MR-002	MR-003
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization, Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 21-05-2021.
- Stability study data of the following batches

21E001	21E002	21E005
14598 vials	14598 vials	14598 vials
05-2021	05-2021	05-2021
07-05-2021	08-05-2021	21-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh Submission by the firm

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure

	system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021

No. of Batches	03	
DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3. Firm has submitted fee 75,000/- (slip number 4621495656) dated 20-07-2022 for change of drug substance manufacturer and of change of stability study batches.

- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

246.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alliance Pharmaceutical Pvt Ltd. 112 A, Hayatabad Industrial Estate, Peshawar**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer

		☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 01-04-2021 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13169: 06-05-2021
	Details of fee submitted	PKR 50,000/-: 07-04-2021
	The proposed proprietary name / brand name	**ALLONEM 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure,

		general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-004	MR-005	MR-006
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 26-05-2021.
- Stability study data of the following batches

21E008	21E009	21E010
10948 vials	10948 vials	10948 vials
05-2021	05-2021	05-2021
24-05-2021	25-05-2021	26-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh submission by the firm:

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA			
Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3. Firm has submitted fee 75,000/- (slip number 774298015996) dated 20-07-2022 for change of drug substance manufacturer and of change of stability study batches.

• **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.		
Decision: Approved. • **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**		
247.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Focus & Rulz Pharmaceuticals Pvt Ltd. 44-Industrial Triangle Kahuta Road, Islamabad**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 07-12-2020 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7100: 03-03-2021
	Details of fee submitted	PKR 50,000/-: 15-12-2020
	The proposed proprietary name / brand name	**MEROVITE 500 mg Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA			
Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-001	MR-002	MR-003
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization, Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

	stability chambers (real time and accelerated)	

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 21-05-2021.
- Stability study data of the following batches

21E001	21E002	21E005
14598 vials	14598 vials	14598 vials
05-2021	05-2021	05-2021
07-05-2021	08-05-2021	21-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh Submission by the firm

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard,

	container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- **Firm has not submitted fee for change of drug substance manufacturer and of change of stability study batches.**
- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

248.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Focus & Rulz Pharmaceuticals Pvt Ltd. 44-Industrial Triangle Kahuta Road, Islamabad**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Contract manufacturing agreement dated 07-12-2020 is submitted
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.

	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17786: 25-06-2021
	Details of fee submitted	PKR 50,000/-: 15-12-2020
	The proposed proprietary name / brand name	**MEROVITE 1g Injection IV**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-004	MR-005	MR-006
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 26-05-2021.
- Stability study data of the following batches

21E008	21E009	21E010
10948 vials	10948 vials	10948 vials
05-2021	05-2021	05-2021
24-05-2021	25-05-2021	26-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

- Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 25th June 2021.

Decision of 316th meeting of Registration Board:

Deferred for following: • Submission of differential fee Rs. 25,000/- for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 25th June 2021. • Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board. • Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
Fresh submission by the firm:	
Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.

Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

• **Firm has not submitted differential fee and fee for change of drug substance manufacturer and of change of stability study batches.** • **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.		
Decision: Approved. • **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**		
249.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Variant Pharmaceuticals Pvt Ltd. Plot No. 5, M2-Pharma Zone Lahore, Sharikpur Road, Sheikhupura**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 10-11-2020.
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17793: 25-06-2021
	Details of fee submitted	PKR 50,000/-: 09-04-2021
	The proposed proprietary name / brand name	**VARINUM 500mg IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..500mg (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 10ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem

	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their

		product against the comparator i.e. Meronem 500mg injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-001	MR-002	MR-003
Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization, Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 21-05-2021.
- Stability study data of the following batches

21E001	21E002	21E005
14598 vials	14598 vials	14598 vials
05-2021	05-2021	05-2021
07-05-2021	08-05-2021	21-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of differential fee Rs. 25,000/- for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 25th June 2021.
- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh Submission by the firm

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and

	its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 500mg injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH Accelerated: $40^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E001	21E002	21E005
Batch Size	14084 vials	14084 vials	14084 vials
Manufacturing Date	05-2021	05-2021	05-2021

Date of Initiation	07-05-2021	08-05-2021	21-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- **Firm has not submitted differential fee and fee for change of drug substance manufacturer and of change of stability study batches.**
- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

250.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Variant Pharmaceuticals Pvt Ltd. Plot No. 5, M2-Pharma Zone Lahore, Sharikpur Road, Sheikhupura**
	Name, address of Manufacturing site.	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate Rawat Islamabad.

	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Firm has submitted copy of contract manufacturing agreement with applicant firm dated 10-11-2020.
	GMP status of the firm	Firm has been granted new DML by way of formulation dated 06-11-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 06-11-2019 specifying Dry Vial Injection section (Carbapenem).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17792: 25-06-2021
	Details of fee submitted	PKR 50,000/-: 09-04-2021
	The proposed proprietary name / brand name	**VARINUM 1g IV Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……..1g (Blended with sodium carbonate)
	Pharmaceutical form of applied drug	Glass vial filled with almost white powder along with 20ml ampoule of WFI further packed in unit carton.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Meronem Injection by ICI Pakistan Ltd.
	Name and address of API manufacturer.	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India.		
API Lot No.	UIMRPS19021		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH Accelerated: $40^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MR-004	MR-005	MR-006

Batch Size	350 vials	350 vials	350 vials
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	07-01-2020	07-01-2020	07-01-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. DC/A-1/WHO-GMP/2020/1961) issued by Drugs control organization Governmnet of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" for import of meropenem 3Kg from M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India issued by AD (I&E) DRAP field office. The license was issued on 02-01-2020. • Firm has submitted copy of commercial invoice dated 02-01-2020 specifying import of 3Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for only single day 01-07-2020.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.

Firm has initially submitted stability study data of trial batches for the contract manufacturing. As per the decision of 312nd meeting of Registration Board the firm was asked to submit product development and stability study data of commercial batches manufactured by M/s Bio-Next Pharmaceuticals.

Firm has submitted tability study data of commercial batches but the batches were manufactured using drug substance from Shenzhen Haibin Pharmaceuticals. Firm has submitted following documents:

- Audit trail report
- Process validation report dated 26-05-2021.
- Stability study data of the following batches

21E008	21E009	21E010
10948 vials	10948 vials	10948 vials
05-2021	05-2021	05-2021
24-05-2021	25-05-2021	26-05-2021

However, the firm has not provided complete data of new drug substance and drug product required as per the CTD guidance document.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of differential fee Rs. 25,000/- for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 25th June 2021.
- Submission of complete data of drug substance as well as drug product in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.
- Submission of fee of Rs. 75,000 for revision in stability data as well as change of source of drug substance, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

Fresh submission by the firm:

Name and address of API manufacturer.	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product,

	specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Meronem 1g injection of Pfizer Limited.
Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	Shenzhen Haibin Pharmaceutical Co., Ltd. No. 2003, Shenyan Road, Yantian District, Shenzhen City, Guangdong Province, P.R China.		
API Lot No.	8MT2103173		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21E008	21E009	21E010
Batch Size	10563 vials	10563 vials	10563 vials
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	24-05-2021	25-05-2021	26-05-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No Product Specific Inspection has been conducted since it is a new license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. GD20190927) issued by China Food and Drug Administration dated 04-01-2019. The certificate is valid till 03-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 22-04-2021 specifying import of 160Kg meropenem. The invoice is signed by AD (I&E) DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Firm has initially submitted stability study data of three trial batches manufactured using drug substance manufactured by M/s Rajasthan Antibiotics Ltd. Plot No. 619 & 630 RIICO Industrial Area Bhiwadi – District Alwar Rajasthan India. Later the firm submitted 6 months stability study data of three commercial batches along with complete module 2 and module 3.

- **Firm has not submitted differential fee and fee for change of drug substance manufacturer and of change of stability study batches.**
- **The specifications of the firm are not as per USP since it does not contain test for sodium contents. Firm has not performed the test for sodium content at batch release or even during the stability studies**.

Decision: Approved.

- **The Board decided that the registration letter will be issued after revision of drug product specification as per USP including test for sodium content along with submission of applicable fee that is 75,000/- for revision of specifications and change of source of drug substance as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **The Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility Capacity assessment of M/s Bio-Next Pharmaceuticals, Rawat.**

251.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Swiss Pharmaceuticals (Pvt) Ltd. A/159, SITE, Super Highway Karachi.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-05-2020 is submitted.
	GMP status of the firm	**Swiss Pharmaceuticals:** 18-10-2018: GMP compliance level is rated as GOOD." **Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 2478: 21-01-2021
	Details of fee submitted	PKR 50,000/-: 11-12-2020
	Proposed proprietary name/brand name	**MEPEN 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……500mg
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with sea green color flip off seal along with 10ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process

		control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Merrem 500mg Injection of Pfizer.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/BMPM/0990917 S1/BMPM/1031017		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17L078	17L079	17M319
Batch Size	7692 vials	7692 vials	7692 vials
Manufacturing Date	11-2017	11-2017	11-2017
Date of Initiation	04-12-2017	05-12-2017	29-12-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 23-10-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/0990917. The commercial invoice is attested by AD (I&E) DRAP field office. Firm has

		submitted copy of commercial invoice cleared dated 03-11-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/BMPM/1031017. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Provide name and address of the applicant i.e. M/s Swiss Pharmaceuticals (Pvt) Ltd as per the address mentioned on Drug Manufacturing License (DML) along with submission of requisite fee (if applicable), since the address mentioned on section 1.3.1 is different from that mentioned in the DML.	Firm has revised the address of applicant on Form 5F without submission of any fee.
Provide correct label claim as per the innovator / reference product in section 1.5.2 along with submission of requisite fee, since the submitted label claim is incomplete and it does not specify the sodium carbonate component.	Firm has submitted revised label claim as per the reference product without submission of fee.
Provide copies of IR spectra of the drug substance in section 3.2.S.3.1 as per the guidance document approved by Registration Board which specifies that "Drug substance /Active Pharmaceutical Ingredients that are described in an officially recognized pharmacopoeia it is generally sufficient to provide copies of the IR spectrum.	Firm has submitted copies of IR spectra of drug substance from the API manufacturer.
Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance manufacturer's specification and testing method separately for meropenem trihydrate, sodium carbonate and meropenem for injection without specifying the exact specifications of their drug substance. Further specifications and method of analysis from drug product manufacturer is not submitted.
Justify why the test of content of sodium is not included in the specifications of drug substance.	Firm has revised the specifications and added test of sodium. The specifications have been revised without submission of fee.
Justify the acceptance criteria of assay "NLT 78% as meropenem on dried basis", since this is not in line with the USP monograph.	Meropenem for injection is a combination of meropenem with sodium carbonate so after subtraction of sodium carbonate and water contents the limit is NLT 78%.

Justify the flow rate of 1.0ml/min for the assay test of drug substance, since USP recommends flow rate to be 1.5ml/min.	Firm has revised the specifications and changed the flow rate to 1.5ml/min. The specifications have been revised without submission of fee.
Provide complete method of standard and sample preparation in assay test of drug substance. Just mentioning the final concentration without specifying the initial quantity of material taken and the dilution steps is not permitted by any guidelines.	Firm has submitted revised specification and testing method. As per revised testing method the sample preparation method is totally different from that specified in USP monograph.
As per the assay method of drug substance, the sample solution is nominally 0.1mg/ml of meropenem in mobile phase. While as per USP monograph the sample solution preparation method is entirely different which involves initial reconstitution with water prior to dilution with mobile phase. Justify how the tests performed by your method can be considered acceptable under the USP monograph.	Firm has submitted revised specification and testing method. As per revised testing method the sample preparation method is totally different from that specified in USP monograph. Firm took meropenem sample equivalent to 50mg in 50ml volumetric flask and make up the volume with mobile phase.
The USP monograph under the assay method specifies that sample should be hold for 1-2 hours at 25± 1°C before testing, while your method does not mention the same. Justify how your method could be considered as complying with USP monograph.	Firm has now mentioned this statement in their testing method.
Justify the submission of batch analysis of 3 batches of drug substance instead of providing the report of validation studies of the analytical method in section 3.2.S.4.3. Further justify how the drug substance testing was carried out without performing verification studies of the analytical method of drug substance as recommended by USP monograph.	Method verification for the product is performed and we use same testing method for the drug substance. Since it is ready to fill powder so for this reason we did not perform method validation of API.
Justify why the test of sodium carbonate content and sodium content is not performed for the batch of drug substance S1/BMPM/0990917 (testing performed on 31-10-2017) and batch number S1/BMPM/1031017 (testing performed on 16-11-2017).	Initially in 2017 we do not hve atomic absorption so we consider this value from manufacturer COA, now we purchased atomic absorption which is used for the determination of sodium content.
Justify how the results of assay of drug substance on dried basis is obtained, since this method (formula) is not mentioned in your analytical method nor specified in USP.	Firm has submitted that testing method has been revised and all required formulas are incorporated.
USP specifies tailing factor NMT 1.5 in the system suitability requirements, while the tailing factor values obtained in your chromatograms of drug substance show results greater than 1.5. Justify how the test was performed without complying the system suitability requirements as per USP monograph.	Testing method is revised as per current USP and revised testing method followed now and tailing factor value reviewed during the checking of testing results and testing report. Firm has not justified the previous analysis in which tailing factor was above 1.5.
The standard solution and the sample solution analysis for drug substance testing was performed using different HPLC equipment and software. Justify how the analysis could be considered	We run standard solution and sample solution both, whenever we perform the testing of any API or finished product on same HPLC, which makes the achieved results reliable and we check the system

reliable if the standard solution are run in different equipment.	suitability parameters in all routine testing to comply the requirement. Firm has not provided any scientific justification.
Justify the HPLC testing of sample solution using detector 220nm while the USP recommends that testing be performed at 300nm.	Testing method is revised as per current USP and revised testing method provided. Firm has not provided any justification for testing of stability batches for which testing was conducted at 200nm. All these batches are now expired as well.
As per the raw data sheets, the value of potency of meropenem in meropenem reference standard is 73.91%. Justify how this reference standard was used in the testing of drug substance which is very low purity and contents.	The potency is based on as is basis which is used for the testing of drug substance.
Provide COA of reference standard / working standard used in the testing of drug substance.	Firm has submitted certificate of USP reference standard. However, the testing method of the firm specifies that meropenem working standard is used.
Justify how 707mg of meropenem as trihydrate blended with sodium carbonate contains 500mg of meropenem.	The calculation provided by the firm does not incorporate the sodium carbonate contents.
Provide details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.	Not submitted
Justify why complete tests as mentioned in USP are not performed in pharmaceutical equivalence.	Not submitted
Provide data in section 3.2.P.2.6 as per the guidance document approved by Registration Board which specifies that "Compatibility studies for the dry powder for injections and dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product."	Not submitted
Justify why the test of content of sodium and loss on drying is not mentioned in the specifications of the drug product provided in section 3.2.P.5.1.	Testing method revised as per current USP and revised testing method provided and implemented for onward testing.
Justify the sample solution preparation method under the assay test of drug product is different from that mentioned in USP monograph.	Testing method revised as per current USP and revised testing method provided and implemented for onward testing.
Justify why the calculation formula of assay content of drug product is different from that specified in USP monograph.	Testing method revised as per current USP and revised testing method provided and implemented for onward testing.
Justify the submission of COA of commercial batch (S1/BMPM/0990917 and S1/BMPM/1031017) in section 3.2.P.6 as the reference standard.	Firm has submitted certificate of USP reference standard. However, the testing method of the firm specifies that meropenem working standard is used.
Justify how meropenem (trihydrate) for injection is used as reference standard since the USP recommends that meropenem (base) should be used as reference standard for assay test of meropenem for injection.	We used meropenem (trihydrate) as working standard after standardizing it against USP reference standard.

Submit data in section 3.2.P.8 as per the guidance document approved by Registration Board which specifies that "Summary of additional stability studies (if applicable) e.g. in-use studies for drug products which are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided".	Firm has only provided a statement of shelf life after reconstitution. No data has been submitted. The reference product specify the shelf life after reconstitution as 3 hours at room temperature while the firm has claimed 12 hours even without any data.
Justify why the test of content of sodium, completeness and clarity of solution, loss on drying and sterility test is not included in the stability studies of the product.	Testing parameters are not completely followed in stability studies only assay and pH test is performed.
The results of assay test of meropenem for the batch No. 17L078 show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time). Provide scientific justification for this upward trend keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.	This increase in assay may be due to the API content vial used for assay testing has filled weight of higher limit. Firm has not provided any scientific justification
You have imported 20Kg meropenem for injection in the packing of 5Kg aluminium container. Justify how the batches of 5.4Kg were developed using the same container.	Firm submitted that they have imported 20 Kg (5kg container x 4) while in each batch 5.4 Kg was used. Firm has not submitted any justification from where that extra 0.4Kg was added in each batch.
Provide Batch Manufacturing Record (BMR) for all the three stability batches.	Firm has submitted copy of BMR of the three stability batches.

Decision of 312th meeting of Registration Board:

Registration Board delibrated the case in detail and observed that the contract manufacturer has not performed complete product development studies, the specifications adopted by the manufacturer throughout stability studies were not according to USP and that the stability batches have also expired. Accordingly, the Board deferred for following submissions:

- Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.
- Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,
- Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.
- Scientific justification for having analytical method of drug product without specifying that "*sample should be hold for 1-2 hours at 25± 1°C before testing*" which is recommended in USP monograph.
- Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.
- Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.
- Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.

- Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.
- Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.
- Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.
- Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.
- Scientific justification for not performing compatability studies of the drug product with the recommended diluent.
- Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.
- Scientific justification for using an entirely different formula for calculation of assay resultsof commercial batches from that specified in USP monograph.
- Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.
- Scientific justification for the results of assay test of meropenem for the batch No. 17L078 which show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time) keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.
- Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.
- Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.
- Submission of fee for pre-registration changes in the drug product specifcations.

Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly. The Board further directed the manufacturer to comply USP Specifications for already registered drug products.

Response by the firm:

Reason for deferment	**Response by the firm**
Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.	Specifications and Analytical Procedure of Drug Substance by API manufacturer is provided.
Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,	As mentioned in USP monograph of Meropenem for Injection edition 2018 and 2019, retention time should be between 6 to 8 minutes. We were following same criteria regarding flow rate i.e. 1.5ml but due to typographic error flow rate of 1.0ml was mentioned in test method which has been corrected now.
Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.	Sample solution preparation was performed as USP monograph but step of reconstitution with water was not previously part of sample solution preparation. Said step has been incorporated in revised test method. Copy of revised test method is also provided.
Scientific justification for having analytical method of drug product without specifying that "sample should be hold for 1-2 hours at 25±	Due to typographic error these details of hold time after sample preparation was missed in finished product testing method. Testing method has been revised as per current USP monograph

1°C before testing" which is recommended in USP monograph.	
Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.	We have checked all chromatograms of raw material testing as well as stability testing but found no peak tailing greater than 1.5. Particular details regarding tailing factor was not previously mentioned in the testing method, which is now incorporated in revised testing method of both drug substance and drug product. Copy of revised test method is also provided.
Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.	We use to run standard solution and sample solution both (whenever we perform the testing of any API or Finished product) on same HPLC system, as it makes results more reliable and also verifies system suitability parameters in all-routine testing. We have tested assay and impurities on two separate systems having different softwares, may be this was confusion factor while data review.
Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.	We have followed USP monograph for testing of assay of drug substance as well as impurities. USP monograph specifies 300nm for assay testing of drug substance while 220nm for impurities testing in drug substance.
Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.	The potency is on as is basis of Meropenem for injection, which has been standardized against the primary standard (Meropenem base) and is used as working standard in routine testing.
Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.	Below is the calculation of fill weight if Meropenem 500mg: As per attached COA, Average water content = 10.5% Average sodium bicarbonate content = 18.5% By adding both contents, 10.5 + 18.5 = 29% By subtracting both contents, 100% - 29% = 71% For Merem 500mg = $\frac{500 \times 100}{71}$ = 704.22mg/vial
Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.	Firm has provided details for meropenem 1gm injection
Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.	All tests that are mentioned in USP could not perform during pharmaceutical equivalence due to limited quantity of innovator sample. Therefore, we have included only all major test while performing pharmaceutical equivalence.
Scientific justification for not performing compatibility studies of the drug product with the recommended diluent.	Compatibility studies of Merem were performed but it was not made part of dossier during submission. Detailed compatibility studies of Merem against its innovator i.e. Merrem was performed with all its recommended diluents. Study results are also provided.

Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.	In 2017, we did not have Atomic Absorption there test of content of sodium is not part of specifications of product. Moreover we have now revised specification and LOD and content of sodium has been incorporated in revised specifications.
Scientific justification for using an entirely different formula for calculation of assay results of commercial batches from that specified in USP monograph.	Formula of content of drug product is elaborated with context to standard and sample preparation procedure which has now been updated as per USP format. Copy of revised test method and USP monograph is also provided.
Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.	Testing parameters like sodium contents, loss on drying has not performed because they can be monitored indirectly. The justifications given as below: • Sodium is the part of Sodium carbonate which in this mixture of meropenem for injection acts as a buffer and controls the pH of the mixture. A pH drift will depict the change in buffer contents, as Sodium being metal does not degrade in ordinary conditions. • Loss on drying has a direct impact on the active ingredient stability/degradation. Assay determination depicts the impact cause by this parameter. • In physical check of stability samples we use to perform this test after reconstitution with prescribed amount of water but this test was not separately mentioned in stability data. As for as sterility is concerned it was not part of stability testing. We have revised our stability protocols and included all critical Quality attributes in stability testing and implemented for onward stability testing.
Scientific justification for the results of assay test of meropenem for the batch No. 17L078 which show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time) keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.	Assay results of initial time point of 17L078 batch are significantly low than all remaining samples tested during whole stability. This is because of low filled weight vial of finished product tested at zero time point. As far as results of all other time points are concerned there is a little difference between assays results i.e. hardly one to two percent. Therefore, speculation regarding deviation from USP monograph is completely ruled out as same method has been applied while testing other stability batches and no such trend has been seen there.
Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.	During interpretation of data from BMR while preparation of dossier 5.4kg has been mistakenly considered batch size by regulatory person. Actual batch size as stated in BMR is 5.0kg. Moreover meropenem as ready to fill powder is imported in container of 5.0kg.

Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.	Field Service Report dated 25-10-2019 is provided from Rays Technologies. In report it is mentioned that IQ, OQ and PQ of the instrument is perfomed and the instrument is handed over to user in working condition. However no details of the equipment / instrument is provide.
Submission of fee for pre-registration changes in the drug product specifications.	Firm has submitted fee 7500/- dated 05-11-2021 for change in specifications
Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly. The Board further directed the manufacturer to comply USP Specifications for already registered drug products.	Firm has not submitted product development and stability study data of new batches in which the development and testing is carried out as per USP specifications from initial time point.

Decision of 313rd meeting of Registration Board:

Registration Board deliberated that the commercial batches manufactured by the manufacturer i.e. Global Pharmaceuticals was not developed and tested as per the USP monograph. Keeping in view the USP monograph, public assessment report of the innovator product and the data submitted by the firm, the Board decided to defer the case and advised the manufacturer to perform product development studies keeping in view the innovator product and product testing and stability studies by complying USP monograph and submit data upon completion of 6 months stability studies.

Submission by the firm:

The firm on 13-01-2022 submitted new response against the decision of 312nd meeting of Registration Board instead of complying the decision of 313rd meeting of Registration Board.

In the new submission, the firm has changed the source of drug substance from M/s Sterile India Pvt Ltd. India to M/s Shenzhen Haibin Pharmaceutical Co. Ltd China. Furthermore, the firm has submitted stability data of following new batches:

Batch No.	Batch size	Mfg date	Stability initiation date
21A057	7072 Vials	01-2021	23-01-2021
21D216	7072 Vials	04-2021	06-05-2021
21E156	7072 vials	05-2021	01-06-2021

Firm has submitted data which shows that the product testing has been conducted as per revised specs and calculation formula however firm has revised their specifications after 312nd meeting which was conducted on 14-16 Septeber 2021 and the revised specifications were considered by the Board in its 313rd meeting held on 16-18 November 2021.

Decision of 316th meeting of Registration Board:

Deferred for submission of complete data of drug substance as well as drug product as per revised specifications in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.

Response by the firm:

Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted module 2 and module 3 along with stability study data, the details of which are as under:			
STABILITY STUDY DATA			
Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.		
API Lot No.	682107003		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A169	22A363	22A364
Batch Size	7418 vials	7418 vials	7418 vials
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	25-01-2022	25-01-2022	25-01-2022
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.
- GMP certificate / insepection report of the contract manufacturer is not available within last three years.

Decision: Approved.

- **Registration Board decided that registration letter will be issued after submission of applicable fee 75,000/ for change of source as well as submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**

252.	Name, address of Applicant / Marketing Authorization Holder	M/s Swiss Pharmaceuticals (Pvt) Ltd. A/159, SITE, Super Highway Karachi.
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-05-2020 is submitted.
	GMP status of the firm	**Swiss Pharmaceuticals:** 18-10-2018: GMP compliance level is rated as GOOD." **Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022 issued on the basis of inspection dated 03-01-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000417 of M/s Global Pharmaceuticals Islamabad dated 18-12-2017 specifying reallocation of dry powder injection (carbapenem) section is place of withdrawn Biotech section (BSF)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 2479: 21-01-2021
	Details of fee submitted	PKR 50,000/-: 11-12-2020
	Proposed proprietary name / brand name	MEPEN 1g Injection

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem trihydrate eq to meropenem……1g
	Pharmaceutical form of applied drug	White to off white powder filled in clear glass vials with brown color flip off seal along with 20ml WFI ampoule.
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Merrem 500mg Injection of Pfizer.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Sterile India Pvt Ltd. Plot No. 100& 118-G, Phase-IV, Sector-56, HSIIDC, Industrial Estate Kundli District Sonepat Haryana India.		
API Lot No.	S1/MPM/01860817		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	17K282	17K283	17K238
Batch Size	3533 vials	3533 vials	3533 vials
Manufacturing Date	10-2017	10-2017	10-2017
Date of Initiation	20-10-2017	25-10-2017	19-10-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/3739 issued by Food and Drugs Administration Haryana dated 21-05-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 25-09-2017 specifying import of 20Kg (4x5Kg) Meropenem for injection for Batch No. S1/MPM/01860817. Commercial invoice is attested by AD (I&E) DRAP field office.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time & accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Provide name and address of the applicant i.e. M/s Swiss Pharmaceuticals (Pvt) Ltd as per the address mentioned on Drug Manufacturing License (DML) along with submission of requisite fee (if applicable), since the address mentioned on section 1.3.1 is different from that mentioned in the DML.	Firm has revised the address of applicant on Form 5F without submission of any fee.
Provide correct label claim as per the innovator / reference product in section 1.5.2 along with submission of requisite fee, since the submitted label claim is incomplete and it does not specify the sodium carbonate component.	Firm has submitted revised label claim as per the reference product without submission of fee.
Provide copies of IR spectra of the drug substance in section 3.2.S.3.1 as per the guidance document approved by Registration Board which specifies that "Drug substance /Active Pharmaceutical Ingredients that are described in an officially recognized pharmacopoeia it is generally sufficient to provide copies of the IR spectrum.	Firm has submitted copies of IR spectra of drug substance from the API manufacturer.
Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted drug substance manufacturer's specification and testing method separately for meropenem trihydrate, sodium carbonate and meropenem for injection without specifying the exact specifications of their drug substance. Further specifications and method of analysis from drug product manufacturer is not submitted.
Justify why the test of content of sodium is not included in the specifications of drug substance.	Firm has revised the specifications and added test of sodium. The specifications have been revised without submission of fee.
Justify the acceptance criteria of assay "NLT 78% as meropenem on dried basis", since this is not in line with the USP monograph.	Meropenem for injection is a combination of meropenem with sodium carbonate so after substraction of sodium carbonate and water contents the limit is NLT 78%.
Justify the flow rate of 1.0ml/min for the assay test of drug substance, since USP recommends flow rate to be 1.5ml/min.	Firm has revised the specifications and changed the flow rate to 1.5ml/min. The specifications have been revised without submission of fee.
Provide complete method of standard and sample preparation in assay test of drug substance. Just mentioning the final concentration without specifying the initial quantity of material taken and the dilution steps is not permitted by any guidelines.	Firm has submitted revised specification and testing method. As per revised testing method the sample preparation method is totally different from that specified in USP monograph.

As per the assay method of drug substance, the sample solution is nominally 0.1mg/ml of meropenem in mobile phase. While as per USP monograph the sample solution preparation method is entirely different which involves initial reconstitution with water prior to dilution with mobile phase. Justify how the tests performed by your method can be considered acceptable under the USP monograph.	Firm has submitted revised specification and testing method. As per revised testing method the sample preparation method is totally different from that specified in USP monograph. Firm took meropenem sample equivalent to 50mg in 50ml volumetric flask and make up the volume with mobile phase.
The USP monograph under the assay method specifies that sample should be hold for 1-2 hours at 25± 1°C before testing, while your method does not mention the same. Justify how your method could be considered as complying with USP monograph.	Firm has now mentioned this statement in their testing method.
Justify the submission of batch analysis of 3 batches of drug substance instead of providing the report of validation studies of the analytical method in section 3.2.S.4.3. Further justify how the drug substance testing was carried out without performing verification studies of the analytical method of drug substance as recommended by USP monograph.	Method verification for the product is performed and we use same testing method for the drug substance. Since it is ready to fill powder so for this reason we did not perform method validation of API.
Justify how the results of assay of drug substance on dried basis is obtained, since this method (formula) is not mentioned in your analytical method nor specified in USP.	Firm has submitted that testing method has been revised and all required formulas are incorporated.
USP specifies tailing factor NMT 1.5 in the system suitability requirements, while the tailing factor values obtained in your chromatograms of drug substance show results greater than 1.5. Justify how the test was performed without complying the system suitability requirements as per USP monograph.	Testing method is revised as per current USP and revised testing method followed now and tailing factor value reviewed during the checking of testing results and testing report. Firm has not justified the previous analysis in which tailing factor was above 1.5
The standard solution and the sample solution analysis for drug substance testing was performed using different HPLC equipment and software. Justify how the analysis could be considered reliable if the standard solution are run in different equipment.	We run standard solution and sample solution both, whenever we perform the testing of any API or finished product on same HPLC, which makes the achieved results reliable and we check the system suitability parameters in all routine testing to comply the requirement. Firm has not provided any scientific justification.
Justify the HPLC testing of sample solution using detector 220nm while the USP recommends that testing be performed at 300nm.	Testing method is revised as per current USP and revised testing method provided. Firm has not provided any justification for the testing of stability batches for which testing was conducted at 200nm. All these batches are now expired as well.
As per the raw data sheets, the value of potency of meropenem in meropenem reference standard is 73.91%. Justify how this reference standard was used in the testing of drug substance which is very low purity and contents.	The potency is based on as is basis which is used for the testing of drug substance.
Provide COA of reference standard / working standard used in the testing of drug substance.	Firm has submitted certificate of USP reference standard.

	However, the testing method of the firm specifies that meropenem working standard is used.
Justify how 1413mg of meropenem as trihydrate blended with sodium carbonate contains 1g of meropenem.	The calculation provided by the firm does not incorporate the sodium carbonate contents.
Provide details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.	Not submitted
Justify why complete tests as mentioned in USP are not performed in pharmaceutical equivalence.	Not submitted
Provide data in section 3.2.P.2.6 as per the guidance document approved by Registration Board which specifies that "Compatibility studies for the dry powder for injections and dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product."	Not submitted
Justify why the test of content of sodium and loss on drying is not mentioned in the specifications of the drug product provided in section 3.2.P.5.1.	Testing method revised as per current USP and revised testing method provided and implemented for onward testing.
Justify the sample solution preparation method under the assay test of drug product is different from that mentioned in USP monograph.	Testing method revised as per current USP and revised testing method provided and implemented for onward testing.
Justify why the calculation formula of assay content of drug product is different from that specified in USP monograph.	Testing method revised as per current USP and revised testing method provided and implemented for onward testing.
Justify the submission of COA of commercial batch (S1/BMPM/0990917 and S1/BMPM/1031017) in section 3.2.P.6 as the reference standard.	Firm has submitted certificate of USP reference standard. However, the testing method of the firm specifies that meropenem working standard is used.
Justify how meropenem (trihydrate) for injection is used as reference standard since the USP recommends that meropenem (base) should be used as reference standard for assay test of meropenem for injection.	We used meropenem (trihydrate) as working standard after standardizing it against USP reference standard.
Submit data in section 3.2.P.8 as per the guidance document approved by Registration Board which specifies that "Summary of additional stability studies (if applicable) e.g. in-use studies for drug products which are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided".	Firm has only provided a statement of shelf life after reconstitution. No data has been submitted. The reference product specify the shelf life after reconstitution as 3 hours at room temperature while the firm has claimed 12 hours even without any data.
Justify why the test of content of sodium, completeness and clarity of solution, loss on drying and sterility test is not included in the stability studies of the product.	Testing parameters are not completely followed in stability studies only assay and pH test is performed.
Provide Batch Manufacturing Record (BMR) for all the three stability batches.	Firm has submitted copy of BMR of the three stability batches.
Decision of 312nd meeting of Registration Board:	

Registration Board delibrated the case in detail and observed that the contract manufacturer has not performed complete product development studies, the specifications adopted by the manufacturer throughout stability studies were not according to USP and that the stability batches have also expired. Accordingly, the Board deferred for following submissions:

- Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.
- Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,
- Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.
- Scientific justification for having analytical method of drug product without specifying that "*sample should be hold for 1-2 hours at 25± 1°C before testing*" which is recommended in USP monograph.
- Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.
- Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.
- Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.
- Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.
- Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.
- Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.
- Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.
- Scientific justification for not performing compatability studies of the drug product with the recommended diluent.
- Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.
- Scientific justification for using an entirely different formula for calculation of assay resultsof commercial batches from that specified in USP monograph.
- Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.
- Scientific justification for the results of assay test of meropenem for the batch No. 17L078 which show upward trend (i.e. increase in assay values with time) throughout the stability studies (both accelerated and real time) keeping in view the fact that the testing method was not exactly as per USP monograph, the reference standard meropenem (trihydrate) for injection was used instead of meropenem (base), the contents of sodium, as well as sodium carbonate was not determined at any time point during stability studies and loss on drying is also not performed during the stability studies.
- Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.
- Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.
- Submission of fee for pre-registration changes in the drug product specifcations.

Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly. The Board further directed the manufacturer to comply USP Specifications for already registered drug products.

Response by the firm:

Reason for deferment	Response by the firm
Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug Product manufacturer.	Specifications and Analytical Procedure of Drug Substance by API manufacturer is provided.
Scientific justification for using flow rate of 1.0ml/min for assay testing of your commercial batches since USP recommends flow rate to be 1.5ml/min,	As mentioned in USP monograph of Meropenem for Injection edition 2018 and 2019, retention time should be between 6 to 8 minutes. We were following same criteria regarding flow rate i.e. 1.5ml but due to typographic error flow rate of 1.0ml was mentioned in test method which has been corrected now.
Scientific justification for having the method of sample solution preparation for the commercial batches which is entirely different from that specified in USP monograph.	Sample solution preparation was performed as USP monograph but step of reconstitution with water was not previously part of sample solution preparation. Said step has been incorporated in revised test method. Copy of revised test method is also provided.
Scientific justification for having analytical method of drug product without specifying that "sample should be hold for 1-2 hours at 25± 1°C before testing" which is recommended in USP monograph.	Due to typographic error these details of hold time after sample preparation was missed in finished product testing method. Testing method has been revised as per current USP monograph
Scientific justification for releasing the commercial batch of drug product and during its stability studies even after having the value of tailing factor above 1.5, since USP monograph specifies tailing factor NMT 1.5 in the system suitability requirements.	We have checked all chromatograms of raw material testing as well as stability testing but found no peak tailing greater than 1.5. Particular details regarding tailing factor was not previously mentioned in the testing method, which is now incorporated in revised testing method of both drug substance and drug product. Copy of revised test method is also provided.
Scientific justification for using different HPLC equipment and software for the standard solution and the sample solution analysis.	We use to run standard solution and sample solution both (whenever we perform the testing of any API or Finished product) on same HPLC system, as it makes results more reliable and also verifies system suitability parameters in all-routine testing. We have tested assay and impurities on two separate systems having different softwares, may be this was confusion factor while data review.
Scientific justification for HPLC testing of your commercial batches using UV detector at 220nm while the USP recommends that testing be performed at 300nm.	We have followed USP monograph for testing of assay of drug substance as well as impurities. USP monograph specifies 300nm for assay testing of drug substance while 220nm for impurities testing in drug substance.
Scientific justification for using reference / working standard having a potency of 73.91% for the analysis of commercial batches.	The potency is on as is basis of Meropenem for injection, which has been standardized against the primary standard (Meropenem base) and is used as working standard in routine testing.
Scientific justification for having a master formulation containing 707mg of meropenem trihydrate blended with sodium carbonate which is equivalent to 500mg meropenem.	Below is calculation of fill weight if Meropenem 1gm: As per attached COA, Average water content = 10.5% Average sodium bicarbonate content = 18.5% By adding both contents, 10.5 + 18.5 = 29%

	By subtracting both contents, 100% - 29% = 71% For Merem 1g = $\frac{1000 \times 100}{71}$ = 1408.45mg/vial
Provision of details including batch number, expiry date and name of manufacturer of the innovator product along with pharmaceutical equivalence was performed.	Product Name: Merrem for injection 1g Batch Number: ZEF0068 Manufacturing Date: 09-2015 Expiry Date: 08-2019 Name of manufacturer is not mentioned.
Scientific justification why complete tests as mentioned in USP monograph were not performed in pharmaceutical equivalence studies.	All tests that are mentioned in USP could not perform during pharmaceutical equivalence due to limited quantity of innovator sample. Therefore, we have included only all major test while performing pharmaceutical equivalence.
Scientific justification for not performing compatibility studies of the drug product with the recommended diluent.	Compatibility studies of Merem were performed but it was not made part of dossier during submission. Detailed compatibility studies of Merem against its innovator i.e. Merrem was performed with all its recommended diluents. Study results are also provided
Scientific justification for not performing the test of sodium content and loss on drying for the analysis of commercial batches of the drug product.	In 2017, we did not have Atomic Absorption there test of content of sodium is not part of specifications of product. Moreover we have now revised specification and LOD and content of sodium has been incorporated in revised specifications.
Scientific justification for using an entirely different formula for calculation of assay results of commercial batches from that specified in USP monograph.	Formula of content of drug product is elaborated with context to standard and sample preparation procedure which has now been updated as per USP format. Copy of revised test method & USP monograph is also provided.
Scientific justification for not performing test of content of sodium, completeness and clarity of solution, loss on drying and sterility test during the stability studies of the product.	Testing parameters like sodium contents, loss on drying has not performed because they can be monitored indirectly. Justifications given as below: • Sodium is the part of Sodium carbonate which in this mixture of meropenem for injection acts as a buffer and controls the pH of the mixture. A pH drift will depict the change in buffer contents, as Sodium being metal does not degrade in ordinary conditions. • Loss on drying has a direct impact on the active ingredient stability/degradation. Assay determination depicts the impact cause by this parameter. • In physical check of stability samples we use to perform this test after reconstitution with prescribed amount of water but this test was not separately mentioned in stability data. As for as sterility is concerned it was not part of stability testing. We have revised our stability protocols and included all critical Quality attributes in stability testing and implemented for onward stability testing.

Scientific justification how three batches have been manufactured using 5Kg containers while each batch required 5.4Kg drug substance.	During interpretation of data from BMR while preparation of dossier 5.4kg has been mistakenly considered batch size by regulatory person. Actual batch size as stated in BMR is 5.0kg. Moreover meropenem as ready to fill powder is imported in container of 5.0kg.
Evidence of purchase of atomic absorption spectrophotometer including commercial invoice and Installation Qualification (IQ) and Operational Qualification (OQ) of atomic absorption.	Field Service Report dated 25-10-2019 is provided from Rays Technologies. In report it is mentioned that IQ, OQ and PQ of the instrument is perfomed and the instrument is handed over to user in working condition. However no details of the equipment / instrument is provide.
Submission of fee for pre-registration changes in the drug product specifications.	Firm has submitted fee 7500/- dated 05-11-2021 for revision of specifications.
Keeping in view the above, the Board decided that the submitted stability study data is not acceptable and directed the manufacturer to either perform complete product development and stability studies or submit the aforementioned data as per USP specifications and submit data accordingly. The Board further directed the manufacturer to comply USP Specifications for already registered drug products.	Firm has not submitted product development and stability study data of new batches in which the development and testing is carried out as per USP specifications from initial time point.

Decision of 313rd meeting of Registration Board:

Registration Board deliberated that the commercial batches manufactured by the manufacturer i.e. Global Pharmaceuticals was not developed and tested as per the USP monograph. Keeping in view the USP monograph, public assessment report of the innovator product and the data submitted by the firm, the Board decided to defer the case and advised the manufacturer to perform product development studies keeping in view the innovator product and product testing and stability studies by complying USP monograph and submit data upon completion of 6 months stability studies.

Submission by the firm:

The firm on 13-01-2022 submitted new response against the decision of 312nd meeting of Registration Board instead of complying the decision of 313rd meeting of Registration Board.

In the new submission, the firm has changed the source of drug substance from M/s Sterile India Pvt Ltd. India to M/s Shenzhen Haibin Pharmaceutical Co. Ltd China. Furthermore, the firm has submitted stability data of following new batches:

Batch No.	Batch size	Mfg date	Stability initiation date
21A243	3538 Vials	01-2021	03-02-2021
21E154	3538 Vials	05-2021	29-05-2021
21E155	3538 vials	05-2021	29-05-2021

Firm has submitted data which shows that the product testing has been conducted as per revised specs and calculation formula however firm has revised their specifications after 312nd meeting which was conducted on 14-16 Septeber 2021 and the revised specifications were considered by the Board in its 313rd meeting held on 16-18 November 2021.

Decision of 316th meeting of Registration Board:

Deferred for submission of complete data of drug substance as well as drug product as per revised specifications in module-2 and module-3 as per the Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.

Response by the firm:

Now the firm has submitted following data of three newly manufactured batches. Firm has also changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.

Firm has also submitted module 2 and module 3 along with stability study data, the details of which are as under:

STABILITY STUDY DATA			
Manufacturer of API	M/s CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China.		
API Lot No.	682107003		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22A335	21M270	21M271
Batch Size	3709 vials	3709 vials	3709 vials
Manufacturing Date	01-2022	12-2021	12-2021
Date of Initiation	10-01-2022	30-12-2021	30-12-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. Inspection date: 14th March, 2019 The report shows that: • The HPLC software is 21 CFR compliant. • The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. HE20180065) issued by China Food and Drugs Administration dated 17-08-2018. The certificate is valid till 16-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice cleared dated 13-09-2021 specifying import of 200Kg Meropenem for Batch No. 682107002 and 682107003. The commercial invoice is attested by AD (I&E) DRAP field office.

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Firm has changed the source of drug substance to CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co. Ltd. No. 88, Yangzi Road, Shijiazhuang Economic and Technological Development Zone, Hebei Province PR. China. **Firm has not submitted any fee for change of source as well as submission of stability study data of new batches**.
- GMP certificate / insepection report of the contract manufacturer is not available within last three years.

Approved.

- **Registration Board decided that registration letter will be issued after submission of applicable fee that is 75,000/- for change of source as well as submission of stability study data of new batches as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**

253.	Name, address of Applicant / Marketing Authorization Holder	**M/s Sami Pharmaceuticals, F-95, SITE, Karachi.**
	Name, address of Manufacturing site.	M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8323 dated 15-03-2021
	Details of fee submitted	PKR 50,000/-: dated 08.01.2021
	The proposed proprietary name / brand name	**D-Tres oral 400 IU Drops**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each drop contains: Cholecalciferol (Vitamin D3) Ph. Eur….400 IU (10µg) Innovator Specs
	Pharmaceutical form of applied drug	Oral drops

	Pharmacotherapeutic Group of (API)	Vitamin D ATC code: A11CC05
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	10ml, 15 ml, 20 ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SAPVIT D3 Oral Drops Solution
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP Certificate issued date 11-08-2020
	Name and address of API manufacturer.	FERMENTA BIOTECH LIMITED Plot No. Z-109 B & C, SEEZ II, Dahej Taluka – Vagra, Distt. Bharuch 392 130 Gujarat, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cholecalciferol is present in Ph. Eur. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances and specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5 ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence not performed due to the unavailability of the innovator sample, CDP is not applicable		
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		FERMENTA BIOTECH LIMITED, Plot NO. Z-109B & C, SEZ-II, DEHAJ, TAL_VAGRA, Dist. Bharuch, India		
API Lot No.		CLC0419047		
Description of Pack (Container closure system)		Glass bottle USP Type-III with dropper applicator		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		Lab-01	Lab-02	Lab-03
Batch Size		2000 ml	2000 ml	2000 ml
Manufacturing Date		Jan 2020	Jan 2020	Jan 2020
Date of Initiation		24-01-2020	24-01-2020	24-01-2020
No. of Batches		03		
Administrative Portion				
13.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted the relevant document.		
14.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 2062043 issued by Food and drug control administration valid till 17/06/2023		
15.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying import of 10 kg of Cholecalciferol (Batch # CLC0419047). (invoice # RV1002000056) attested by AD (I&E), Karachi dated 09/05/2020		
16.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
17.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted		
18.	Record of Digital data logger for temperature and humidity monitoring of	Submitted		

	stability chambers (real time and accelerated)	

Remarks OF Evaluator:

	Shortcomings	Reply of the firm
2.3.S.4.3	The drug product manufacturer has performed impurity and residual solvent testing in the drug substance. The firm did not perform the method validation/verification for the same	We performed assay method validation of the drug substance as per CTD requirement. Validation of Impurity and residual solvent testing is performed by drug substance manufacturer.
3.2.P.1	Justification/scientific rationale is required for addition of 20% overage along with submission of stability assay report of the latest time point	Some active pharmaceutical ingredients including several vitamins in certain dosage forms or packaging condition may be susceptible to degrade or deteriorate and may not remain their native form over the shelf life of product. Degradation or deterioration of vitamins is one of the major factors that lead manufacturer to require excess amount of vitamins in their products, to ensure the amount of the drug substance meets the requirement of 100% of the label claim amount throughout the shelf life of the product. (**Referred ANNEXURE –I** Pharmacopeial Forum Vol.42.42 (3) [May-June 2016], Stimuli to the Revision Process, Factors to Consider in Setting Adequate Overages of Vitamins and Minerals in Dietary Supplements). Outside the U.S., many jurisdictions recognize the minimum value as 80-90% of label claim. For example, the Danish and Korean authorities allow a shelf-life minimum of 80% of label claim for added vitamins and minerals, and the United Kingdom allows -50% for water soluble vitamins and minerals, and -30% for oil soluble vitamins. U.S.-designed products with inputs typically 10-50% higher than the label claim to meet 100% minimum requirement at end of shelf life can exceed upper specifications limits for non-U.S. countries with maximum overage limits. (**Referred ANNEXURE –II** Council for Responsible Nutrition-Docket No.FDA-2012-N-1210; Food labelling: Revision of the Nutrition and Supplement Facts Labels, Page No.27). For development of our product i.e. D-Tres 400 IU/Drop, 20% overage of cholecalciferol (vitamin D_3) was taken to compensate initial process loss followed by the expected loss in assay during stability studies. The initial test results and stability trending of our product shows about 3% initial process loss and 3 to 4% loss in assay under accelerated condition as well as in long term condition. Moreover, 20% overage was not fixed, as mentioned above, it is a global practice to take overages for vitamins during development studies. However, after evaluation of the stability data and stability study report of the latest time period i.e. 18 months it is observed that our product is stable and no further loss in assay observed after 18 month.

<table>
<tr><td></td><td></td><td>(Referred ANNEXURE –III Stability trending of our product i.e. D-Tres 400 IU/Drop).
Therefore, based on the above data and stability trend analysis of our product, we recommend to reduce the overage of cholecalciferol (vitamin D_3) from 20% to 5%. However, this 5% overage will not effect safety and efficacy of product, because this 5% overage is well within the tolerable upper intake levels recommend for Vitamin D (Referred ANNEXURE –IV National Institutes of Health).</td></tr>
<tr><td>3.2.P.2.1</td><td>The theoretical dispensed weight of cholecalciferol is 12,000 IU per ml (without overages), while it is 14,400 IU per ml in the reference product. Justification is required</td><td>We have developed our product D-Tres 400 IU/Drop against the reference listed drug (RLD) i.e. Sapvit-D3 14,400 IU/ml Oral Drops, Solution (400 IU/ Drop marketed by M/s. Fresenius Kabi Limited UK.
The literate data of RLD shows that one ml of RLD is equivalent to 36 drops. 1 drop of RLD is equivalent to 400 IU (10 µg) cholecalciferol (vitamin D_3). As 0.025 µg Cholecalciferol is equivalent to 1 IU Cholecalciferol so, 360 µg is equivalent to 14,400 IU cholecalciferol (vitamin D_3) for 36 drops which is equivalent to one ml
Furthermore, please note that One ml of our product contains 30 drops. However, the label claim of Cholecalciferol per drop is same as of the RLD i.e. One drop of our product is equivalent to 400 IU (10 µg) cholecalciferol (vitamin D_3). As 0.025 µg Cholecalciferol is equivalent to 1 IU Cholecalciferol so, 300 µg is equivalent to 12,000 IU cholecalciferol (vitamin D_3) for 30 drops which is equivalent to one ml.
(Referred ANNEXURE –V Package leaflet: Information for the user, Sapvit-D3 14,400 IU/ml Oral Drops, Solution (400 IU/ Drop), page no.5)
The comparative analysis of D-Tres 400 IU/Drop against Sapvit-D3 14,400 IU/ml Oral Drops, Solution (400 IU/ Drop) is mention below
<table>
<tr><th>SAMI's Product
D-Tres 400IU/Drop</th><th>RLD
Sapvit-D3 14,400 IU/ml Oral D
Solution (400 IU/ Drop)</th></tr>
<tr><td>1ml contains 30 drops</td><td>1ml contains 36 drops</td></tr>
<tr><td>1drop contains 400 IU (10 µg) cholecalciferol (vitamin D_3)</td><td>1drop contains 400 IU (10 µg) cholecalciferol (vitamin D_3)</td></tr>
<tr><td>30 drops =12,000 IU (300 µg)</td><td>36 drops =14,400 IU (360 µg)</td></tr>
</table>
Based on the above details we can conclude that our product contain the same labelled amount of cholecalciferol as of the reference listed drug (RLD) i.e. 400 IU (10 µg) cholecalciferol (vitamin D_3) per drop</td></tr>
<tr><td>3.2.P.2.2.1</td><td>You have not performed pharmaceutical equivalence. Justification is required</td><td>The reference product is not available in Pakistan. We have tried to arrange it from the country of origin but unfortunately not succeeded.
Please note that the dosage form is oral solution for which BE studies also exempted (See reference guideline of FDA "Guidance for Industry, Bioavailability and Bioequivalence Studies Submitted in NDAs or INDs",
Solutions and Other Solubilized Dosage Forms
"For oral solutions, elixirs, syrups, tinctures, or other solubilized forms, in vivo BA and/or BE are generally self-evident and a requirement of in vivo data for a product may</td></tr>
</table>

<table>
<tr><td></td><td></td><td>be waived (21 CFR 320.22(b)(3)). In such instances, the applicant would be deemed to have complied with and fulfilled any requirement for in vivo data. Although a comparative study is not necessary, characterization of the pharmacokinetics of the drug is required (21 CFR 314.50(d)(3)). In addition, in vivo BE studies that compare different solution formulations are waived based on the assumptions that release of drug substance from the drug product is self-evident and that the solutions do not contain any excipients that significantly affect drug absorption. However, there are certain excipients that may alter the BA (e.g., sorbitol may reduce the BA of drugs, and vitamin E may enhance the BA) in amounts sometimes used in oral liquid dosage forms. In this case, evaluation of in vivo BA and/or BE may be required".
Please also note that our formulation is similar to the innovator in the following,
1. API: Same as that of Reference listed drug.
2. Dosage form: Same as that of Reference listed drug.
3. Indication: Same as that of Reference listed drug.
4. Excipients: Same as that of Reference listed drug .
5. Label claim: Same as that of Reference listed drug.
However, for assay and other chemical / microbiological attributes, we have tested the product according to the general monograph of pharmacopeia and complied.</td></tr>
<tr><td>3.2.P.4.1</td><td>The coconut oil is available in pharmacopeia. The drug product manufacturer has claimed in-house specifications; and did not perform the chromium test.
Justification is required</td><td>Yes, it is available in BP and testing was done according to the BP specifications. As per our procedure for excipients, we do not mention the material reference on the specifications.
The missing Chromium test performed and incorporated in our specifications.</td></tr>
<tr><td>3.2.P.5.1</td><td>Pharmacopeial monograph for the Cholecalciferol solution has the different vehicle / solvent from the innovator and our formulation is based on reference listed drug (RLD), which using only API and medium chain triglyceride (coconut oil). Therefore we cannot claim it Pharmacopeial and claim it as</td><td>Pharmacopeial monograph for the Cholecalciferol solution has the different vehicle / solvent from the innovator and our formulation is based on reference listed drug (RLD), which using only API and medium chain triglyceride (coconut oil). Therefore we cannot claim it Pharmacopeial and claim it as Innovator specifications.
Please see below the difference of the formulations
<table>
<tr><th>Pharmacopeia</th><th>Innovator</th><th>SAMI</th></tr>
<tr><td>edible vegetable oil</td><td>Medium chai triglyceride (Fractionated coconut oil)</td><td>Medium chai triglyceride (Fractionated coconut oil)</td></tr>
<tr><td>Polysorbate 80 or</td><td>-</td><td>-</td></tr>
<tr><td>Propylene Glycol</td><td>-</td><td>-</td></tr>
</table>
</td></tr>
</table>

	Innovator specifications.	
3.2.P.5.1	Filled volume/weight variation test has not been performed	We have already performed filled volume test but not submitted to you as this is the part of our in-process testing. Please find attached the in-process report for your ready reference
3.2.P.5.2	The applied drug product is available in pharmacopeia. The drug product manufacturer has validated their own testing method for the assay. Justification is required	As already mentioned in 3.2.P.5.1, the product available in pharmacopeia has different vehicle / solvent from the innovator. Our formulation is based on innovator. Therefore, we use the in-house developed, validated method.
3.2.P.5.6	The drug product manufacturer has performed additional tests (other than those mentioned in the pharmacopeia). The specifications for such tests shall be justified	Pharmacopoeia tests are the minimum requirement. As per general pharmacopoeial monograph, additional tests can be performed according to the nature of substance and considering the formulation.
3.2.P.8.3	You shall clarify whether the stability was conducted placing the bottles upright or inverted	The product is placed in inverted position.

Decision of 316th meeting of Registration Board:

Deferred for following:

- Pharmaceutical equivalence studies of the applied product along with innovator / reference product.
- Evidence of approval of applied formulation as a pharmaceutical drug product in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.
- Scientific justification that the applied formulation is equivalent to the innovator's product in terms of cholecalciferol contents per ml as well as per drop.

Response by the firm:

Sr. No	Reason for deferment	Response by the firm
1.	Pharmaceutical equivalence studies of the applied product along with innovator / reference product.	We have developed our product D-Tres 400 IU/Drop against the reference listed drug (RLD) i.e. Sapvit-D3 Oral Drops solution (400 IU/ Drop) marketed by M/s. Fresenius Kabi Limited UK. However, due to unavailability of the reference product, pharmaceutical Equivalence has been performed against

		Baby Ddrops 400IU per drop - which is similar to our formulation *Reference Document attached* https://health-products.canada.ca/lnhpd-bdpsnh/index-eng.jsp
2.	Evidence of approval of applied formulation as a pharmaceutical drug product in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.	**Sapvit-D3 400 IU/drop oral drops, solution** **Qualitative and Quantitative Composition** One ml (= 36 drops) contains: 14,400 IU (360 microgram) cholecalciferol (vitamin D3) One drop = 400 IU (10 microgram) cholecalciferol (vitamin D3) **Health Products Regulatory Authority (HPRA) Ireland**
3.	Scientific justification that the applied formulation is equivalent to the innovator's product in terms of cholecalciferol contents per ml as well as per drop.	SmPC of the Innovator product clearly mentions that 1 drop is equivalent to 400IU The Leaflet & SmPC of the Innovator product SAPVIT D3 mentions the following dosage guidelines: **The Method of administration mentions that the best way to take** Sapvit-D3 oral drops is to add them drop by drop into the mouth or, if necessary, administer with a spoon and some liquid. **Prevention of vitamin D deficiency:** The usual daily dose is: For newborns, infants and children from the second week of life to the age of 3 years: between 1-2 drops For children aged 4 years and above and adolescents: between 1-3 drops For adults aged 19 to 70 years: between 1-4 drops For elderly people aged above 70 years: between 2-4 drops **Treatment of rickets** The total amount of required vitamin D depends on the severity of the disease. In existing rickets, treatment is started with a preparation with a higher concentration of vitamin D for the initial treatment. Subsequently, the usual dose is between 2 to 12 drops of Sapvit-D3 daily. **Treatment of vitamin D deficiency** The usual daily dose is: For children and adolescents: 5 drops daily for 6 weeks, then between 1-3 drops daily For adults aged 19 to 70 years and elderly people aged above 70 years: 15 drops daily for 8 weeks, then between 3-5 drops daily **Adjunct to osteoporosis treatment of patients who are at risk of vitamin D deficiency**

		The usual daily dose is: For adults aged 19 years and above: between 2-4 drops daily or between 14-26 drops weekly. **Based on the dosage guidelines for multiple conditions as mentioned above, SAPVIT D3 is available in 12.5 ml (corresponding to 450 drops) or 25 ml (corresponding to 900 drops), whereas our product D-Tres Oral Drops applied pack size is 10ml.** The literate data of RLD shows that one ml of RLD is equivalent to 36 drops. 1 drop of RLD is equivalent to 400 IU (10 µg) cholecalciferol (vitamin D_3). As 0.025 µg Cholecalciferol is equivalent to 1 IU Cholecalciferol so, 360 µg is equivalent to 14,400 IU cholecalciferol (vitamin D_3) for 36 drops which is equivalent to one ml. Furthermore, please note that One ml of our product contains 30 drops. However, the label claim of Cholecalciferol per drop is same as of the RLD i.e. One drop of our product is equivalent to 400 IU (10 µg) cholecalciferol (vitamin D_3). As 0.025 µg Cholecalciferol is equivalent to 1 IU Cholecalciferol so, 300 µg is equivalent to 12,000 IU cholecalciferol (vitamin D_3) for 30 drops which is equivalent to one ml. Finally, the firm summarized that their per drop content is same as that of the reference product.

Decision: Deferred for following points:

- **Clarification since the concentration of Cholecaliferole per mL of the innovator's product is 360ug (Eq. to 14,440IU) while the applied product contains 30ug (12,000IU) per mL.**
- **Confirmation of RDA value for Cholecalciferole.**

254.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Aspin Pharma (Pvt) Ltd. Plot No. 10 & 25 Sector 20, Korangi Industrial Area Karachi.**
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)

		Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 21-01-2021 is submitted.
	GMP status of the firm	**Stallion Pharmaceuticals:** Firm has submitted GMP certificate issued on the basis of inspection dated 22-09-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000783 of M/s Stallion Pharma Islamabad dated 08-02-2016 specifying dry powder injection Vial (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7086: 03-03-2021
	Details of fee submitted	PKR 70,000/-: 19-01-2021
	The proposed proprietary name / brand name	**ASPINEM 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White or almost white, hygroscopic, crystalline, powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 500mg Injection of Pfizer Pakistan Ltd.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.
API Lot No.	1705205135 1705205096 1705203623
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T7003	T7004	T7005
Batch Size	7800 vials	7800 vials	7570 vials
Manufacturing Date	09-2017	10-2017	11-2017
Date of Initiation	25-09-2017	13-11-2017	16-11-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

- Firm has submitted fee 70,000 for the application of contract manufacturing

Shortcomings communicated	**Response by the firm**
Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted copy of analytical method of drug substance from the drug product manufacturer. The analytical method is issued on 20-07-2021.
Submit data in section 3.2.S.4.3 as per the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be	Firm has submitted report of verification studies of the analytical method of drug substance. However, the verification studies were conducted on 21-01-2021 while the analytical method of drug substance was issued by the drug product manufacturer on 20-07-2021.

submitted". Further justify how the analysis of drug substance was conducted without performing verification studies of the analytical method of drug substance.	
Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification)".	Firm has submitted COA of the drug substance generated by drug product manufacturer only, while the COA of drug substance manufacturer is not submitted.
Submit COA of reference standard / working standard including source and lot number which is actually used in the testing of drug substance and drug product.	Firm has submitted COA of working standard from drug substance manufacturer which has been standardized against USP reference standard. However drug product manufacturer is using working standard of meropenem Batch No. SI/MPM/00060120 manufactured by M/s Sterile India.
Justify the master formulation containing 570mg of meropenem trihydrate for manufacturing of 500mg meropenem for injection, since the drug substance contains meropenem blended with 15.10 to 16.50% w/w of sodium carbonate.	Firm has submitted calculation to justify the filled weight. As per calculations submitted by the firm the weight 570mg per vial is calculated on theoretical basis considering that the drug substance has 100% assay, while the actual dispensing is to be made on the basis of actual % assay of the meropenem.
Justify the use of 5% overage in the formulation, since the justification submitted in this regard is not supported by any guidelines.	We hereby justify that in development stage we added 5% extra meropenem sterile powder for injection in initial batches. After completion of stability study degradation is no more than 2 – 3% within the limit assay range is 90 – 120% so no more 5% meropenem sterile powder for injection is added.
Submit results of compatibility studies in section 3.2.P.2.6.	Firm has submitted result of compatibility studies of the drug product with WFI.
Justify how the time and temperature of sterilization cycle is directly selected without any protocols for its validation.	Firm has submitted summary report of autoclave machine re qualification instead of providing justification.
Provide detailed method of sample stock solution preparation instead of mentioning the general statement "Constitute a container of Meropenem for Injection with a volume of water, corresponding to the quantity of solvent specified in the labelling".	Firm has not submitted complete method of analysis of the drug product in which the method of sample solution preparation is explained.
Justify why the formula for calculation of assay contents of meropenem is different than that mentioned in USP monograph.	Firm has submitted that we are using potency of working standard as percentage. USP taking the potency in mg/mg which is

	converted into percentage by multiplying this ratio with 100. Firm has submitted calculation to justify that their formula is equivalent to USP. However, the USP formula used by the firm is different from that specified in USP.
Analytical method verification studies have not been conducted and evaluated in the light of USP general chapters and ICH guidelines.	Firm has submitted verification studies of the analytical method dated 21-01-2021, while the analytical method of the drug product was revised and updated on 12-07-2021.
Justify why the drug product specifications does not contain the test for sodium contents as recommended by USP.	In Meropenem trihydrate injection label claim is as meropenem while trihydrate and sodium considered as impurity. We are verifying the meropenem by HPLC and due to unavailability of the atomic absorption we were verifying the sodium content by titration method. Moreover, for verification purpose, we analysed sodium content from PCSI and Citi Pharma with atomic absorption. And now we have atomic absorption in our facility and we have changed our SOP accordingly and now we are conducting each and every analysis of sodium content in our facility as per USP monograph.
Justify the test of accuracy in analytical method validation without specifying the concentrations of the solution which are analysed for accuracy. Further justify the use of solutions having low, medium, and high concentration of sample without specifying their exact concentration. Such words are not recommended by any scientific guidelines.	Firm has submitted that we had performed the accuracy by making a concentration of standard preparation and three concentrations. The concentrations used by the firm for accuracy test is 0.16mg/ml, 0.20mg/ml and 0.24mg/ml. As per the analytical method the standard solution concentration is 0.11mg/ml and the concentration used by the firm to study accuracy does not include the said concentration.
Linearity and range have been studied from 70% to 120% of the solution wherein the area under curve for 100% solution was 4691449 while in accuracy studies in the same method none of the solution (either low, medium or high concentration) achieved such area although the concentration of the solution is expected to be the same. Justification is required in this regard.	Two different samples were prepared for linearity and accuracy parameter of analytical method verification, for linearity parameter from the first dilution 6 further second dilutions 70%, 80%, 90%, 100%, 110% and 120% were prepared while in accuracy 3 further second dilutions low, medium and high were prepared. Because the weights of the sample are different in linearity and accuracy parameters that's why the area achieved is different for both parameters.
In linearity studies the area under curve for 100% solution was 4691449, while in stability studies the area under curve of the sample solution having exactly same concentration is reported to be 11769485. Justification is required in this regard how such huge difference in area under the curve can exist in the analysis and how this method can be considered reliable and verified.	In linearity the sample solution preparation is different from the sample preparation of finished product. In linearity a concentration of standard taken to prepare first dilution then make second dilution by taking 7ml, 8ml, 9ml, 10ml, 11ml, 12ml from the first dilution, second dilution of 10ml is considered as 100% concentration while in finished good the dilution contain 100mg of sample that's

	why area under curve for 100% solution is different from the area of 100mg in finished product.
The analytical method verification studies have been conducted in January 2021 while the batches were manufactured in 2017. Justification is required in this regard.	In 2017, we had completed analytical method verification by performing three parameters which are linearity, system suitability and specificity while when we submit the CTD dossier we came to know the DRAP requirement of accuracy and repeatability, then we had complete the analytical method verification by performing five parameters which are linearity, system suitability, specificity accuracy and repeatability.
Justify the limit of sodium content in the in house generated COA of drug substance, in which limit of sodium content is taken as 6.0% to 9.3% and the drug substance was passed on the basis of results of 9.12%, while the drug substance manufacturer specifies the limit of sodium content as 6.56% to 7.20%.	In past we were doing sodium content analysis by titration method (due to unavailability of AAS) the result was 9.12% limit of sodium content is 6.0% - 9.3% while the drug substance manufacturer specifies the sodium content as 6.65 to 7.20%. Now we are doing sodium content with AAS according to USP.
As per the submitted results of sodium content in meropenem injection by CITI Pharma, the results of % sodium content is 7.867%, while USP specifies the acceptance criteria to be 80%–120% of the labeled amount of sodium. Justify how your results complies USP specifications keeping in view the labelled amount of sodium in your product.	Firm has not submitted any justification
Justify the use of commercial lot of meropenem for injection as working standard since USP recommends that reference standard should be pure meropenem trihydrate.	The assay of meropenem trihydrate USP reference standard lot# J0K434, is 87.3% meropenem. Similarly by comparing with reference standard we prepare our meropenem trihydrate working standard in which 82.12% is meropenem present. Actually the material used in USP Reference standard and the working standard is the same as meropenem trihydrate because the product label claim is meropenem, therefore we have to calculate the assay against the purity of material as meropenem which is 87.3% in USP Reference standard and 82.12% in working standard.
Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Firm has not submitted details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Further documents confirming import of these relevant batches are also required.
Provide data of stability batches properly arranged and supported by respective documents including analytical report / COA, raw data sheet and respective chromatograms separately for each time point, since the	Firm has not yet submitted stability study data in proper sequence with COA for each time point, raw data sheets and chromatograms. Raw data sheets are not submitted. Further the calculation formula used for the calculation of

submitted chromatograms and analytical reports are without any proper sequence.	assay result is also different from USP as well as the method of sample and standard solution preparation.
Provide Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	No response submitted by the firm
Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	No response submitted by the firm

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of differential fee as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
- Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.
- Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.
- Scientific justification for use of 5% overage in the formulation.
- Submission of complete protocols of process validation studies of the drug product.
- Submission of detailed method of analysis of the drug product with details of sample solution preparation.
- Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.
- Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
- Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.
- Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.

Response by the firm:

Sr. No	Reason for deferment	Response by the firm
1.	Submission of differential fee as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has submitted differential fee 5,000/- vide slip number 551237597908 dated 20-05-2022.
2.	Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.	Firm has submitted COA of relevant batch of drug substance generated by drug substance manufacturer.
3.	Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.	This firm has submitted that the assay of Meropenem Trihydrate USP reference standard lot # J0k434 is 87.3%. Therefore, we used sterile India material as working Standard having potency 82.02% by using standardization procedure with USP reference standard. Material used for batch

		manufacturing is from Aurobindo China and working standard prepared is of Sterile India having Potency 82.02% COA's for Reference standard & working standard along with standardization procedure is submitted by the firm.
4.	Scientific justification for use of 5% overage in the formulation.	Firm has submitted that an overage is used to cover losses during manufacturing. Initially we used extra 5% of Meropenem to deliver our product with exact quantity of API in injection, the idea behind was to deliver exact quantity of the active substance. After that our product was stable throughout its shelf life so no need to add extra 5% overage. In general, use of an overage of a drug substance to compensate for degradation during manufacture or a product's shelf life, or to extend shelf life, is discouraged. Overages are nothing but the extra quantity of material taken, which is lost during process stage.ICH Q8 guide line, provide a structured way to define product critical quality attributes. We are not using any overage in the manufacturing of Meropenem injection
5.	Submission of complete protocols of process validation studies of the drug product.	Firm has submitted general protocols for process validation. **Firm has not submitted specific protocols for the process validation of applied product.**
6.	Submission of detailed method of analysis of the drug product with details of sample solution preparation.	Firm has submitted detailed method of analysis of the drug product, **However in the submitted method, sample solution preparation method is still not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions.** Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.
7.	Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.	Firm has submitted that they are using the potency of working standard as percentage. USP taking the Potency into mg/mg which is covered into percentage multiplying the ratio with 100 so there is no difference between the USP formula & our standard operating formula further more we have amended our SOP with respect to the formula given in USP. **However, the newly used calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.**

		The new formula is also not exactly as per USP monograph.
8.	Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has now added sodium content test in their specifications. Firm has also submitted fee 7,500/- vide slip number 212267176 dated 20-05-2022. **However, no data regarding the sodium content testing during stability studies is provided.**
9.	Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.	Firm has not justified the previous validation reports, instead the firm has submitted new report in which the analysis is carried out on July 2022. The new report was performed in line with ICH recommendations.
10.	Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.	Firm has submitted data in section 3.2.P.8.3. The evaluation os submitted data is as under:

Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
Documents for the procurement of API with approval from DRAP (in case of import).	**1705205135, 1705205096:** Firm has submitted copy of commercial invoice cleared dated 19-10-2017 specifying import of 20Kg meropenem for lot number 1705205135, 1705205096. The invoice is cleared by AD (I&E) DRAP. **1705203623:** Firm has submitted copy of commercial invoice cleared dated 12-09-2017 specifying import of 15Kg meropenem for lot number 1705203623. The invoice is cleared by AD (I&E) DRAP.
Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record of product testing including HPLC chromatogram and raw data sheets
Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted

	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for stability chambers for accelerated and real time stability study.

Decision: Deferred for following:

- **Clarification for use of 5% overage in sterile products and specifications of the manufactured products in the light of approved specifications and pharmacopoeial monographs.**
- **Capacity assessment of manufacturing and testing facility of M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.**
- **Submission of specific protocols for the process validation of applied product.**
- **Submission of preparation sample solution is required since it is not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions. Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.**
- **Clarification regarding use of formula which is different from the formula as recommended by USP for calculation of assay.**

255.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Aspin Pharma (Pvt) Ltd. Plot No. 10 & 25 Sector 20, Korangi Industrial Area Karachi.**
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 21-01-2021 is submitted.
	GMP status of the firm	**Stallion Pharmaceuticals:** Firm has submitted GMP certificate issued on the basis of inspection dated 22-09-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000783 of M/s Stallion Pharma Islamabad dated 08-02-2016 specifying dry powder injection Vial (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7087: 03-03-2021
	Details of fee submitted	PKR 70,000/-: 19-01-2021

	The proposed proprietary name / brand name	**ASPINEM 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White or almost white, hygroscopic, crystalline, powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.		
API Lot No.	1705205135 1705205096 1705203623		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	U7003	U7004	U7005
Batch Size	3900 vials	7600 vials	3780 vials
Manufacturing Date	09-2017	10-2017	11-2017
Date of Initiation	04-10-2017	14-11-2017	17-11-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

- Firm has submitted fee 70,000 for the application of contract manufacturing

Shortcomings communicated	**Response by the firm**
Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted copy of analytical method of drug substance from the drug product manufacturer. The analytical method is issued on 20-07-2021.
Submit data in section 3.2.S.4.3 as per the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted". Further justify how the analysis of drug substance was conducted without performing verification studies of the analytical method of drug substance.	Firm has submitted report of verification studies of the analytical method of drug substance. However, the verification studies were conducted on 21-01-2021 while the analytical method of drug substance was issued by the drug product manufacturer on 20-07-2021.
Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification)".	Firm has submitted COA of the drug substance generated by drug product manufacturer only, while the COA of drug substance manufacturer is not submitted.

Submit COA of reference standard / working standard including source and lot number which is actually used in the testing of drug substance and drug product.	Firm has submitted COA of working standard from drug substance manufacturer which has been standardized against USP reference standard. However drug product manufacturer is using working standard of meropenem Batch No. SI/MPM/00060120 manufactured by M/s Sterile India.
Justify the master formulation containing 1140mg of meropenem trihydrate for manufacturing of 1g meropenem for injection, since the drug substance contains meropenem blended with 15.10 to 16.50% w/w of sodium carbonate.	Firm has submitted calculation to justify the filled weight. As per calculations submitted by the firm the weight 1140mg per vial is calculated on theoretical basis considering that the drug substance has 100% assay, while the actual dispensing is to be made on the basis of actual % assay of the meropenem.
Justify the use of 5% overage in the formulation, since the justification submitted in this regard is not supported by any guidelines.	We hereby justify that in development stage we added 5% extra meropenem sterile powder for injection in initial batches. After completion of stability study degradation is no more than 2 – 3% within the limit assay range is 90 – 120% so no more 5% meropenem sterile powder for injection is added.
Submit results of compatibility studies in section 3.2.P.2.6.	Firm has submitted result of compatibility studies of the drug product with WFI.
Justify how the time and temperature of sterilization cycle is directly selected without any protocols for its validation.	Firm has submitted summary report of autoclave machine re qualification instead of providing justification.
Provide detailed method of sample stock solution preparation instead of mentioning the general statement "Constitute a container of Meropenem for Injection with a volume of water, corresponding to the quantity of solvent specified in the labelling".	Firm has not submitted complete method of analysis of the drug product in which the method of sample solution preparation is explained.
Justify why the formula for calculation of assay contents of meropenem is different than that mentioned in USP monograph.	Firm has submitted that we are using potency of working standard as percentage. USP taking the potency in mg/mg which is converted into percentage by multiplying this ratio with 100. Firm has submitted calculation to justify that their formula is equivalent to USP. However, the USP formula used by the firm is different from that specified in USP.
Analytical method verification studies have not been conducted and evaluated in the light of USP general chapters and ICH guidelines.	Firm has submitted verification studies of the analytical method dated 21-01-2021, while the analytical method of the drug product was revised and updated on 12-07-2021.
Justify why the drug product specifications does not contain the test for sodium contents as recommended by USP.	In Meropenem trihydrate injection label claim is as meropenem while trihydrate and sodium considered as impurity. We are verifying the meropenem by HPLC and due to unavailability of the atomic absorption we were verifying the sodium content by titration method. Moreover, for verification purpose, we analysed sodium content from PCSI and Citi Pharma with atomic absorption. And now

	we have atomic absorption in our facility and we have changed our SOP accordingly and now we are conducting each and every analysis of sodium content in our facility as per USP monograph.
Justify the test of accuracy in analytical method validation without specifying the concentrations of the solution which are analysed for accuracy. Further justify the use of solutions having low, medium, and high concentration of sample without specifying their exact concentration. Such words are not recommended by any scientific guidelines.	Firm has submitted that we had performed the accuracy by making a concentration of standard preparation and three concentrations. The concentrations used by the firm for accuracy test is 0.16mg/ml, 0.20mg/ml and 0.24mg/ml. As per the analytical method the standard solution concentration is 0.11mg/ml and the concentration used by the firm to study accuracy does not include the said concentration.
Linearity and range have been studied from 70% to 120% of the solution wherein the area under curve for 100% solution was 4691449 while in accuracy studies in the same method none of the solution (either low, medium or high concentration) achieved such area although the concentration of the solution is expected to be the same. Justification is required in this regard.	Two different samples were prepared for linearity and accuracy parameter of analytical method verification, for linearity parameter from the first dilution 6 further second dilutions 70%, 80%, 90%, 100%, 110% and 120% were prepared while in accuracy 3 further second dilutions low, medium and high were prepared. Because the weights of the sample are different in linearity and accuracy parameters that's why the area achieved is different for both parameters.
In linearity studies the area under curve for 100% solution was 4691449, while in stability studies the area under curve of the sample solution having exactly same concentration is reported to be 11769485. Justification is required in this regard how such huge difference in area under the curve can exist in the analysis and how this method can be considered reliable and verified.	In linearity the sample solution preparation is different from the sample preparation of finished product. In linearity a concentration of standard taken to prepare first dilution then make second dilution by taking 7ml, 8ml, 9ml, 10ml, 11ml, 12ml from the first dilution, second dilution of 10ml is considered as 100% concentration while in finished good the dilution contain 100mg of sample that's why area under curve for 100% solution is different from the area of 100mg in finished product.
The analytical method verification studies have been conducted in January 2021 while the batches were manufactured in 2017. Justification is required in this regard.	In 2017, we had completed analytical method verification by performing three parameters which are linearity, system suitability and specificity while when we submit the CTD dossier we came to know the DRAP requirement of accuracy and repeatability, then we had complete the analytical method verification by performing five parameters which are linearity, system suitability, specificity accuracy and repeatability.
Justify the limit of sodium content in the in house generated COA of drug substance, in which limit of sodium content is taken as 6.0% to 9.3% and the drug substance was passed on the basis of results of 9.12%, while	In past we were doing sodium content analysis by titration method (due to unavailability of AAS) the result was 9.12% limit of sodium content is 6.0% - 9.3% while the drug substance manufacturer specifies the sodium content as 6.65 to 7.20%. Now we are

the drug substance manufacturer specifies the limit of sodium content as 6.56% to 7.20%.	doing sodium content with AAS according to USP.
As per the submitted results of sodium content in meropenem injection by CITI Pharma, the results of % sodium content is 7.867%, while USP specifies the acceptance criteria to be 80%–120% of the labeled amount of sodium. Justify how your results complies USP specifications keeping in view the labelled amount of sodium in your product.	Firm has not submitted any justification
Justify the use of commercial lot of meropenem for injection (batch number SI/MPM/00060120) manufactured by sterile India as working standard since USP recommends that reference standard should be pure meropenem trihydrate.	The assay of meropenem trihydrate USP reference standard lot# J0K434, is 87.3% meropenem. Similarly by comparing with reference standard we prepare our meropenem trihydrate working standard in which 82.12% is meropenem present. Actually the material used in USP Reference standard and the working standard is the same as meropenem trihydrate because the product label claim is meropenem, therefore we have to calculate the assay against the purity of material as meropenem which is 87.3% in USP Reference standard and 82.12% in working standard.
Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Firm has not submitted details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Further documents confirming import of these relevant batches are also required.
Provide data of stability batches properly arranged and supported by respective documents including analytical report / COA, raw data sheet and respective chromatograms separately for each time point, since the submitted chromatograms and analytical reports are without any proper sequence.	Firm has not yet submitted stability study data in proper sequence with COA for each time point, raw data sheets and chromatograms. Raw data sheets are not submitted. Further the calculation formula used for the calculation of assay result is also different from USP as well as the method of sample and standard solution preparation.
Provide Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	No response submitted by the firm
Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	No response submitted by the firm

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of differential fee as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.

- Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.
- Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.
- Scientific justification for use of 5% overage in the formulation.
- Submission of complete protocols of process validation studies of the drug product.
- Submission of detailed method of analysis of the drug product with details of sample solution preparation.
- Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.
- Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
- Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.
- Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.

Response by the firm:

Sr. No	Reason for deferment	Response by the firm
1.	Submission of differential fee as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has submitted differential fee 5,000/- vide slip number 658476562996 dated 20-05-2022.
2.	Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.	Firm has submitted COA of relevant batch of drug substance generated by drug substance manufacturer.
3.	Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.	This firm has submitted that the assay of Meropenem Trihydrate USP reference standard lot # J0k434 is 87.3%. Therefore, we used sterile India material as working Standard having potency 82.02% by using standardization procedure with USP reference standard. Material used for batch manufacturing is from Aurobindo China and working standard prepared is of Sterile India having Potency 82.02% COA's for Reference standard & working standard along with standardization procedure is submitted by the firm.
4.	Scientific justification for use of 5% overage in the formulation.	Firm has submitted that an overage is used to cover losses during manufacturing. Initially we used extra 5% of Meropenem to deliver our product with exact quantity of API in injection, the idea behind was to deliver exact quantity of the active substance. After that our product was stable throughout its shelf life so no need to add extra 5% overage.

		In general, use of an overage of a drug substance to compensate for degradation during manufacture or a product's shelf life, or to extend shelf life, is discouraged. Overages are nothing but the extra quantity of material taken, which is lost during process stage.ICH Q8 guide line, provide a structured way to define product critical quality attributes. We are not using any overage in the manufacturing of Meropenem injection
5.	Submission of complete protocols of process validation studies of the drug product.	Firm has submitted general protocols for process validation. **Firm has not submitted specific protocols for the process validation of applied product.**
6.	Submission of detailed method of analysis of the drug product with details of sample solution preparation.	Firm has submitted detailed method of analysis of the drug product, **However in the submitted method, sample solution preparation method is still not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions.** Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.
7.	Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.	Firm has submitted that they are using the potency of working standard as percentage. USP taking the Potency into mg/mg which is covered into percentage multiplying the ratio with 100 so there is no difference between the USP formula & our standard operating formula further more we have amended our SOP with respect to the formula given in USP. **However, the newly used calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard. The new formula is also not exactly as per USP monograph.**
8.	Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has now added sodium content test in their specifications. Firm has also submitted fee 7,500/- vide slip number 45752149528 dated 20-05-2022. **However, no data regarding the sodium content testing during stability studies is provided.**
9.	Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.	Firm has not justified the previous validation reports, instead the firm has submitted new report in which the analysis is carried out on July 2022. The new report was performed in line with ICH recommendations.

10.	Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.	Firm has submitted data in section 3.2.P.8.3. The evaluation os submitted data is as under:

Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
Documents for the procurement of API with approval from DRAP (in case of import).	**1705205135, 1705205096:** Firm has submitted copy of commercial invoice cleared dated 19-10-2017 specifying import of 20Kg meropenem for lot number 1705205135, 1705205096. The invoice is cleared by AD (I&E) DRAP. **1705203623:** Firm has submitted copy of commercial invoice cleared dated 12-09-2017 specifying import of 15Kg meropenem for lot number 1705203623. The invoice is cleared by AD (I&E) DRAP.
Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record of product testing including HPLC chromatogram and raw data sheets
Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for stability chambers for accelerated and real time stability study.

Decision: Deferred for following:

- **Clarification for use of 5% overage in sterile products and specifications of the manufactured products in the light of approved specifications and pharmacopoeial monographs.**
- **Capacity assessment of manufacturing and testing facility of M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.**
- **Submission of specific protocols for the process validation of applied product.**
- **Submission of preparation sample solution is required since it is not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions. Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.**

- **Clarification regarding use of formula which is different from the formula as recommended by USP for calculation of assay.**

256.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Genetics Pharmaceuticals (Pvt) Ltd. 539-A, Sundar Industrial Estate, Raiwind Road Lahore.**
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-10-2020 is submitted.
	GMP status of the firm	**Genetics Pharmaceuticals:** Firm has submitted copy of GMP certificate issued on the basis of inspection dated 29-03-2019. **Stallion Pharmaceuticals:** Firm has submitted GMP certificate issued on the basis of inspection dated 22-09-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000783 of M/s Stallion Pharma Islamabad dated 08-02-2016 specifying dry powder injection Vial (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13638: 20-05-2021
	Details of fee submitted	PKR 50,000/-: 30-11-2020
	The proposed proprietary name / brand name	**MEROTOL 500mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……500mg (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White or almost white, hygroscopic, crystalline, powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 500mg Injection of Pfizer Pakistan Ltd.

	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.		
API Lot No.	1705205135 1705205096 1705203623		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T7003	T7004	T7005
Batch Size	7800 vials	7800 vials	7570 vials
Manufacturing Date	09-2017	10-2017	11-2017
Date of Initiation	25-09-2017	13-11-2017	16-11-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**

Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 20th May 2021.	Firm has submitted copy of fee challan dated 28-10-2021 for 25,000/- vide slip number 08343787921
Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted copy of analytical method of drug substance from the drug product manufacturer. The analytical method is issued on 20-07-2021.
Submit data in section 3.2.S.4.3 as per the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted". Further justify how the analysis of drug substance was conducted without performing verification studies of the analytical method of drug substance.	Firm has submitted report of verification studies of the analytical method of drug substance. However, the verification studies were conducted on 21-01-2021 while the analytical method of drug substance was issued by the drug product manufacturer on 20-07-2021.
Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification)".	Firm has submitted COA of the drug substance generated by drug product manufacturer only, while the COA of drug substance manufacturer is not submitted.
Submit COA of reference standard / working standard including source and lot number which is actually used in the testing of drug substance and drug product.	Firm has submitted COA of working standard from drug substance manufacturer which has been standardized against USP reference standard. However drug product manufacturer is using working standard of meropenem Batch No. SI/MPM/00060120 manufactured by M/s Sterile India.
Justify the master formulation containing 570mg of meropenem trihydrate for manufacturing of 500mg meropenem for injection, since the drug substance contains meropenem blended with 15.10 to 16.50% w/w of sodium carbonate.	Firm has submitted calculation to justify the filled weight. As per calculations submitted by the firm the weight 570mg per vial is calculated on theoretical basis considering that the drug substance has 100% assay, while

	the actual dispensing is to be made on the basis of actual % assay of the meropenem.
Justify the use of 5% overage in the formulation, since the justification submitted in this regard is not supported by any guidelines.	We hereby justify that in development stage we added 5% extra meropenem sterile powder for injection in initial batches. After completion of stability study degradation is no more than 2 – 3% within the limit assay range is 90 – 120% so no more 5% meropenem sterile powder for injection is added.
Submit results of compatibility studies in section 3.2.P.2.6.	Firm has submitted result of compatibility studies of the drug product with WFI.
Justify how the time and temperature of sterilization cycle is directly selected without any protocols for its validation.	Firm has submitted summary report of autoclave machine re qualification instead of providing justification.
Provide detailed method of sample stock solution preparation instead of mentioning the general statement "Constitute a container of Meropenem for Injection with a volume of water, corresponding to the quantity of solvent specified in the labelling".	Firm has not submitted complete method of analysis of the drug product in which the method of sample solution preparation is explained.
Justify why the formula for calculation of assay contents of meropenem is different than that mentioned in USP monograph.	Firm has submitted that we are using potency of working standard as percentage. USP taking the potency in mg/mg which is converted into percentage by multiplying this ratio with 100. Firm has submitted calculation to justify that their formula is equivalent to USP. However, the USP formula used by the firm is different from that specified in USP.
Analytical method verification studies have not been conducted and evaluated in the light of USP general chapters and ICH guidelines.	Firm has submitted verification studies of the analytical method dated 21-01-2021, while the analytical method of the drug product was revised and updated on 12-07-2021.
Justify why the drug product specifications does not contain the test for sodium contents as recommended by USP.	In Meropenem trihydrate injection label claim is as meropenem while trihydrate and sodium considered as impurity. We are verifying the meropenem by HPLC and due to unavailability of the atomic absorption we were verifying the sodium content by titration method. Moreover, for verification purpose, we analysed sodium content from PCSI and Citi Pharma with atomic absorption. And now we have atomic absorption in our facility and we have changed our SOP accordingly and now we are conducting each and every analysis of sodium content in our facility as per USP monograph.
Justify the test of accuracy in analytical method validation without specifying the concentrations of the solution which are analysed for accuracy. Further justify the use of solutions having low, medium, and high concentration of sample without specifying their exact concentration. Such words are not recommended by any scientific guidelines.	Firm has submitted that we had performed the accuracy by making a concentration of standard preparation and three concentrations. The concentrations used by the firm for accuracy test is 0.16mg/ml, 0.20mg/ml and 0.24mg/ml. As per the analytical method the standard solution concentration is 0.11mg/ml and the

	concentration used by the firm to study accuracy does not include the said concentration.
Linearity and range have been studied from 70% to 120% of the solution wherein the area under curve for 100% solution was 4691449 while in accuracy studies in the same method none of the solution (either low, medium or high concentration) achieved such area although the concentration of the solution is expected to be the same. Justification is required in this regard.	Two different samples were prepared for linearity and accuracy parameter of analytical method verification, for linearity parameter from the first dilution 6 further second dilutions 70%, 80%, 90%, 100%, 110% and 120% were prepared while in accuracy 3 further second dilutions low, medium and high were prepared. Because the weights of the sample are different in linearity and accuracy parameters that's why the area achieved is different for both parameters.
In linearity studies the area under curve for 100% solution was 4691449, while in stability studies the area under curve of the sample solution having exactly same concentration is reported to be 11769485. Justification is required in this regard how such huge difference in area under the curve can exist in the analysis and how this method can be considered reliable and verified.	In linearity the sample solution preparation is different from the sample preparation of finished product. In linearity a concentration of standard taken to prepare first dilution then make second dilution by taking 7ml, 8ml, 9ml, 10ml, 11ml, 12ml from the first dilution, second dilution of 10ml is considered as 100% concentration while in finished good the dilution contain 100mg of sample that's why area under curve for 100% solution is different from the area of 100mg in finished product.
The analytical method verification studies have been conducted in January 2021 while the batches were manufactured in 2017. Justification is required in this regard.	In 2017, we had completed analytical method verification by performing three parameters which are linearity, system suitability and specificity while when we submit the CTD dossier we came to know the DRAP requirement of accuracy and repeatability, then we had complete the analytical method verification by performing five parameters which are linearity, system suitability, specificity accuracy and repeatability.
Justify the limit of sodium content in the in house generated COA of drug substance, in which limit of sodium content is taken as 6.0% to 9.3% and the drug substance was passed on the basis of results of 9.12%, while the drug substance manufacturer specifies the limit of sodium content as 6.56% to 7.20%.	In past we were doing sodium content analysis by titration method (due to unavailability of AAS) the result was 9.12% limit of sodium content is 6.0% - 9.3% while the drug substance manufacturer specifies the sodium content as 6.65 to 7.20%. Now we are doing sodium content with AAS according to USP.
As per the submitted results of sodium content in meropenem injection by CITI Pharma, the results of % sodium content is 7.867%, while USP specifies the acceptance criteria to be 80%–120% of the labeled amount of sodium. Justify how your results complies USP specifications keeping in view the labelled amount of sodium in your product.	Firm has not submitted any justification
Justify the use of commercial lot of meropenem for injection as working standard since USP recommends that reference	The assay of meropenem trihydrate USP reference standard lot# J0K434, is 87.3% meropenem. Similarly by comparing with

standard should be pure meropenem trihydrate.	reference standard we prepare our meropenem trihydrate working standard in which 82.12% is meropenem present. Actually the material used in USP Reference standard and the working standard is the same as meropenem trihydrate because the product label claim is meropenem, therefore we have to calculate the assay against the purity of material as meropenem which is 87.3% in USP Reference standard and 82.12% in working standard.
Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Firm has not submitted details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Further documents confirming import of these relevant batches are also required.
Provide data of stability batches properly arranged and supported by respective documents including analytical report / COA, raw data sheet and respective chromatograms separately for each time point, since the submitted chromatograms and analytical reports are without any proper sequence.	Firm has not yet submitted stability study data in proper sequence with COA for each time point, raw data sheets and chromatograms. Raw data sheets are not submitted. Further the calculation formula used for the calculation of assay result is also different from USP as well as the method of sample and standard solution preparation.
Provide Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	No response submitted by the firm
Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	No response submitted by the firm

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.
- Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.
- Scientific justification for use of 5% overage in the formulation.
- Submission of complete protocols of process validation studies of the drug product.
- Submission of detailed method of analysis of the drug product with details of sample solution preparation.
- Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.
- Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
- Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.

- Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.

Response by the firm:

Sr. No	Reason for deferment	Response by the firm
1.	Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.	Firm has submitted COA of relevant batch of drug substance generated by drug substance manufacturer.
2.	Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.	This firm has submitted that the assay of Meropenem Trihydrate USP reference standard lot # J0k434 is 87.3%. Therefore, we used sterile India material as working Standard having potency 82.02% by using standardization procedure with USP reference standard. Material used for batch manufacturing is from Aurobindo China and working standard prepared is of Sterile India having Potency 82.02% COA's for Reference standard & working standard along with standardization procedure is submitted by the firm.
3.	Scientific justification for use of 5% overage in the formulation.	Firm has submitted that an overage is used to cover losses during manufacturing. Initially we used extra 5% of Meropenem to deliver our product with exact quantity of API in injection, the idea behind was to deliver exact quantity of the active substance. After that our product was stable throughout its shelf life so no need to add extra 5% overage. In general, use of an overage of a drug substance to compensate for degradation during manufacture or a product's shelf life, or to extend shelf life, is discouraged. Overages are nothing but the extra quantity of material taken, which is lost during process stage.ICH Q8 guide line, provide a structured way to define product critical quality attributes. We are not using any overage in the manufacturing of Meropenem injection
4.	Submission of complete protocols of process validation studies of the drug product.	Firm has submitted general protocols for process validation. **Firm has not submitted specific protocols for the process validation of applied product.**
5.	Submission of detailed method of analysis of the drug product with details of sample solution preparation.	Firm has submitted detailed method of analysis of the drug product, **However in the submitted method, sample solution preparation method is still not clear in terms of exact volume of water used to**

		reconstitute the contents of vial and then how to make further dilutions. Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.
6.	Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.	Firm has submitted that they are using the potency of working standard as percentage. USP taking the Potency into mg/mg which is covered into percentage multiplying the ratio with 100 so there is no difference between the USP formula & our standard operating formula further more we have amended our SOP with respect to the formula given in USP. **However, the newly used calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard. The new formula is also not exactly as per USP monograph.**
7.	Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has now added sodium content test in their specifications. Firm has also submitted fee 7,500/- vide slip number 212267176 dated 20-05-2022. **However, no data regarding the sodium content testing during stability studies is provided.**
8.	Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.	Firm has not justified the previous validation reports, instead the firm has submitted new report in which the analysis is carried out on July 2022. The new report was performed in line with ICH recommendations.
9.	Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.	Firm has submitted data in section 3.2.P.8.3. The evaluation os submitted data is as under:

Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
Documents for the procurement of API with approval from DRAP (in case of import).	**1705205135, 1705205096:** Firm has submitted copy of commercial invoice cleared dated 19-10-2017

		specifying import of 20Kg meropenem for lot number 1705205135, 1705205096. The invoice is cleared by AD (I&E) DRAP. **1705203623:** Firm has submitted copy of commercial invoice cleared dated 12-09-2017 specifying import of 15Kg meropenem for lot number 1705203623. The invoice is cleared by AD (I&E) DRAP.
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record of product testing including HPLC chromatogram and raw data sheets
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for stability chambers for accelerated and real time stability study.

Decision: Deferred for following:

- **Clarification for use of 5% overage in sterile products and specifications of the manufactured products in the light of approved specifications and pharmacopoeial monographs.**
- **Capacity assessment of manufacturing and testing facility of M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.**
- **Submission of specific protocols for the process validation of applied product.**
- **Submission of preparation sample solution is required since it is not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions. Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.**
- **Clarification regarding use of formula which is different from the formula as recommended by USP for calculation of assay.**

257.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Genetics Pharmaceuticals (Pvt) Ltd. 539-A, Sundar Industrial Estate, Raiwind Road Lahore.**
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) Copy of agreement for contract manufacturing of pharmaceutical products between contract giver and acceptor dated 29-10-2020 is submitted

	GMP status of the firm	**Genetics Pharmaceuticals:** Firm has submitted copy of GMP certificate issued on the basis of inspection dated 29-03-2019. **Stallion Pharmaceuticals:** Firm has submitted GMP certificate issued on the basis of inspection dated 22-09-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 000783 of M/s Stallion Pharma Islamabad dated 08-02-2016 specifying dry powder injection Vial (carbapenem) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 16253: 11-06-2021
	Details of fee submitted	PKR 50,000/-: 30-11-2020
	The proposed proprietary name / brand name	**MEROTOL 1g Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as trihydrate)……1g (blended with sodium carbonate)
	Pharmaceutical form of applied drug	White or almost white, hygroscopic, crystalline, powder filled in clear glass vials
	Pharmacotherapeutic Group of (API)	Carbapenem antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Merrem Injection **(USFDA** Approved)
	For generic drugs (me-too status)	Merrem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Meronem 1g Injection of Pfizer Pakistan Ltd.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Aurobindo Pharma Limited Unit-V, Plot No. 68-70, 73-91, 95, 96, 260, 261 I.D.A Chemical Zone, Pashamylaram, Patancheru Mandal, Sanga Reddy District Telangana, India.
API Lot No.	1705205135 1705205096 1705203623
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	U7003	U7004	U7005
Batch Size	3900 vials	7600 vials	3780 vials
Manufacturing Date	09-2017	10-2017	11-2017
Date of Initiation	04-10-2017	14-11-2017	17-11-2017
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 11th June 2021.	Firm has submitted fee challan dated 28-12-2021 for 25,000/- vide slip number 16540367178
Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Firm has submitted copy of analytical method of drug substance from the drug product manufacturer. The analytical method is issued on 20-07-2021.
Submit data in section 3.2.S.4.3 as per the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity,	Firm has submitted report of verification studies of the analytical method of drug substance. However, the verification studies were conducted on 21-01-2021 while the

accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted". Further justify how the analysis of drug substance was conducted without performing verification studies of the analytical method of drug substance.	analytical method of drug substance was issued by the drug product manufacturer on 20-07-2021.
Submit data in section 3.2.S.4.4 as per the guidance document approved by Registration Board which specifies that "Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture. A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification)".	Firm has submitted COA of the drug substance generated by drug product manufacturer only, while the COA of drug substance manufacturer is not submitted.
Submit COA of reference standard / working standard including source and lot number which is actually used in the testing of drug substance and drug product.	Firm has submitted COA of working standard from drug substance manufacturer which has been standardized against USP reference standard. However drug product manufacturer is using working standard of meropenem Batch No. SI/MPM/00060120 manufactured by M/s Sterile India.
Justify the master formulation containing 1140mg of meropenem trihydrate for manufacturing of 1g meropenem for injection, since the drug substance contains meropenem blended with 15.10 to 16.50% w/w of sodium carbonate.	Firm has submitted calculation to justify the filled weight. As per calculations submitted by the firm the weight 1140mg per vial is calculated on theoretical basis considering that the drug substance has 100% assay, while the actual dispensing is to be made on the basis of actual % assay of the meropenem.
Justify the use of 5% overage in the formulation, since the justification submitted in this regard is not supported by any guidelines.	We hereby justify that in development stage we added 5% extra meropenem sterile powder for injection in initial batches. After completion of stability study degradation is no more than 2 – 3% within the limit assay range is 90 – 120% so no more 5% meropenem sterile powder for injection is added.
Submit results of compatibility studies in section 3.2.P.2.6.	Firm has submitted result of compatibility studies of the drug product with WFI.
Justify how the time and temperature of sterilization cycle is directly selected without any protocols for its validation.	Firm has submitted summary report of autoclave machine re qualification instead of providing justification.
Provide detailed method of sample stock solution preparation instead of mentioning the general statement "Constitute a container of Meropenem for Injection with a volume of	Firm has not submitted complete method of analysis of the drug product in which the method of sample solution preparation is explained.

water, corresponding to the quantity of solvent specified in the labelling".	
Justify why the formula for calculation of assay contents of meropenem is different than that mentioned in USP monograph.	Firm has submitted that we are using potency of working standard as percentage. USP taking the potency in mg/mg which is converted into percentage by multiplying this ratio with 100. Firm has submitted calculation to justify that their formula is equivalent to USP. However, the USP formula used by the firm is different from that specified in USP.
Analytical method verification studies have not been conducted and evaluated in the light of USP general chapters and ICH guidelines.	Firm has submitted verification studies of the analytical method dated 21-01-2021, while the analytical method of the drug product was revised and updated on 12-07-2021.
Justify why the drug product specifications does not contain the test for sodium contents as recommended by USP.	In Meropenem trihydrate injection label claim is as meropenem while trihydrate and sodium considered as impurity. We are verifying the meropenem by HPLC and due to unavailability of the atomic absorption we were verifying the sodium content by titration method. Moreover, for verification purpose, we analysed sodium content from PCSI and Citi Pharma with atomic absorption. And now we have atomic absorption in our facility and we have changed our SOP accordingly and now we are conducting each and every analysis of sodium content in our facility as per USP monograph.
Justify the test of accuracy in analytical method validation without specifying the concentrations of the solution which are analysed for accuracy. Further justify the use of solutions having low, medium, and high concentration of sample without specifying their exact concentration. Such words are not recommended by any scientific guidelines.	Firm has submitted that we had performed the accuracy by making a concentration of standard preparation and three concentrations. The concentrations used by the firm for accuracy test is 0.16mg/ml, 0.20mg/ml and 0.24mg/ml. As per the analytical method the standard solution concentration is 0.11mg/ml and the concentration used by the firm to study accuracy does not include the said concentration.
Linearity and range have been studied from 70% to 120% of the solution wherein the area under curve for 100% solution was 4691449 while in accuracy studies in the same method none of the solution (either low, medium or high concentration) achieved such area although the concentration of the solution is expected to be the same. Justification is required in this regard.	Two different samples were prepared for linearity and accuracy parameter of analytical method verification, for linearity parameter from the first dilution 6 further second dilutions 70%, 80%, 90%, 100%, 110% and 120% were prepared while in accuracy 3 further second dilutions low, medium and high were prepared. Because the weights of the sample are different in linearity and accuracy parameters that's why the area achieved is different for both parameters.
In linearity studies the area under curve for 100% solution was 4691449, while in stability studies the area under curve of the sample solution having exactly same concentration is	In linearity the sample solution preparation is different from the sample preparation of finished product. In linearity a concentration of standard taken to prepare first dilution then

reported to be 11769485. Justification is required in this regard how such huge difference in area under the curve can exist in the analysis and how this method can be considered reliable and verified.	make second dilution by taking 7ml, 8ml, 9ml, 10ml, 11ml, 12ml from the first dilution, second dilution of 10ml is considered as 100% concentration while in finished good the dilution contain 100mg of sample that's why area under curve for 100% solution is different from the area of 100mg in finished product.
The analytical method verification studies have been conducted in January 2021 while the batches were manufactured in 2017. Justification is required in this regard.	In 2017, we had completed analytical method verification by performing three parameters which are linearity, system suitability and specificity while when we submit the CTD dossier we came to know the DRAP requirement of accuracy and repeatability, then we had complete the analytical method verification by performing five parameters which are linearity, system suitability, specificity accuracy and repeatability.
Justify the limit of sodium content in the in house generated COA of drug substance, in which limit of sodium content is taken as 6.0% to 9.3% and the drug substance was passed on the basis of results of 9.12%, while the drug substance manufacturer specifies the limit of sodium content as 6.56% to 7.20%.	In past we were doing sodium content analysis by titration method (due to unavailability of AAS) the result was 9.12% limit of sodium content is 6.0% - 9.3% while the drug substance manufacturer specifies the sodium content as 6.65 to 7.20%. Now we are doing sodium content with AAS according to USP.
As per the submitted results of sodium content in meropenem injection by CITI Pharma, the results of % sodium content is 7.867%, while USP specifies the acceptance criteria to be 80%–120% of the labeled amount of sodium. Justify how your results complies USP specifications keeping in view the labelled amount of sodium in your product.	Firm has not submitted any justification
Justify the use of commercial lot of meropenem for injection (batch number SI/MPM/00060120) manufactured by sterile India as working standard since USP recommends that reference standard should be pure meropenem trihydrate.	The assay of meropenem trihydrate USP reference standard lot# J0K434, is 87.3% meropenem. Similarly by comparing with reference standard we prepare our meropenem trihydrate working standard in which 82.12% is meropenem present. Actually the material used in USP Reference standard and the working standard is the same as meropenem trihydrate because the product label claim is meropenem, therefore we have to calculate the assay against the purity of material as meropenem which is 87.3% in USP Reference standard and 82.12% in working standard.
Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Firm has not submitted details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Further documents confirming import of these relevant batches are also required.

Provide data of stability batches properly arranged and supported by respective documents including analytical report / COA, raw data sheet and respective chromatograms separately for each time point, since the submitted chromatograms and analytical reports are without any proper sequence.	Firm has not yet submitted stability study data in proper sequence with COA for each time point, raw data sheets and chromatograms. Raw data sheets are not submitted. Further the calculation formula used for the calculation of assay result is also different from USP as well as the method of sample and standard solution preparation.
Provide Reference of previous approval of applications with stability study data of the firm (if any)	No response submitted by the firm
Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	No response submitted by the firm
Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	No response submitted by the firm

Decision of 316th meeting of Registration Board:

Deferred for following:

- Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.
- Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.
- Scientific justification for use of 5% overage in the formulation.
- Submission of complete protocols of process validation studies of the drug product.
- Submission of detailed method of analysis of the drug product with details of sample solution preparation.
- Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.
- Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
- Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.
- Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.

Response by the firm:

Sr. No	Reason for deferment	Response by the firm
1.	Submission of COA of relevant batch of drug substance from drug substance manufacturer used in the manufacturing of batches for which stability study data is submitted.	Firm has submitted COA of relevant batch of drug substance generated by drug substance manufacturer.
2.	Scientific justification for using commercial batch manufactured by M/s Sterile India as working standard.	This firm has submitted that the assay of Meropenem Trihydrate USP reference standard lot # J0k434 is 87.3%. Therefore, we used sterile India material as working Standard having potency 82.02% by using standardization procedure with USP reference standard. Material used for batch

		manufacturing is from Aurobindo China and working standard prepared is of Sterile India having Potency 82.02% COA's for Reference standard & working standard along with standardization procedure is submitted by the firm.
3.	Scientific justification for use of 5% overage in the formulation.	Firm has submitted that an overage is used to cover losses during manufacturing. Initially we used extra 5% of Meropenem to deliver our product with exact quantity of API in injection, the idea behind was to deliver exact quantity of the active substance. After that our product was stable throughout its shelf life so no need to add extra 5% overage. In general, use of an overage of a drug substance to compensate for degradation during manufacture or a product's shelf life, or to extend shelf life, is discouraged. Overages are nothing but the extra quantity of material taken, which is lost during process stage.ICH Q8 guide line, provide a structured way to define product critical quality attributes. We are not using any overage in the manufacturing of Meropenem injection
4.	Submission of complete protocols of process validation studies of the drug product.	Firm has submitted general protocols for process validation. **Firm has not submitted specific protocols for the process validation of applied product.**
5.	Submission of detailed method of analysis of the drug product with details of sample solution preparation.	Firm has submitted detailed method of analysis of the drug product, **However in the submitted method, sample solution preparation method is still not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions.** Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.
6.	Scientific justification for using calculation formula for assay testing which is different from that specified in USP monograph.	Firm has submitted that they are using the potency of working standard as percentage. USP taking the Potency into mg/mg which is covered into percentage multiplying the ratio with 100 so there is no difference between the USP formula & our standard operating formula further more we have amended our SOP with respect to the formula given in USP. **However, the newly used calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.**

		The new formula is also not exactly as per USP monograph.
7.	Revision of drug product specifications in the light of USP monograph and inclusion of test for sodium content along with submission of fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	Firm has now added sodium content test in their specifications. Firm has also submitted fee 7,500/- vide slip number 45752149528 dated 20-05-2022. **However, no data regarding the sodium content testing during stability studies is provided.**
8.	Scientific justification for the analytical method verification studies of the drug product which is not performed as per ICH guidelines.	Firm has not justified the previous validation reports, instead the firm has submitted new report in which the analysis is carried out on July 2022. The new report was performed in line with ICH recommendations.
9.	Submission of stability study data of three commercial batches in section 3.2.P.8.3 as per the 6-points checklist provided in Form 5-F guidance document (PE&R/GL/AF/004) approved by the Registration Board.	Firm has submitted data in section 3.2.P.8.3. The evaluation os submitted data is as under:

Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 3298/E1/2019) issued by Drugs Control Administration, Government of Telangana dated 11-02-2020. The certificate is valid till 3 years from the date of issue.
Documents for the procurement of API with approval from DRAP (in case of import).	**1705205135, 1705205096:** Firm has submitted copy of commercial invoice cleared dated 19-10-2017 specifying import of 20Kg meropenem for lot number 1705205135, 1705205096. The invoice is cleared by AD (I&E) DRAP. **1705203623:** Firm has submitted copy of commercial invoice cleared dated 12-09-2017 specifying import of 15Kg meropenem for lot number 1705203623. The invoice is cleared by AD (I&E) DRAP.
Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record of product testing including HPLC chromatogram and raw data sheets
Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted

	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for stability chambers for accelerated and real time stability study.

Decision: Deferred for following:

- **Clarification for use of 5% overage in sterile products and specifications of the manufactured products in the light of approved specifications and pharmacopoeial monographs.**
- **Capacity assessment of manufacturing and testing facility of M/s Stallion Pharmaceuticals (Pvt) Ltd. 581, Sundar Industrial Estate, Raiwind Road Lahore.**
- **Submission of specific protocols for the process validation of applied product.**
- **Submission of preparation sample solution is required since it is not clear in terms of exact volume of water used to reconstitute the contents of vial and then how to make further dilutions. Furthermore, the calculation formula use weight of sample and standard while USP recommends to use concentration of sample and standard.**
- **Clarification regarding use of formula which is different from the formula as recommended by USP for calculation of assay.**

258. CAPACITY ASSESSMENT INSPECTION REPORT OF M/S VISION PHARMACEUTICALS (PVT.) LTD

GENERAL INFORMATION

Name of manufacturer	M/s. Vision Pharmaceuticals (Pvt.) Ltd
Physical Address	Plot No. 22 – 23, Industrial Triangle Kahuta Road, Islamabad
DML No.	000517
Date of inspection	15.06.2022
Purpose of inspection	Assessment and confirmation of manufacturing capacity with reference to DRAP, Islamabad letter No.
Dosage Form/Sections Included	I. Sterile Dry Powder Injection Vial (GENERAL) II. Sterile Dry Powder Injection Vial (STEROID)
Name of inspector (s)	I. Muhammad Haseeb Tariq, Assistant Director PEC, PE&R Division. II. Dr Farhadullah, Assistant Director PEC, PE&R Division.
Name of Firm's Representative (s) accompanying during inspection	I. Dr. Waseem Shahzad (Head of Quality Operations) II. Mr. Shaukat Iqbal (Manager Quality Control)

Manufacturing and testing record/data was evaluated from **January 2021 to December 2021** for the said purpose. The details of capacity calculations are as under:

NUMBER OF PRODUCTS MANUFACTURED BY THE FIRM

Category	No of products registered for self-manufacturing	No of products registered for contract manufacturing	Total

Sterile Dry Powder Injection Vial (General)	15	17	32
Sterile Dry Powder Injection Vial (Steroid)	04	00	04
Total products	**19**	**17**	**36**

SECTION WISE MANUFACTURING CAPACITY

1. CAPACITY OF STERILE DRY POWDER INJECTION VIAL (GENERAL)

Step wise capacity of Sterile Dry Powder Injection Vial (GENERAL)	**Maximum production Capacity (vials)**	
	Per day (8 hour working shift)	**Per month** (26 working days)
Vial Washing - Per single shift of 8 working hours (Load per Day)	25,000	650,000
Depyrogenation Capacity- Per Single shift of 8 working hours (Load per Day)	35,826	931,476
Filling and Sealing Capacity – Per single shift of 8 working hours (Load per Day)	30,000	780,000
Packing Capacity – Per single shift of 8 working hours (Load per Day)	20,000	520,000

***Note:** Limiting step in this process is **Packing** for calculating Utilized Capacity.*

Quarter Wise capacity utilized in Sterile Dry Powder Injection Vial (GENERAL)			
Quarter	**Actual Production (Vials)**	**Capacity (Vials)**	**Capacity utilized in (%)**
I (1st January – 31st March 2021)	474,030	1,560,000	30.3 %
II (1st April – 30th June 2021)	871,948	1,560,000	55.8 %
III (1st July – 30th September 2021)	430,320	1,560,000	27.5 %
IV (1st October – 31st December 2021)	741,563	1,560,000	47.5 %
Average Capacity Utilized for January – December 2021 in %			**40.27 %**

Manufacturing Capacity Utilized (average): 40.27 %
Manufacturing Capacity Available (average): 59.72 %

2. CAPACITY OF STERILE DRY POWDER INJECTION VIAL (STEROID)

Step wise capacity of Sterile Dry Powder Injection Vial (STEROID)	**Maximum production Capacity (vials)**	
	Per day (8 hour working shift)	**Per month** (26 working days)
Vial Washing - Per single shift of 8 working hours (Load per Day)	40,000	1,040,000
Depyrogenation Capacity- Per Single shift of 8 working hours (Load per Day)	40,000	1,040,000

Filling and Sealing Capacity – Per single shift of 8 working hours (Load per Day)	40,000	1,040,000
Packing Capacity – Per single shift of 8 working hours (Load per Day)	20,000	5,20,000

Note: Limiting step in this process is Packing for calculating Utilized Capacity.

Quarter Wise capacity utilized in Sterile Dry Powder Injection Vial (STEROID)			
Quarter	**Actual Production (Vials)**	**Capacity (Vials)**	**Capacity utilized in (%)**
I (1st January – 31st March 2021)	194,418	1,560,000	12.4%
II (1st April – 30th June 2021)	96,955	1,560,000	6.21%
III (1st July – 30th September 2021)	278,531	1,560,000	17.85%
IV (1st October – 31st December 2021)	197,903	1,560,000	12.68%
Average Capacity Utilized for January – December 2021 in %			**12.28%**

Manufacturing Capacity Utilized (average): 12.28%
Manufacturing Capacity Available (average): 87.71%

CAPACITY OF QUALITY CONTROL DEPARTMENT

Quality Control Equipment Detail			
Sr. No	**Equipment**	**Qty.**	**Capacity per day (tests)**
1.	HPLC Hitachi (Auto Sampler)	1	03
2.	HPLC Waters (Auto Sampler)	1	03
3.	HPLC Waters (Auto Sampler)	1	03
4.	HPLC Shimadzu	1	02
5.	HPLC Shimadzu	1	02
6.	Spectrophotometer	1	20
7.	Sterility Testing	1 Lab	12
8.	Moisture Analyzer	1	50
9.	Total Organic carbon Analyzer	1	10
10.	Karl Fischer	1	30
11.	pH meter	2	100
12.	Conductivity Meter	1	50
13.	Weighing balance	2	100
14.	Liquid particle Counter	1	50
15.	Hot Incubator (30- 35^{o}C) 750 Liters	1	175

16.	Cool Incubator (20- 25°C) 750 Liters	1	750
17.	Hot Incubator (30- 35°C) 108 Liters	1	108
18.	Hot Incubator (30- 35°C) 100 Liters	1	224
19.	Hot Incubator (55- 60°C) 74 Liters	1	Only for BET 300
20.	Cool Incubator (20- 25°C) 126 Liters	1	150
21.	Hot Incubator 37°C ± 1 °C 74 Liters	1	For Biological Indicators
22.	Dry Heat Sterilizer 250 °C	1	200
23.	Refrigerator	1	-----
24.	Autoclave	1	10
25.	Autoclave	1	10
26.	Air born particle counter	1	50
27.	Air sampler	1	50
28.	FTIR	1	20
29.	Polarimeter	1	15
30.	Dissolution Apparatus	3	15
31.	Stability Chamber (Accelerated)	2	600L
32.	Stability Chamber (Real time)	5	1500L

The details of the total registered products of the firm with respect to the method of testing is provided below:

Total No of registered Products	**No of Products with official Monograph (USP/BP/JP)**	**No of Products with In-house/Innovator specs**	**No of product currently on HPLC**	**No of products to be shifted to HPLC**
36	08 USP/03 BP	25	36/ 36 currently	NA

The firm has two separate Drug Manufacturing License i.e. DML by way of formulation and DML by way of semi-basic manufacturing, however the firm has a single QC laboratory which caters for all stages of testing for all type of products manufactured in both licensed facilities.

HPLCs Capacity Calculation Quarter Wise
(Average 2 – 3 tests/day/HPLC)
TOTAL 05 HPLC (13 tests per day)*
26 working days

* Firm has 5 HPLC systems which is used to test all products manufactured either as formulation in one DML or as semi basic products in other DML. Under the semi-basic facility the firm also manufacture pellets including sustained release, delayed release and dual delayed release pellets etc which requires extensive testing and dissolution studies. Further the formulation side also contain various sections which also requires product testing through HPLC.

Keeping in view the above, the panel members were of the opinion that the two sections i.e. Sterile Dry Powder Injection Vial (General) and Sterile Dry Powder Injection Vial (Steroid) will have at least 25% testing load of the whole Quality Control Laboratory. So keeping in view this factor the total HPLC capacity was reduced to 25% to check the testing capacity for these two sections.

Quarter	Average testing capacity / Quarter	Raw material tests	Product tests	Stability tests	Total tests	Capacity utilized (%)
I (1st Jan – 31st Mar 2021)	253	8	48	6	62	24.50 %
II (1st Apr – 30th June 2021)	253	12	60	8	80	31.60 %
III (1st July – 30th Sept 2021)	253	15	40	10	65	25.69 %
IV (1st Oct – 31st Dec 2021)	253	10	54	8	72	28.45 %
Average capacity						**27.56 %**

HPLC Testing Capacity Utilized (average): 27.56 %
HPLC Testing Capacity Available (average): 72.44 %

Sterility testing capacity of the firm was also reduced to 25% of the total capacity for calculating the overall capacity for these two sections.

Sterility Testing Capacity Calculation Quarter Wise (Average 12 tests/day)			
Quarter	Average capacity/ Quarter	Test Performed	Capacity Utilized %
I (1st Jan – 31st Mar 2021)	234	62	26.49%
II (1st Apr – 30th June 2021)	234	80	34.18%
III (1st July – 30th Sept 2021)	234	65	27.77%
IV (1st Oct – 31st Dec 2021)	234	72	30.76%
Average capacity available:			**29.8%**

Sterility Testing Capacity Utilized (average): 29.8%
Sterility Testing Capacity Available (average): 70.2%

Sterility testing capacity of the firm was also reduced to 25% of the total capacity for calculating the overall capacity for these two sections.

Bacterial Endotoxin Test Capacity Calculation Quarter Wise (Average 200 tests / day)			
Quarter	Average capacity/ Quarter	Test Performed	Capacity Utilized %
I (1st Jan – 31st Mar 2021)	3900	158	4.05%
II (1st Apr – 30th June 2021)	3900	200	5.12%

III (1st July – 30th Sep 2021)	3900	145	3.71%
IV (1st Oct – 31st Dec 2021)	3900	188	4.82%
Average capacity available:			**4.42%**

BET Testing Capacity Utilized (average): 4.42 %
BET Testing Capacity Available (average): 95.57 %

Hot and Cold Incubator Testing Capacity

The testing capacity of hot and cold incubators was determined at maximum production load during the study period i.e. January – December 2021.

	INCUBATOR TOTAL 08 INCUBATOR				
Incubator Name	**Use**	**capacity at a time for incubation**	**Media used for testing (Maximum production load)**	**Capacity utilized (%)**	**Capacity Available (%)**
	Test				
Hot incubator for sterility	**for sterility**	175 bottles for 14 days	07 test per day	4 %	96 %
Cool incubator for sterility	**for sterility**	175 bottles for 14 days	07 test per day	4 %	96 %
Cool incubator for media plates	**For Bio burden test**	150 plates for 5 days	03 test per day	2 %	98 %
Hot incubator for media plates	**For area monitoring**	270 plates for 3 days	80 plates per day	29.6 %	70.4 %
Hot incubator for incubation	**For Bio burden/ area monitoring**	288 plates for 3 days	80 plates per day	27.7 %	72.3 %
Hot incubator for biological indicators	**For biological indicators**	300 tubes for 2 days	20 tubes per day	6.6 %	93.4 %
Hot incubator for BET	**BET**	216 for 1 hour	30 test per day	15 %	85 %
Dry heat sterilizer	**Sterilization**	360 plates per day	80 plates per day	22.2 %	77.8 %

Observations by the Inspection Panel:

- The panel observed that the firm has two separate Drug Manufacturing License i.e. DML by way of formulation and DML by way of semi-basic manufacturing, however the firm has a single QC laboratory which caters for all stages of testing for all type of products manufactured in both licensed facilities.
- At the time of receiving of drug substance (containing multiple containers of sterile drug substances) the firm perform complete analysis including physical, chemical and microbiological tests using the sample vial / pouch provided with the containers.
- However, before production of commercial batches, the firm only performs BET test for the drug substance instead of performing complete testing for each container.
- The representatives of the firm informed the panel that incase of non-pharmacopoeial drug products, they were using UV methods for analysis, however they have switched all such products to HPLC method / innovator's specifications.
- During review of specifications of drug substance and drug product it was observed that the firm

has mentioned an alternate method (UV method) for assay testing in some cases. Upon clarification the firm's representatives informed that they use this alternate method only for identification test of those drug substances which are already manufactured and released within their own facility having DML by way of semi-basic manufacturing.

- It was also observed that the firm was using diluents for reconstitution of the drug products other than those recommended by innovator product in certain cases like esomeprazole powder for solution for injection/infusion etc.

CONCLUSION

The manufacturing capacity (installed, utilized and unutilized) and overall capacity of the analytical equipment of M/s Vision Pharmaceuticals (Pvt.) Ltd Plot No. 22 – 23, Industrial Triangle Kahuta Road, Islamabad, was assessed based on the data and record provided by the firm, interview of the personnel and visit of the premises. The installed and utilized capacity of the manufacturing and analytical equipment used for testing of products has been given in detail above for record and further necessary action.

Dr. Farhad Ullah Assistant Director, PEC, PE&R Division DRAP, Islamabad	**Dr. Muhammad Haseeb Tariq**, Assistant Director, PEC, PE&R Division DRAP, Islamabad

ANNEXURES:

Annexure 1	• Total number of registered products of the firm, • Total number registered product for each aforementioned section • Existing registered products on contract manufactured by the firm in aforementioned sections
Annexure 2	• List of all quality control equipment along with its testing capacity • Total number of QC, IPQC and stability study tests performed in each quarter
Annexure 3	• List of qualified personnel working in production, Quality control and Quality assurance department
Annexure 4	• List of production equipment along with capacity
Annexure 5	• List of all production batches of each product manufactured in each quarter from January to December 2021.
Annexure 6	• Calibration certificate of dryer and autoclave.

Decision: Registration Board discussed the inspection report in details. Deliberations were made on used and available manufacturing and quality control capacity keeping in view all registered product and currently applied products. After thorough deliberation, the Board decided to allow contract manufacturing from M/s Vision Pharmaceuticals (Pvt) Ltd Plot No. 22 – 23, Industrial Triangle Kahuta Road, Islamabad for following sections:

- **Sterile Dry Powder Injection Vial (General)**
- **Sterile Dry Powder Injection Vial (Steroid)**

Agenda of Evaluator PEC-IV

Case no. 01 Registration applications on Form 5F for local manufacturing of (Human) drugs

a. New cases

259.	Name, address of Applicant / Marketing Authorization Holder	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23834 dated: 31-08-2021
	Details of fee submitted	PKR 20,000/- dated: 08/03/2021 PKR 10,000/- dated: 11/05/2020
	The proposed proprietary name / brand name	Montisim 5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each chewable tablet contains: Montelukast as sodium…….5mg
	Pharmaceutical form of applied drug	Red colored, Round shaped, chewable tablet
	Pharmacotherapeutic Group of (API)	Leukotriene receptor antagonist
	Reference to Finished product specifications	USP
	Proposed Pack size	2×7’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Montelukast 5mg chewable tablet, Accord Healthcare Limited, United Kingdom, MHRA Approved.
	For generic drugs (me-too status)	Montiget 5mg chewable tablet, Getz Pharma (Pvt) Ltd. Reg# 034837
	GMP status of the Finished product manufacturer	Copy of cGMP issued on 23-07-202 on the basis of evaluation conducted on 09-07-2020
	Name and address of API manufacturer.	ZHEJIANG TIANYU PHARMCEUTICALS CO., LTD. No. 15, Donghai 5th Avenue, Zhejiang Provincial chemical and medical Raw Materials Base Linhai Zone, Taizhou City.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of montelukast sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (Sulfoxide impurity, Cis Isomer, methylketone, methylstyrene and total impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (201310301, 201310302, 201310303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Singulair 5mg tablet Batch No# S018860 by Merck Sharp & Dohme limited UK by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Singulair 5mg tablet by Merck Sharp & Dohme limited UK in Acid media (pH 1.0-1.2) & Acetate buffer 4.5pH and Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision and specificity.
STABILITY STUDY DATA		
Manufacturer of API	ZHEJIANG TIANYU PHARMCEUTICALS CO., LTD.	

	No. 15, Donghai 5th Avenue, Zhejiang Provincial chemical and medical Raw Materials, Base Linhai Zone, Taizhou City.		
API Lot No.	11001-181210		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20TRn006	20TRn009	20TRn010
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	10-2020	11-2020	11-2020
Date of Initiation	23-11-2020	23-11-2020	23-11-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No . ZJ20180033 issued by China food and Drug Control administration valid until 14.03.2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of form 3, form 7 and commercial invoice (Invoice# TY119146 Dated: 28-02-2019 with received quantity i.e. 15 kg) of Montelukast Batch No# 11001-181210 with attestation of DRAP Lahore dated: 11-03-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.1	Differential fee according to as per notification No.F.7-11/2012-	Differential fee of Rs:10000/- deposit slip # 34803402245 dated: 11-05-2022 submitted

		B&A/DRAP dated 13-07-2012	
2.	1.3.5.	GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.	Latest cGMP certificate submitted
3.	1.5.15 – 1.5.20	Submit Original Commitment	Signed original commitments submitted.
4.	2.3.R.1.1	Assay of Drug substance mentioned is 94.24% while in Certificate of Analysis of Drug substance Assay is 99.39%. Clarification is required.	Assay result 94.24% is result of montelukast on as is basis (the content of montelukast in montelukast sodium API), while the result 99.39% in Certificate of analysis of Drug substance under assay is result on dried basis.
5.	3.2.S.4.2	USP specify montelukast dicyclohexylamine as reference standard in drug substance assay testing while you have used montelukast sodium as reference standard. Clarification is required.	We used montelukast sodium as working standard which was standardized against Montelukast dicyclohexylamine CRS Lot#Y0001436 B#2. CoA of montelukast dicyclohexylamine Reference standard is given under section 3.2.P.6 Reference standard or materials and also attached (As the primary reference standards are costly and have small quantities, reference standards used in routine test of batch/product analysis are made in-house against primary reference standard. The in-house reference standards are working/secondary reference standards).
6.	3.2.P.5.2	• USP specify montelukast dicyclohexylamine as reference standard in drug product analytical testing method while you have used montelukast sodium as working standard. Clarification is required.	We used montelukast sodium as working standard which was standardized against Montelukast dicyclohexylamine CRS Lot#Y0001436 B#2. CoA of montelukast dicyclohexylamine Reference standard is given under section 3.2.P.6 Reference standard or materials and also attached (As the primary reference standards are costly and have small quantities, reference standards used in routine test of batch/product analysis are made in-house against primary reference standard. The in-house reference standards are working/secondary reference standards).
7.	3.2.P.8	• Reference of previous approval of applications with stability study data of the firm (if any). • Compliance Record of HPLC software 21CFR	• NA • Real time stability data summary sheets are attached. • Compliance record of HPLC Software 21CFR and audit trail reports on product testing are attached.

		& audit trail reports on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) • Documents for the procurement of API with approval from DRAP (in case of import).	• Record of digital data logger for temperature and humidity monitoring of stability chambers is attached. • Import documents submitted.

Decision: Registration Board deferred the case for Scientific justification for use of montelukast sodium as working standard instead of montelukast dicyclohexylamine specified by USP monograph.

260.	Name, address of Applicant / Marketing Authorization Holder	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23836 dated: 31-08-2021
	Details of fee submitted	PKR 20,000/- dated: 22-02-2021 PKR 10,000/- dated: 11/05/2020
	The proposed proprietary name / brand name	Montisim 10mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Montelukast as sodium…….10mg
	Pharmaceutical form of applied drug	Yellow colored, Round shaped, film coated tablet
	Pharmacotherapeutic Group of (API)	Leukotriene receptor antagonist
	Reference to Finished product specifications	USP
	Proposed Pack size	2×7’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Montelukast 10mg tablet, Accord Healthcare Limited, United Kingdom, MHRA Approved.

	For generic drugs (me-too status)	Montiget 10mg tablet, Getz Pharma (Pvt) Ltd. Reg# 034838
	GMP status of the Finished product manufacturer	Copy of cGMP issued on 23-07-202 on the basis of evaluation conducted on 09-07-2020
	Name and address of API manufacturer.	ZHEJIANG TIANYU PHARMCEUTICALS CO., LTD. No. 15, Donghai 5th Avenue, Zhejiang Provincial chemical and medical Raw Materials Base Linhai Zone, Taizhou City.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of montelukast sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (Sulfoxide impurity, Cis Isomer, methylketone, methylstyrene and total impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (201310301, 201310302, 201310303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Singulair 10mg tablet Batch No# S032494 by Merk Sharp & Dohme limited UK by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Singulair 10mg tablet by Merk Sharp &

		Dohme limited UK in Acid media (pH 1.0-1.2) & Acetate buffer 4.5pH and Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision and specificity.

STABILITY STUDY DATA			
Manufacturer of API	ZHEJIANG TIANYU PHARMCEUTICALS CO., LTD. No. 15, Donghai 5th Avenue, Zhejiang Provincial chemical and medical Raw Materials, Base Linhai Zone, Taizhou City.		
API Lot No.	11001-181210		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20TRn003	20TRn007	20TRn008
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	11-11-2020	11-11-2020	11-11-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No . ZJ20180033 issued by China food and Drug Control administration valid until 14.03.2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of form 3, form 7 and commercial invoice (Invoice# TY119146 Dated: 28-02-2019 with received quantity i.e. 15 kg) of Montelukast Batch No# 11001-181210 with attestation of DRAP Lahore dated: 11-03-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity	Submitted

	monitoring of stability chambers (real time and accelerated)	

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.1	Differential fee according to as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2012	Differential fee of Rs:10000/- deposit slip # 34803402245 dated: 11-05-2022 submitted
2.	1.3.5.	GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.	Latest cGMP certificate submitted
3.	1.5.15 – 1.5.20	Submit Original Commitment	Signed original commitments submitted.
4.	2.3.R.1.1	Assay of Drug substance mentioned is 94.24% while in Certificate of Analysis of Drug substance Assay is 99.39%. Clarification is required.	Assay result 94.24% is result of montelukast on as is basis (the content of montelukast in montelukast sodium API), while the result 99.39% in Certificate of analysis of Drug substance under assay is result on dried basis.
5.	3.2.S.4.2	USP specify montelukast dicyclohexylamine as reference standard in drug substance assay testing while you have used montelukast sodium as reference standard. Clarification is required.	We used montelukast sodium as working standard which was standardized against Montelukast dicyclohexylamine CRS Lot#Y0001436 B#2. CoA of montelukast dicyclohexylamine Reference standard is given under section 3.2.P.6 Reference standard or materials and also attached (As the primary reference standards are costly and have small quantities, reference standards used in routine test of batch/product analysis are made in-house against primary reference standard. The in-house reference standards are working/secondary reference standards).
6.	3.2.P.5.2	• USP specify montelukast dicyclohexylamine as reference standard in drug product analytical testing method while you have used montelukast sodium as working standard. Clarification is required.	We used montelukast sodium as working standard which was standardized against Montelukast dicyclohexylamine CRS Lot#Y0001436 B#2. CoA of montelukast dicyclohexylamine Reference standard is given under section 3.2.P.6 Reference standard or materials and also attached (As the primary reference standards are costly and have small quantities, reference standards used in routine test of batch/product analysis are made in-house against primary reference standard. The in-house reference standards are working/secondary reference standards).
7.	3.2.P.8	• Reference of previous approval of	• NA

		applications with stability study data of the firm (if any). • Submit real time • stability summary sheets for Compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) • Documents for the procurement of API with approval from DRAP (in case of import).	• Real time stability data summary sheets are attached. • Compliance record of HPLC Software 21CFR and audit trail reports on product testing are attached. • Record of digital data logger for temperature and humidity monitoring of stability chambers is attached. • Import documents submitted.

Decision: Registration Board deferred the case for Scientific justification for use of montelukast sodium as working standard instead of montelukast dicyclohexylamine specified by USP monograph.

261.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.24703 dated 07/09/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 8066123845
	The proposed proprietary name / brand name	Diampa M XR 5mg + 1000mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended-release tablet contains: Empagliflozin…..5mg Metformin HCl USP…..1000mg
	Pharmaceutical form of applied drug	Light yellow colored oblong shaped biconvex, film coated tablet plain on both sides.
	Pharmacotherapeutic Group of (API)	Combination of oral blood glucose lowering drugs(Anti-diabetic)

	Reference to Finished product specifications	Getz Pharma Specs.
	Proposed Pack size	14's (2×7's) & 28's (4×7's)
	Proposed unit price	Rs. 982/- (14's) Rs. 1964/- (28's)
	The status in reference regulatory authorities	Synjardy XR 5mg + 1g tablet by M/s Boehringer Ingelheim, USA. USFDA Approved.
	For generic drugs (me-too status)	Erli Plus XR 5mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., Karachi. (Reg. No. 105273)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18,237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Empagliflozin: Official monograph of Empagliflozin is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance Metformin HCl: Official monograph of Metformin HCl is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances,

		specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Empagliflozin:** Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (130701, 130702, 130801) **Metformin HCl:** Real time: 30˚C ± 2˚C / 75% ± 5%RH for 60 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (A-72611405016, A-72611405017, A-72611405018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is ErliPlus XR 5mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd. by performing quality tests (Appearance, Average Weight, Assay, Dissolution). CDP has been performed against the same brand that is ErliPlus XR 5mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., in Acidic media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The f2 values are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	**Empagliflozin:**Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18, 237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.
API Lot No.	Empagliflozin: 20191130 (0000171936) Metformin HCl: A-32611910002 (0000173980) & A-81412001039 (0000176216)
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's & 28's)
Stability Storage Condition	Real time: 30˚C ± 2˚C / 75% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	532DS01	532DS02	532DS03
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	25.06.2020	05.08.2020	05.08.2020
Date of Initiation	25.09.2020	09.10.2020	25.09.2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December, 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of Drug Manufacturing License no. Su 20160324 issued by Jiangsu Drug Administration (Huai'an Inspection Branch) valid till 06-12-2025. **Metformin HCl:** Copy of GMP Certificate No. SD20190888 issued by CFDA, China valid till 12-03-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# JXCAVIR-20191003AP) dated : 03-01-2020 cleared by DRAP Karachi office dated 07.01-2020 specifying import 20Kg Empagliflozin: (Batch# 20191130). **Metformin HCl:** Firm has submitted copy of invoic (invoice# JC202002009-1) dated : 18-03-2020 cleared by DRAP Karachi office dated 07.04.2020 specifying import of Metformin Hcl (Batch# A-81412001039). Firm has submitted copy of invoice (invoice# JC201910012-2) dated : 30-12-2019 cleared by DRAP Karachi office dated 07.01-2020 specifying import of Metformin HCl (Batch# A-32611910002).

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Remarks OF Evaluator: Gap bew mfg and stability start

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2.	Strength of Active ingredient shall be stated clearly. For example, each tablet contains,	Firm submitted Label claim as follows: Each extended-release tablet contains: Empagliflozin…..5mg Metformin HCl USP…..1000mg
2.	2.3.R.1.1	In BMR of batch # 532DS03 batch no of drug substance Metformin HCl # 0000176216 while in stability summary sheets it is mentioned as batch # 000013980. Clarify which batch of drug substance is used in manufacturing of 532DS03.	Batch no # 0000176216 of Metformin HCl is used in manufacturing of 532DS03 and accordingly revised corrected stability summary sheets are submitted.
3.	1.6.5	Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. Or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin for Empagliflozin	Valid Drug Manufacturing License of Empagliflozin issued by Jiangsu Drug Administration, China valid till 06.12.2025.
4.	3.2.S.4.3	Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both drug substance(s) Empagliflozin & Metformin HCl) Shall be submitted.	Firm has submitted Analytical method verification studies, without performance of accuracy parameter. Firm has submitted following justification: "This is to bring to your kind attention that we have used 100% API without any placebo in Analytical Method Verification Studies of Empagliflozin and Metformin HCl, therefore, requirement of accuracy is not applicable. Further, we have performed linearity to check area response of the sample as the concentration of the sample

			raised within working range of sample i.e., 50% - 150%."
5.	3.2.P.2.2.1	CDP has been performed with different strength. Clarification is required.	Comparative dissolution profile (CDP) with Erliplus XR Tablets 5mg + 1000mg (Batch No # 1B133) manufactured by Pharmevo (Pvt) Limited, submitted.
6.	3.2.P.5.1	In specification of dissolution testing time for Empagliflozin Q is not mentioned	Updated finished product specifications submitted.
7.	3.2.P.8	Documents for the procurement of Metformin HCl for batch # (Batch# A-81412001039). with approval from DRAP	Documents for the procurement of Metformin HCl for batch # (Batch# A-81412001039). with approval from DRAP submitted.

Decision: Approved with innovator's specification..

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

262.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.24704 dated 07/09/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 2281658200
	The proposed proprietary name / brand name	Diampa M XR 10mg + 1000mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended-release tablet contains: Empagliflozin…..10mg Metformin HCl USP…..1000mg
	Pharmaceutical form of applied drug	Pink colored oblong shaped biconvex, film coated tablet plain on both sides.
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Getz Pharma Specs.

	Proposed Pack size	14's (2×7's) & 28's (4×7's)
	Proposed unit price	Rs. 1160/- (14's) Rs. 2137/- (28's)
	The status in reference regulatory authorities	Synjardy XR 10mg + 1g tablet by M/s Boehringer Ingelheim, USA. USFDA Approved.
	For generic drugs (me-too status)	Erli Plus XR 10mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., Karachi. (Reg. No. 105274)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18,237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Empagliflozin: Official monograph of Empagliflozin is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance Metformin HCl: Official monograph of Metformin HCl is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its

		verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Empagliflozin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (130701, 130702, 130801) **Metformin HCl:** Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (A-72611405016, A-72611405017, A-72611405018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is ErliPlus XR 10mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd. by performing quality tests (Appearance, Average Weight, Assay, Dissolution). CDP has been performed against the same brand that is ErliPlus XR 10mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., in Acidic media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	**Empagliflozin:** Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18, 237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.
API Lot No.	Empagliflozin: 20191205 (0000174101) Metformin HCl: A-22612002008 (0000177796) A-81412001039 (0000176216)
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's & 28's)
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	536DS01	536DS02	536DS03
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	10.07.2020	12.08.2020	12.08.2020
Date of Initiation	25.09.2020	25.09.2020	25.09.2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December, 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of Drug Manufacturing License no. Su 20160324 issued by Jiangsu Drug Administration (Huai'an Inspection Branch) valid till 06-12-2025. **Metformin HCl:** Copy of GMP Certificate No. SD20190888 issued by CFDA, China valid till 12-03-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# JXCAVIR-200212) dated : 02-03-2020 cleared by DRAP Karachi office dated 05.03-2020 specifying import 10Kg Empagliflozin: (Batch# 20191205). **Metformin HCl:** Firm has submitted copy of form 7 and invoice (invoice# JC202002010-1) dated : 09-04-2020 cleared by DRAP Karachi office dated 22.04.2020 specifying import 9 of Metformin HCl (Batch# A-22612002008). Firm has submitted copy of invoice (invoice# JC202002009-1) dated : 18-03-2020 cleared by DRAP Karachi office dated 07.04.2020 specifying import of Metformin HCl (Batch# A-81412001039)

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2.	Strength of Active ingredient shall be stated clearly. For example, each tablet contains,	Firm submitted Label as follows: Each extended-release tablet contains: Empagliflozin…..10mg Metformin HCl USP…..1000mg
2.	2.3.R.1.1	In BMR of batch # 536DS01 batch no of drug substance Metformin HCl # 0000176216 mentioned while in stability summary sheets it is mentioned as batch # (0000177796). Clarify which batch of drug substance is used in manufacturing of 536DS01.	0000176216 of Metformin HCl is used in manufacturing of 536DS01 and accordingly revised corrected stability summary sheets are submitted.
3.	1.6.5	Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. Or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin for Empagliflozin	Valid Drug Manufacturing License of Empagliflozin issued by Jiangsu Drug Administration, China valid till 06.12.2025.
4.	3.2.S.4.3	Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both drug substance(s) Empagliflozin & Metformin HCl) Shall be submitted.	Firm has submitted Analytical method verification studies, without performance of accuracy parameter. Firm has submitted following justification: "This is to bring to your kind attention that we have used 100% API without any placebo in Analytical Method Verification Studies of Empagliflozin and Metformin HCl, therefore, requirement of accuracy is not applicable. Further, we have performed linearity to check area response of the

			sample as the concentration of the sample raised within working range of sample i.e., 50% - 150%."
5.	3.2.S.4.4	Submit Certificate of analysis for Empagliflozin batch #(20191205) by drug substance manufacturer and drug product manufacturer.	Certificate of analysis of Empagliflozin batch # (20191205) by drug substance manufacturer and drug product manufacturer is attached.
6.	3.2.P.2.2.1	CDP has been performed with different strength. Clarification is required.	Comparative dissolution profile (CDP) with Erliplus XR Tablets 10mg + 1000mg (Batch No # 1D0683) manufactured by Pharmevo (Pvt) Limited, submitted
7.	3.2.P.5.1	In specification of dissolution testing time for Empagliflozin Q is not mentioned	Updated finished product specifications submitted.
8.	3.2.P.8	• Documents for the procurement of Empagliflozin for batch #(0000174101) with approval from DRAP. • Documents for the procurement of Metformin HCl for batch # (A-81412001039) with approval from DRAP	Documents for the procurement of Empagliflozin for batch # (0000174101) and Metformin HCI for batch # (Batch# A-81412001039) with approval from DRAP are attached.

Decision: Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

263.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No.24705 dated 07/09/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 86219844
	The proposed proprietary name / brand name	Diampa M XR 12.5mg + 1000mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended-release tablet contains: Empagliflozin…..12.5mg Metformin HCl USP…..1000mg
	Pharmaceutical form of applied drug	Red colored oblong shaped biconvex, film-coated tablet plain on both sides.
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Getz Pharma Specs.
	Proposed Pack size	14's (2×7's) & 28's (4×7's)
	Proposed unit price	Rs. 1162/- (14's) Rs. 2278/- (28's)
	The status in reference regulatory authorities	Synjardy XR 12.5mg + 1g tablet by M/s Boehringer Ingelheim, USA. USFDA Approved.
	For generic drugs (me-too status)	Erli Plus XR 12.5mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., Karachi. (Reg. No. 105275)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18,237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Empagliflozin: Official monograph of Empagliflozin is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance Metformin HCl: Official monograph of Metformin HCl is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Empagliflozin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (130701, 130702, 130801) **Metformin HCl:** Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (A-72611405016, A-72611405017, A-72611405018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is ErliPlus XR 12.5mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd. by performing quality tests (Appearance, Average Weight, Assay, Dissolution). CDP has been performed against the same brand that is ErliPlus XR 12.5mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., in Acidic media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	**Empagliflozin:**Jiangsu Yongan Pharmaceutical Co., Ltd.	

	No. 18, 237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.		
API Lot No.	Empagliflozin: 20191205 (0000174101), 20191130 (0000171936), 20190322 (0000161733) Metformin HCl: A-81412001039 (0000176216), A-22612002008 (0000177796)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's & 28's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	537DS02	537DS04	537DS06
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	17.07.2020	12.08.2020	02.10.2020
Date of Initiation	25.09.2020	16.10.2020	16.10.2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December, 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of Drug Manufacturing License no. Su 20160324 issued by Jiangsu Drug Administration (Huai'an Inspection Branch) valid till 06-12-2025. **Metformin HCl:** Copy of GMP Certificate No. SD20190888 issued by CFDA, China valid till 12-03-2024.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of form 7 and invoice (invoice# JXCAVIR-200212) dated : 02-03-2020 cleared by DRAP Karachi office dated 05.03-2020 specifying import 10Kg Empagliflozin: (Batch# 20191205). Firm has submitted copy of form 7 and invoice (invoice# CAVIR-20190303AP) dated : 28-03-2019 cleared by DRAP Karachi office dated 05.04-2019 specifying import 10Kg Empagliflozin: (Batch# 20190322). Firm has submitted copy of invoice (invoice# JXCAVIR-20191003AP) dated : 03-01-2020 cleared by DRAP Karachi office dated 07.01-2020 specifying import 20Kg Empagliflozin: (Batch# 20191130). **Metformin HCl:** Firm has submitted copy of invoic (invoice# JC202002010-1) dated : 09-04-2020 cleared by DRAP Karachi office dated 22.04.2020 specifying import 9 of Metformin HCl (Batch# A-22612002008). Firm has submitted copy of invoice (invoice# JC202002009-1) dated : 18-03-2020 cleared by DRAP Karachi office dated 04.04.2020 specifying import of Metformin HCl (Batch# A-81412001039)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2.	Strength of Active ingredient shall be stated clearly. For example, each tablet contains,	Firm submitted Label as follows: Each extended-release tablet contains: Empagliflozin…..12.5mg Metformin HCl USP…..1000mg
2.	1.6.5	Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. Or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by	Valid Drug Manufacturing License of Empagliflozin issued by Jiangsu Drug Administration, China valid till 06.12.2025.

		relevant regulatory authority of country of origin for Empagliflozin	
3.	3.2.S.4.3	Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both drug substance(s) Empagliflozin & Metformin HCl) Shall be submitted.	Firm has submitted Analytical method verification studies, without performance of accuracy parameter. Firm has submitted following justification: "This is to bring to your kind attention that we have used 100% API without any placebo in Analytical Method Verification Studies of Empagliflozin and Metformin HCl, therefore, requirement of accuracy is not applicable. Further, we have performed linearity to check area response of the sample as the concentration of the sample raised within working range of sample i.e., 50% - 150%."
4.	3.2.S.4.4	Submit Certificate of analysis for Empagliflozin batch # (20191205 & 0000161733) by drug substance manufacturer and drug product manufacturer.	Certificate of analysis of Empagliflozin batch # ((20191205 & 0000161733) by drug substance manufacturer and drug product manufacturer are attached.
5.	3.2.P.2.2.1	CDP has been performed with different strength. Clarification is required.	Comparative dissolution profile (CDP) with Erliplus XR Tablets 12.5mg + 1000mg (Batch No # 1D062) manufactured by Pharmevo (Pvt) Limited, submitted
6.	3.2.P.5.1	In specification iof dissolution testing time for Empagliflozin Q is not mentioned	Updated finished product specifications submitted.
7.	3.2.P.8	• Documents for the procurement of Empagliflozin for batch (0000174101 and 0000161733) with approval from DRAP. • Documents for the procurement of Metformin HCl for batch # (A-81412001039 and A-22612002008) with approval from DRAP	Documents for the procurement of Empagliflozin for batch # (0000174101 and 0000161733) and Metformin HCI for batch # (Batch# A-81412001039 and B# A-22612002008) with approval from DRAP are attached.

Decision: Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

264.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30 Sectors 27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.24061 dated 01/09/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 241056944018
	The proposed proprietary name / brand name	Diampa M XR 25mg + 1000mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended-release tablet contains: Empagliflozin…..25mg Metformin HCl USP…..1000mg
	Pharmaceutical form of applied drug	Yellow colored, oblong shaped, biconvex film coated tablet, plain on both sides.
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Getz Pharma Specs.
	Proposed Pack size	14's (2×7's)
	Proposed unit price	Rs. 1178/- (14's)
	The status in reference regulatory authorities	Synjardy XR 25mg + 1g tablet by M/s Boehringer Ingelheim, USA. USFDA Approved.
	For generic drugs (me-too status)	Erli Plus XR 25mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., Karachi. (Reg. No. 105276)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18,237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Empagliflozin: Official monograph of Empagliflozin is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance Metformin HCl: Official monograph of Metformin HCl is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Empagliflozin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (130701, 130702, 130801) **Metformin HCl:** Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (A-72611405016, A-72611405017, A-72611405018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is ErliPlus XR 25mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd. by performing quality tests (Appearance, Average Weight, Assay, Dissolution). CDP has been performed against the same brand that is ErliPlus XR 25mg + 1000mg Tablet by M/s PharmEvo (Pvt.) Ltd., in Acidic media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The f2 values are in the acceptable range..
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:**Jiangsu Yongan Pharmaceutical Co., Ltd. No. 18, 237 provincial highway, Jiangsu Huai'an Economic Development, China. **Metformin HCl:** Shouguang Fukang Pharmaceutical Co., Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang, Shandong, China.		
API Lot No.	Empagliflozin: 20191205 (0000174101), 20190322 (0000161733) Metformin HCl: A-32611910002 (0000173980), A-81412001039 (0000176216)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's & 28's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	533DS02	533DS03	533DS05
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	03.07.2020	05.08.2020	15.09.2020
Date of Initiation	25.09.2020	09.10.2020	09.10.2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December, 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available.

		• Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of Drug Manufacturing License no. Su 20160324 issued by Jiangsu Drug Administration (Huai'an Inspection Branch) valid till 06-12-2025. **Metformin HCl:** Copy of GMP Certificate No. SD20190888 issued by CFDA, China valid till 12-03-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of form 7 and invoice (invoice# JXCAVIR-200212) dated : 02-03-2020 cleared by DRAP Karachi office dated 05.03-2020 specifying import 10Kg Empagliflozin: (Batch# 20191205). Firm has submitted copy of form 7 and invoice (invoice# CAVIR-20190303AP) dated : 28-03-2019 cleared by DRAP Karachi office dated 05.04-2019 specifying import 10Kg Empagliflozin: (Batch# 20190322). **Metformin HCl:** Firm has submitted copy of invoic (invoice# JC201910012-2) dated : 30-12-2019 cleared by DRAP Karachi office dated 07.01.2020 specifying import 9 of Metformin HCl (Batch# A-32611910002). Firm has submitted copy of invoice (invoice# JC202002009-1) dated : 18-03-2020 cleared by DRAP Karachi office dated 04.04.2020 specifying import of Metformin HCl (Batch# A-81412001039).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2.	Strength of Active ingredient shall be stated clearly. For example, each tablet contains,	Firm submitted Label as follows: Each extended-release tablet contains: Empagliflozin…..25mg

			Metformin HCl USP…..1000mg
2.	2.3.R.1.1	In BMR of batch # 533DS05 batch no of drug substance Empagliflozin # 0000174101 and Metformin HCl# 0000176216 mentioned while in stability summary sheets it is mentioned as batch Empagliflozin # 0000171936 and Metformin HCl #0000177796. Clarify which batch of drug substance's are used in manufacturing of 533DS05.	Batch no: 0000174101 of Empagliflozin and Batch no: 0000176216 of Metformin HCl is used in manufacturing of 533DS05 and accordingly revised corrected stability summary sheets are submitted.
3.	1.6.5	Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. Or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin for Empagliflozin	Valid Drug Manufacturing License of Empagliflozin issued by Jiangsu Drug Administration, China valid till 06.12.2025.
4.	3.2.S.4.3	Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both drug substance(s) Empagliflozin & Metformin HCl) Shall be submitted.	Firm has submitted Analytical method verification studies, without performance of accuracy parameter. Firm has submitted following justification: "This is to bring to your kind attention that we have used 100% API without any placebo in Analytical Method Verification Studies of Empagliflozin and Metformin HCl, therefore, requirement of accuracy is not applicable. Further, we have performed linearity to check area response of the sample as the concentration of the sample raised within working range of sample i.e., 50% - 150%."
5.	3.2.S.4.4	Submit Certificate of analysis for Empagliflozin batch # (20191205 & 0000161733) by drug substance manufacturer and drug product manufacturer.	Certificate of analysis of Empagliflozin batch # ((20191205 & 0000161733) by drug substance manufacturer and drug product manufacturer are attached.
6.	3.2.P.5.1	In specification of dissolution testing time for Empagliflozin Q is not mentioned	Updated finished product specifications submitted.

7.	3.2.P.8	• Documents for the procurement of Empagliflozin for batch # (0000174101 and 0000161733) with approval from DRAP. • Documents for the procurement of Metformin HCl for batch # (A-81412001039) with approval from DRAP	Documents for the procurement of Empagliflozin for batch # (0000174101 and 0000161733) and Metformin HCI for batch # (Batch# A-81412001039) with approval from DRAP. Are attached.

Decision: Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

265.	Name, address of Applicant / Marketing Authorization Holder	"M/s Hilton Pharma (Pvt.) Ltd. Plot No. 13-14, Sector-15, Korangi, Industrial Area, Karachi."
	Name, address of Manufacturing site.	"M/s Hilton Pharma (Pvt.) Ltd. Plot No. 13-14, Sector 15, Korangi, Industrial Area, Karachi."
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23218 Dated: 25-08-2021
	Details of fee submitted	PKR 30,000/- Dated: 16-06-2021
	The proposed proprietary name / brand name	Racehil Granules for suspension 10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet Contains: Racecadotril …… 10mg
	Pharmaceutical form of applied drug	Granules for suspension
	Pharmacotherapeutic Group of (API)	Antidiarrheal
	Reference to Finished product specifications	Innovator
	Proposed Pack size	8's, 10's, 16's, 20's, 30's
	Proposed unit price	As per DPC

	The status in reference regulatory authorities	Hidrasec® 10mg by France Approved.
	For generic drugs (me-too status)	"Hidrasec® 10mg" Sachet by M/s Abbott Laboratories Reg# 087082
	GMP status of the Finished product manufacturer	Section for Capsule (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020
	Name and address of API manufacturer.	**Racecadotril:** **M/s SVK Laboratories Private Limited** D-16, Phase-I, IDA-Jeedimetla Hyderabad-500055 Telangana State-India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data on CTD format related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications and analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	**Stability study conditions:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months **Racecadotril**: Batches #: (RCL/00415, RCL/00515, RCL/00615)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturing process and process control, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Hidrasec® Granules for suspension 10mg manufactured by Sophatrex 21 Rue du pressoir , France for Abbott Laboratories The firm has submitted the comparative dissolution with Hidrasec® Granules for suspension 10mg manufactured by Sophatrex 21 Rue du pressoir ,

		France for Abbott Laboratories. and dissolution profile in Acid media (pH- 1.2) Acetate Buffer (pH-4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including, Specificity, linearity, range, accuracy, Precision Repeatability, Intermediate precision, Robustness, System Suitability.

STABILITY STUDY DATA			
Manufacturer of API	M/s SVK Laboratories Private Limited D-16, Phase-I, IDA-Jeedimetla Hyderabad-500055 Telangana State-India.		
API Lot No.	RCL/0050919		
Description of Pack (Container closure system)	Alu-Alu paper foil		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RAC-419105-4	RAC-419105-5	RAC-419105-6
Batch Size	1000 Sachet	1000 Sachet	1000 Sachet
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	21-05-2020	21-05-2020	21-05-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No (39250/TS/2020) issued by Drugs control administration Telangana (DCA) valid until 26.05.2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy commercial invoice (Invoice# EXP/2019-20/010 Dated: 05-12-2019 with received quantity i.e. 2 kg) of Racecadotril Batch No# RCL/0050919 with attestation of DRAP Karachi dated: 16-12-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have maintained manual logs of all tests.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	In BMR potency of Drug substance mentioned on As is basis is 100.96% while in COA 99.49% . Clarification is required.	In BMR potency of Drug Substance on As is basis was taken 100.96% for trial batches. The actual potency of API was 99.49%. In fact 100.96% potency was erroneously taken from 20.0g docket sample of API received for initial testing purpose. Please find enclosed data of docket sample including with raw data as your ready reference. However, both docket sample for initial testing and API received for trial batches have potency results within the specification limit i.e. 98 – 102% (on dried basis). The difference is minor and that is 1.47%, which does not effect stability data as all assay results are well within limits. "In continuation of our letter no. SA/MI/05-22/78 (Racehil Granules for Suspension) submitted on 12.05.2022. As required, we explain the point No. 2.3.R.1.1, vendor sample from manufacturer for testing/evaluation purpose is termed as docket sample. Potency of docket sample was used mistakenly instead of potency of API. However, there is no significant difference in potency of docket sample & API used for trial batches"
2.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed	All quality tests (mentioned in section 3.2.P.5.1) were tested for test product (Racehil Granules for Oral Suspension 30mg) and innovator (Hidrasec Granules For Oral Suspension 30mg) and found to be satisfactory and comparable.
9.	3.2.P.5.1	Dissolution testing not included in specification.	Dissolution test has been included in specification, enclosed.

Decision: Approved with innovator's specification.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		
266.	Name, address of Applicant / Marketing Authorization Holder	"M/s Hilton Pharma (Pvt.) Ltd. Plot No. 13-14, Sector-15, Korangi, Industrial Area, Karachi."
	Name, address of Manufacturing site.	"M/s Hilton Pharma (Pvt.) Ltd. Plot No. 13-14, Sector 15, Korangi, Industrial Area, Karachi."
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23217 Dated: 25-08-2021
	Details of fee submitted	PKR 30,000/- Dated: 16-06-2021
	The proposed proprietary name / brand name	Racehil Granules for suspension 30mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet Contains: Racecadotril …… 30mg
	Pharmaceutical form of applied drug	Granules for suspension
	Pharmacotherapeutic Group of (API)	Antidiarrheal
	Reference to Finished product specifications	Innovator
	Proposed Pack size	8's, 10's, 16's, 20's, 30's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Hidrasec® 30mg by France Approved.
	For generic drugs (me-too status)	"Hidrasec® 30mg" Sachet by M/s Abbott Laboratories Reg# 087517
	GMP status of the Finished product manufacturer	Section for Capsule (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020
	Name and address of API manufacturer.	M/s SVK Laboratories Private Limited D-16, Phase-I, IDA-Jeedimetla Hyderabad-500055 Telangana State-India.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data on CTD format related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications and analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Racecadotril: Batches #: (RCL/00415, RCL/00515, RCL/00615)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacturing process and process control, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Hidrasec® Granules for suspension 30mg manufactured by Sophatrex 21 Rue du pressoir , France for Abbott Laboratories The firm has submitted the comparative dissolution with Hidrasec® Granules for suspension 30mg manufactured by Sophatrex 21 Rue du pressoir , France for Abbott Laboratories. and dissolution profile in Acid media (pH 1.2) Acetate Buffer (pH-4.5) & Phosphate Buffer (pH- 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including, Specificity, linearity, range, accuracy, Precision Repeatability, Intermediate precision, Robustness, System Suitability.
STABILITY STUDY DATA		
Manufacturer of API	M/s SVK Laboratories Private Limited D-16, Phase-I, IDA-Jeedimetla Hyderabad-500055 Telangana State-India.	

API Lot No.	RCL/0050919		
Description of Pack (Container closure system)	Alu-Alu paper foil		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RAC-418604-6	RAC-418904-7	RAC-419004-8
Batch Size	500 Sachet	500 Sachet	500 Sachet
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	21-05-2020	21-05-2020	21-05-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No (39250/TS/2020) issued by Drugs control administration Telangana (DCA) valid until 26.05.2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy commercial invoice (Invoice# EXP/2019-20/010 Dated: 05-12-2019 with received quantity i.e. 2 kg) of Racecadotril Batch No# RCL/0050919 with attestation of DRAP Karachi dated: 16-12-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have maintained manual logs of all tests.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	In BMR potency of Drug substance mentioned on As is basis 100.96% while in COA 99.49%	In BMR potency of Drug Substance on As is basis was taken 100.96% for trial batches. The actual potency of API was 99.49%. In fact 100.96% potency was erroneously taken from 20.0g docket sample of API received for initial testing purpose. Please find enclosed data of docket sample including

			with raw data as your ready reference. However, both docket sample for initial testing and API received for trial batches have potency results within the specification limit i.e. 98 – 102% (on dried basis). The difference is minor and that is 1.47%, which does not effect stability data as all assay results are well within limits. "In continuation of our letter no. SA/MI/05-22/78 (Racehil Granules for Suspension) submitted on 12.05.2022. As required, we explain the point No. 2.3.R.1.1, vendor sample from manufacturer for testing/evaluation purpose is termed as docket sample. Potency of docket sample was used mistakenly instead of potency of API. However, there is no significant difference in potency of docket sample & API used for trial batches"
2.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed	All quality tests (mentioned in section 3.2.P.5.1) were tested for test product (Racehil Granules for Oral Suspension 30mg) and innovator (Hidrasec Granules For Oral Suspension 30mg) and found to be satisfactory and comparable
10.	3.2.P.5.1	Dissolution testing not included in specification.	Dissolution test has been included in specification, enclosed.

Decision: Approved with innovator's specification..

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.F**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

267.	Name, address of Applicant / Marketing Authorization Holder	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals 7KM Pasrur Road Sialkot
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23838 dated: 31-08-2021
	Details of fee submitted	PKR 30,000/- dated: 04/08/2021
	The proposed proprietary name / brand name	Dentofin 100mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Flurbiprofen…….100mg
	Pharmaceutical form of applied drug	Blue color, round, biconvex, film coated tablets
	Pharmacotherapeutic Group of (API)	Anti-inflammatory and anti-rheumatic (NSAID)
	Reference to Finished product specifications	USP
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Flurbiprofen 100mg film coated tablet, Pharmacia and Upjohn, USFDA Approved.
	For generic drugs (me-too status)	ANSAID 100mg tablet, Pfizer Pakistan Limited Reg# -12299
	GMP status of the Finished product manufacturer	Copy of cGMP issued on 23-07-202 on the basis of evaluation conducted on 09-07-2020
	Name and address of API manufacturer.	Hy-Gro Chemicals Pharmtek Private Limited, Plot No. 174, Progressive Industrial Society, IDA Bollaram, Jinnaram (Mandal), Sanga Reddy (District), Telangana, INDIA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of flurbiprofen is present in B.P. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (Impurity A, B, C, D, E, Unknown and total impurities), specifications, analytical procedures

		and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Innovator that is ANSAID 100mg tablet by Pfizer Pakistan Ltd by performing quality tests (Identification, Assay, Disintegration, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is ANSAID 100mg tablet by Pfizer Pakistan Ltd in Acid media (pH 1.0-1.2) & Acetate buffer 4.5pH and Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision and specificity.

STABILITY STUDY DATA

Manufacturer of API	Hy-Gro Chemicals Pharmtek Private Limited, Plot No. 174, Progressive Industrial Society, IDA Bollaram, Jinnaram (Mandal), Sanga Reddy (District), Telangana, INDIA.		
API Lot No.	FB-2020/07/41		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (3×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20TRn013	21TRn004	21TRn005
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	12-2020	02-2021	02-2021
Date of Initiation	11-03-2021	11-03-2021	11-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. L.Dis**.** No.69129/Stores/2021 issued by Drug control administration Government of Telangana issued on 18-09-2021 and valid for a period of three years.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.12086/2020/DRAP-AD-G (I&E) dated 26/08/2020 is submitted wherein the permission to import different APIs including Flurbiprofen for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, Form 7 & invoice (invoice# HBD/EXP/84) Dated: 23-09-2020 from Hy-Gro Chemicals Pharmtek Private Limited specifying import 0.7096Kg Flurbiprofen (Batch# FB-2020/07/41). But no approval by DRAP.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.1	Drug substance manufacturer specifications are BP for drug substance while drug product manufacture specifications are USP for drug substance. Clarification is required.	We have changed specification from USP to BP, revised Standard analytical procedure, performed method verification studies as per BP and performed complete analysis of Drug substance as per BP method. Revised standard analytical procedure and specifications, method verification protocol and report and Drug substance analytical record as per BP specification are attached. • (However different batch no mentioned on COA.)
2.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section	Pharmaceutical equivalence study report and analytical record is attached

		3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed	
3.	3.2.P.8	• Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin. • Documents for the procurement of API with approval from DRAP (in case of import). • Compliance Record of HPLC software 21CFR & audit trail reports on product testing • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• GMP certificate of API manufacturer is attached. • For document for procurement of API form 6 submitted (However of different batch no mentioned.) • Compliance record of HPLC software 21CFR & Audit trail reports on product testing are attached. • Record of digital data logger for temperature and humidity monitoring of stability chambers is attached .
4.	In continuation of previous reply firm submitted justification for change of Batch No on COA and import documents as follows: **1.** **"**Flurbiprofen Drug substance was received in Raw material store and RMS in-Charge asked purchase department for CoA (as the soft copy of document is received in purchase dept. and hard copy arrives after few days of receiving of drug substance). Purchase department provided CoA of different Batch No. (FBP-2020/09/24) (mistakenly provided by supplier to purchase department) to RMS and the same Batch number was recorded in all documents in RMS, quality control laboratory and production. **2.** At the time of reply to deficiencies of Dentofin 100mg tablet above issue was detected that the import documents have different batch number (FB-2020/07/41) compared to our record. After investigation above mentioned mistake was traced, correct batch number CoA provided and record was corrected. **3.** As it was observed in deficiencies (performance of test as per USP instead of BP) we performed method verification studies as per drug substance manufacturer specifications (BP) and retested the drug substance as per BP method mentioning correct batch number. Method verification protocol, report, revised SAP for drug substance, testing record and report submitted to your office. **4.** Flurbiprofen drug substance was initially tested by USP method (assay by titration using indicator) on 16-Nov-2020 and Trial batches were manufactured		

	as per USP method results (99.45% on as is basis). Flurbiprofen drug substance was re-tested as per manufacturer specifications by BP method (assay by potentiometric titration) on 15-Jun-2022, assay result (99.16% on as is basis). **5.** The difference of assay result is 0.30% which is due to difference of time between two analysis/tests (1.7 years) and testing method (titration method using indicator versus potentiometric titration).**"**

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in Drug Substance, specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

268.	Name, address of Applicant / Marketing Authorization Holder	M/s Scotmann Pharmaceuticals, 5-D, I-10/3, Industrial Area, Islamabad, Pakistan
	Name, address of Manufacturing site.	M/s Scotmann Pharmaceuticals, 5-D, I-10/3, Industrial Area, Islamabad, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23861 dated 31/08/2021
	Details of fee submitted	PKR 30,000/- dated 07/07/2021
	The proposed proprietary name / brand name	Tanavul Tablets 10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated Tablet contains: Vonoprazan Fumarate eq.to Vonoprazan….10mg
	Pharmaceutical form of applied drug	Film coated tablets
	Pharmacotherapeutic Group of (API)	Potassium-competitive acid blocker
	Reference to Finished product specifications	Manufacturer specification
	Proposed Pack size	7's, 10's, 14's, 20's, 28's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab 10mg Tablets (PMDA Japan Approved)
	For generic drugs (me-too status)	Voniza tablets 10mg Manufacture by Hilton Pharma (Pvt.) Ltd. Reg # 108573

	GMP status of the Finished product manufacturer	cGMP certificate on the basis of inspection and evaluation conducted on 09-11-2020 and valid till 08-11-2022
	Name and address of API manufacturer.	**Name:** Ami Lifesciences Pvt.Ltd. **Address:** Block No. 82/B, Ecp Road, At & Post. Karakhadi, Taluka-Padra, District Vadodara Gujarta, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Vonoprazan Fumarate is not present in any Pharmacopeia. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Long term: 30°C ± 2°C / 65% ± 5%RH for 18 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Voniza Tablets 10mg by Hilton Pharma (Pvt.) Ltd. performing quality tests (Identification, D. time, Dissolution, Assay). CDP has been performed against the same brand that is Voniza Tablets 10mg by Hilton Pharma (Pvt.) Ltd, Dissolution profiles of both products (Voniza Tablets 10mg and Tanavul Tablets 10mg) were compared at three pH (1.2, 4.5, and 6.8) graphically and statistically.

	Analytical method validation/verification of product	Method verification studies have submitted including linearity, Robustness, accuracy, precision (Repeatability), specificity.	
STABILITY STUDY DATA			
Manufacturer of API	**Name:** Ami Lifesciences Pvt.Ltd. **Address:** Block No. 82/B, Ecp Road, At & Post. Karakhadi, Taluka-Padra, District Vadodara Gujarta, India		
API Lot No.	VPF/RD/30720520		
Description of Pack (Container closure system)	Alu-Alu blister with cold aluminum foil (7's, 10's, 14's, 20's, 28's & 30's)		
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Long term: 6 months Accelerated: 6 months		
Frequency	Accelerated: Initial, 3, 6 (Months) Long term: Initial, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	26-12-2020	21-12-2020	21-12-2020
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product "Dascot (Daclatasvir) 30mg Tablets" which was presented in 278th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 26th January, 2018. According to inspection report, following points were confirmed. • The firm has 21CFR compliant HPLC software. • The firm has audit trail reports available. Adequate monitoring and control are available for stability chamber	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No . 22043267 issued by food and Drug Control administration Gandhinagar Gujarat State India valid until 17.04.2025.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 3,Form 6, Form 7 & invoice (invoice# EXP/1/20-21/0217) Dated: 20-08-2020 from Ami life sciences Pvt. Ltd cleared by DRAP Islamabad office dated 09-09-2020 specifying import 300g Vonoprazone Fumarate(Batch# VPF/RD/30720520).	

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Name and address of API manufacturer. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.	Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin is attached.
2.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided
3.	3.2.S.4.1	Copies of the Drug substance specifications by Drug Product manufacturer is required	Copies of the Drug substance specifications by Drug Product manufacturer is attached.
4.	3.2.S.4.2	Copies of the Drug substance analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required	Copies of the Drug substance analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is attached.
5.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance is attached.

		Product manufacturer for drug substance(s) shall be submitted.	
6.	3.2.S.4.4	Certificate of Analysis (CoA) of the same batch used during product development and stability studies from Drug Substance / /Active Pharmaceutical Ingredient manufacture.	Certificate of Analysis (CoA) of the same batch used during product development and stability studies from Drug Substance / /Active Pharmaceutical Ingredient manufacture is submitted.
7.	3.2.P.2.2.1	Pharmaceutical Equivalence and CDP not performed with Innovator. Clarification is required.	The Innovator product was not readily available in the market at the time of performing these studies in Pakistan. Therefore, we selected a comparator product that has been approved by DRAP and is the most widely used brand in Pakistan.
8.	3.2.P.5.2	Justify the adaptation of dissolution parameters including type of apparatus, speed (rpm), dissolution medium, volume and time keeping in view the solubility and pKa of the drug substance, pH – pKa solubility profile and recommendations from general chapters of official pharmacopoeia	Dissolution parameters i.e revolution (50rpm), dissolution media volume (900ml) and time (30 minutes) of Vonaprazan Tablet 10mg and Vonaprazan Tablet 20mg were selected as per USP chapter <1092>. For the selection of dissolution media, the dose solubility ratio of Vonoprazan was performed in pH 1.2, 4.5, and 6.8 buffer. Dose solubility ratio was very high throughout the physiological buffer range i.e. 1mg/ml in pH 6.8 buffers, 10mg/ml in pH 1.2 buffers, and 10.4mg/ml in pH 4.5 buffers. Therefore, we selected a dissolution medium having 6.8 pH as a strict-case scenario. <Reference Attached> Dose solubility volume ratio was calculated by using the following formula: Dose solubility volume: Dose (mg) Solubility (mg/ml)
9.	3.2.P.8	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) submitted.

Decision: Approved with innovator's specification..

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

269.	Name, address of Applicant / Marketing Authorization Holder	M/s Scotmann Pharmaceuticals, 5-D, I-10/3, Industrial Area, Islamabad, Pakistan
	Name, address of Manufacturing site.	M/s Scotmann Pharmaceuticals, 5-D, I-10/3, Industrial Area, Islamabad, Pakistan

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23862 dated 31/08/2021
	Details of fee submitted	PKR 30,000/- dated 07/07/2021
	The proposed proprietary name / brand name	Tanavul Tablets 20mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Each film coated Tablet contains**: Vonoprazan Fumarate eq.to Vonoprazan….20mg
	Pharmaceutical form of applied drug	Film coated tablets
	Pharmacotherapeutic Group of (API)	Potassium-competitive acid blocker
	Reference to Finished product specifications	Manufacturer specification
	Proposed Pack size	7's, 10's, 14's, 20's, 28's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab 20mg Tablets (PMDA Japan Approved)
	For generic drugs (me-too status)	Voniza tablets 20mg Manufacture by Hilton Pharma (Pvt.) Ltd. Reg # 108572
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of inspection and evaluation conducted on 09-11-2020 and valid till 08-11-2022
	Name and address of API manufacturer.	**Name:** Ami Lifesciences Pvt.Ltd. **Address:** Block No. 82/B, Ecp Road, At & Post. Karakhadi, Taluka-Padra, District Vadodara Gujarta, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Vonoprazan Fumarate is not present in any Pharmacopeia. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, tests for impurity related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Long term: 30°C ± 2°C / 65% ± 5%RH for 18 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Voniza Tablets 20mg by Hilton Pharma (Pvt.) Ltd. performing quality tests (Identification, D. time, Dissolution, Assay). CDP has been performed against the same brand that is Voniza Tablets 20mg by Hilton Pharma (Pvt.) Ltd, Dissolution profiles of both products (Voniza Tablets 10mg and Tanavul Tablets 10mg) were compared at three pH (1.2, 4.5, and 6.8) graphically and statistically.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, Robustness, accuracy, precision (Repeatability), specificity.

STABILITY STUDY DATA

Manufacturer of API	**Name:** Ami Lifesciences Pvt.Ltd. **Address:** Block No. 82/B, Ecp Road, At & Post. Karakhadi, Taluka-Padra, District Vadodara Gujarta, India		
API Lot No.	VPF/RD/30720520		
Description of Pack (Container closure system)	Alu-Alu blister with cold aluminum foil (7's, 10's, 14's, 20's, 28's & 30's)		
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Long term: 6 months Accelerated: 6 months		
Frequency	Accelerated: Initial, 3, 6 (Months) Long term: Initial, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	22-12-2020	22-12-2020	22-12-2020

No. of Batches	03

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product "Dascot (Daclatasvir) 30mg Tablets" which was presented in 278th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 26th January, 2018. According to inspection report, following points were confirmed. • The firm has 21CFR compliant HPLC software. • The firm has audit trail reports available. Adequate monitoring and control are available for stability chamber
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No . 19041306 issued by food and Drug Control administration Gandhinagar gujjarat State India valid until 24.04.2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 3,Form 6, Form 7 & invoice (invoice# EXP/1/20-21/0217) Dated: 20-08-2020 from Ami life sciences Pvt. Ltd cleared by DRAP Islamabad office dated 09-09-2020 specifying import 300g Vonoprazone (Batch# VPF/RD/30720520).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Name and address of API manufacturer. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory	Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin is attached.

		authority of country of origin.	
2.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided
3.	3.2.S.4.1	Copies of the Drug substance specifications by Drug Product manufacturer is required	Copies of the Drug substance specifications by Drug Product manufacturer is attached.
4.	3.2.S.4.2	Copies of the Drug substance analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required	Copies of the Drug substance analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is attached.
5.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance is attached.
6.	3.2.S.4.4	Certificate of Analysis (CoA) of the same batch used during product development and stability studies from Drug Substance / /Active Pharmaceutical Ingredient manufacture.	Certificate of Analysis (CoA) of the same batch used during product development and stability studies from Drug Substance / /Active Pharmaceutical Ingredient manufacture is submitted.
7.	3.2.P.2.2.1	Pharmaceutical Equivalence and CDP not performed with Innovator. Clarification is required.	The Innovator product was not readily available in the market at the time of performing these studies in Pakistan. Therefore, we selected a comparator product that has been approved by DRAP and is the most widely used brand in Pakistan.
8.	3.2.P.5.2	Justify the adaptation of dissolution parameters including type of apparatus, speed (rpm),	Dissolution parameters i.e revolution (50rpm), dissolution media volume (900ml) and time (30 minutes) of Vonaprazan Tablet

		dissolution medium, volume and time keeping in view the solubility and pKa of the drug substance, pH – pKa solubility profile and recommendations from general chapters of official pharmacopoeia	10mg and Vonaprazan Tablet 20mg were selected as per USP chapter <1092>. For the selection of dissolution media, the dose solubility ratio of Vonoprazan was performed in pH 1.2, 4.5, and 6.8 buffer. Dose solubility ratio was very high throughout the physiological buffer range i.e. 1mg/ml in pH 6.8 buffers, 10mg/ml in pH 1.2 buffers, and 10.4mg/ml in pH 4.5 buffers. Therefore, we selected a dissolution medium having 6.8 pH as a strict-case scenario. <Reference Attached> Dose solubility volume ratio was calculated by using the following formula: Dose solubility volume: Dose (mg) Solubility (mg/ml)
9.	3.2.P.8	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) submitted.

Decision: Approved with innovator's specification..

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

270.	Name, address of Applicant / Marketing Authorization Holder	M/s Wimits Pharmaceuticals (Pvt) Ltd. Lahore
	Name, address of Manufacturing site.	M/s Wimits Pharmaceuticals (Pvt) Ltd. Plot #129 Sundar Industrial Estate, Raiwind road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33169 dated 21/12/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 1174933702
	The proposed proprietary name / brand name	Metacor 1000mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Metformin HCl …….1000mg

	Pharmaceutical form of applied drug	White colored oval Film coated engraved with 'W' on one side of tablet
	Pharmacotherapeutic Group of (API)	Oral Hypoglycemic agent
	Reference to Finished product specifications	BP
	Proposed Pack size	5×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucophage 1000mg tablet by M/s Martin Dow, USFDA Approved.
	For generic drugs (me-too status)	Neodiper 1g tablet by M/s Sanofi Aventis Reg. No. 026929
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conducted on 08-09-2021
	Name and address of API manufacturer.	M/s AARTI DRUGS LIMITED Plot No 211 & 213, Road -2, G.I.D.C AT & Post Sarigam. City Sarigam– 396 155 Dist. Valsad Gujarat industrial estate India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Metformin Hydrochloride is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A,B,C,E &F, related substances (Xyline), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Glucophage 1g tablet by Martin Dow by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Glucophage 1g tablet by Martin Dow in Acid media (pH-1.2),Acetate Buffer(pH-4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s AARTI DRUGS LIMITED Plot No 211 & 213, Road -2, G.I.D.C AT & Post Sarigam. City Sarigam– 396 155 Dist. Valsad Gujarat industrial estate India.		
API Lot No.	MEF119102522		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (5×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1,2 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TMR002	TMR003	TMR004
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	27-01-2021	28-01-2021	29-01-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 20031933 issued by Food & Drug Control administration Gujrat state India valid till 19-03-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (invoice# EXP/1879/10-20) dated : 01-11-2019 cleared by DRAP Lahore office dated 18.11-2019 specifying import of Metformin HCl (Batch# MEF119102522).

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	U.V method is used
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).
Remarks OF Evaluator: The BP monograph for metformin tablet specifies UV method for assay testing.		
Decision: Approved with BP specification. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
271.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare (Pvt) Ltd. Plot No.33-Sundar Industrial Estate Lahore- Pakistan
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt) Ltd. Plot No.33-Sundar Industrial Estate Lahore- Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33302 dated 09/12/2021
	Details of fee submitted	PKR 75,000/-: Deposit slip # 5095652505
	The proposed proprietary name / brand name	Rupri Tablet 1mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Prucalopride Succinate Eq To Prucaloprid…1mg
	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	High affinity 5HT4 receptor antagonist (Other drugs for constipation ATC code: A06AX05)_
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MOTEGRITY of USFDA approved
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conducted on03-06-2021
	Name and address of API manufacturer.	M/s Kimia Biosciences Limited, (Formerly Known as Laurel Organics Limited)Village Bhondsi Tehsil-Sohna District-Gurgoan Harryana, India
	Evaluation by PEC: Firm applied products Rupri 1mg Tablet (Prucalopride) on form 5D afterward also applied same product on form 5F. Form 5D case was evaluated earlier and presented in 317th meeting of DRB and was approved by DRB.(Case no 57 of 317th meeting). **Firm Response:** With reference to our form 5F application submitted on December 9th, 2021 for our product mentioned in subject this is to explain here that we submitted application of Prucalopride on form 5D as well and it is approve in registration board meeting No 317th for our Horizon Healthcare Pvt Limited Lahore. We hereby request your good office for withdrawal of our submitted application of Prucalopride submitted on form 5F.	
	Decision: Registration Board acceded the firm's request and decided to reject Rupri 1mg Tablet (Prucalopride).	
272.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare (Pvt) Ltd. Plot No.33-Sundar Industrial Estate Lahore- Pakistan
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt) Ltd. Plot No.33-Sundar Industrial Estate Lahore- Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33303 dated 09/12/2021
	Details of fee submitted	PKR 75,000/-: Deposit slip # 842525402
	The proposed proprietary name / brand name	Rupri Tablet 2mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Prucalopride Succinate Eq To Prucaloprid…2mg
	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	High affinity 5HT4 receptor antagonist (Other drugs for constipation ATC code: A06AX05)_

	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MOTEGRITY of USFDA approved
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conducted on03-06-2021
	Name and address of API manufacturer.	M/s Kimia Biosciences Limited, (Formerly Known as Laurel Organics Limited)Village Bhondsi Tehsil-Sohna District-Gurgoan Harryana, India
	Evaluation by PEC: Firm applied products Rupri 2mg Tablet (Prucalopride) on form 5D afterward also applied same product on form 5F. Form 5D case was evaluated earlier and presented in 317th meeting of DRB and was approved by DRB.(Case no 58 of 317th meeting). **Firm Response:** With reference to our form 5F application submitted on December 9th, 2021 for our product mentioned in subject this is to explain here that we submitted application of Prucalopride on form 5D as well and its approve in registration board meeting No 317th for our Horizon Healthcare Pvt Limited Lahore. We hereby request your good office for withdrawal of our submitted application of Prucalopride submitted on form 5F.	
	Decision: Registration Board acceded the firm's request and decided to reject Rupri 2mg Tablet (Prucalopride).	
273.	Name, address of Applicant / Marketing Authorization Holder	M/s Ferozsons Laboratories Ltd. P.O Ferozsons, Amangarh, Nowshera-Khyber Pakhtunkhwa
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Ltd. P.O Ferozsons, Amangarh, Nowshera-Khyber Pakhtunkhwa
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27705 dated 06/10/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 1430213620
	The proposed proprietary name / brand name	Dakardi 5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin propanediol monohydrate eq to Dapagliflozin …….5mg

	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	Antidiabetic Drug (Sodium-glucose co-transporters 2 (SGLT2) inhibitor)
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	10's, 14's, 20's, 28's and 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Farxiga 5mg tablet by AstraZeneca Pharmaceuticals LP Wilmington, DE 19850, USFDA Approved
	For generic drugs (me-too status)	Dapwiz 5mg Tablets by M/s Pharmevo Pvt Ltd. - Karachi, Reg. No. 107374
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conductd on 25-01-2019 and valid for 03 years.
	Name and address of API manufacturer.	M/s Fuxin Long Rui Pharmaceutical Co, Ltd – China Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province – 123000 China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Dapagliflozin is Inhouse, the firm submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, tests for single/total impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (160108, 160124, 160220)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Farxiga 5mg tablet by AstraZeneca Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Farxiga 5mg tablet by AstraZeneca Pharmaceuticals. The dissolution profile of Dakardi 5mg Tablets and Farxiga 5mg Tablet has shown release of more than 85 % in all three Buffer pH 1.2, Phosphate Buffer pH 6.8 and Acetate Buffer pH 4.5 in 30 minutes. And no calculation is required for Similarity factor f2 hence dissolution profile of both Dakardi 5mg tablets and Farxiga 5mg tablet is similar.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical Co, Ltd – China Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province – 123000 China		
API Lot No.	DG-20200107-D01-DG06-01		
Description of Pack (Container closure system)	01 Alu-Alu blister of 14 tablets, packed in cardboard box (Box of 14 tablets)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	DGTab-001	DGTab-002	DGTab-003
Batch Size	1000 tablets	1000 tablets	1000 tablets
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	19-01-2021	19-01-2021	19-01-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product EMPAGEN 10mg & 25mg which was conducted on 24-08-2021 and was presented in 294th meeting of Registration Board held on 9th April , 2020. According to the report following points were confirmed.

		• The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML Registration. No. Liao20150233 issued by Food and Drug Administration of Liaoning Province-China valid till 20/12/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 6 , , DRAP acknowledgment for receiving of dapagliflozin ,form3, form 7 and invoice (invoice#HN200716-L) dated : 16-07-2020 specifying import of Dapagliflozin propanediol monohydrate (Batch# DG-20200107-D01-DG06-01).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.P.5.3	Protocols of analytical validation studies not submitted.	Protocols of analytical validation studies submitted
2.	3.2.P.5.4	In COA's Inhouse specifications mentioned while in section 1.5.6 Innovator specifications claimed. Clarification is required.	Revised COA's with Innovator's specifications are submitted.
3.	3.2.P.8	Submit Commercial invoice with approval from DRAP.	Drug substance was imported against form-6 and the DRAP-Peshawar office was also intimated regarding receiving of the same. Both Copy of form 6 , DRAP acknowledgment for receiving of dapagliflozin are attached. That's why commercial invoice with DRAP approval was not granted.

Decision:

Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Firm shall submit the fee of Rs. 7,500 for revision of specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		
274.	Name, address of Applicant / Marketing Authorization Holder	M/s Ferozsons Laboratories Ltd. P.O Ferozsons, Amangarh, Nowshera-Khyber Pakhtunkhwa
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Ltd. P.O Ferozsons, Amangarh, Nowshera-Khyber Pakhtunkhwa
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27706 dated 06/10/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 9620015101
	The proposed proprietary name / brand name	Dakardi 10mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains; Dapagliflozin propanediol monohydrate eq. to Dapagliflozin…..10mg
	Pharmaceutical form of applied drug	Blue, Round, biconvex coated tablet having "*f*" on one side and plain on other side
	Pharmacotherapeutic Group of (API)	Antidiabetic Drug (Sodium-glucose co-transporters 2 (SGLT2) inhibitor)
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	10's, 14's, 20's, 28's and 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Farxiga 10mg tablet by AstraZeneca Pharmaceuticals LP Wilmington, DE 19850, USFDA Approved
	For generic drugs (me-too status)	Dapwiz 10mg Tablets by M/s Pharmevo Pvt Ltd. - Karachi, Reg. No. 107375
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conductd on 25-01-2019 and valid for 03 years.
	Name and address of API manufacturer.	M/s Fuxin Long Rui Pharmaceutical Co, Ltd – China Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province – 123000 China

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Dapagliflozin is Inhouse, the firm submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, tests for single/total impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (160108, 160124, 160220)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Farxiga 10mg tablet by AstraZeneca Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Farxiga 10mg tablet by AstraZeneca Pharmaceuticals. The dissolution profile of Dakardi 10mg Tablets and Farxiga 10mg Tablet has shown release of more than 85 % in all three Buffer pH 1.2, Phosphate Buffer pH 6.8 and Acetate Buffer pH 4.5 in 30 minutes. And no calculation is required for Similarity factor f2 hence dissolution profile of both Dakardi 10mg tablets and Farxiga 10mg tablet is similar.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical Co, Ltd – China Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province – 123000 China		
API Lot No.	DG-20200107-D01-DG06-01		
Description of Pack (Container closure system)	01 Alu-Alu blister of 14 tablets, packed in cardboard box (Box of 14 tablets)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	DGTab-004	DGTab-005	DGTab-006
Batch Size	750 tablets	750 tablets	750 tablets
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	19-01-2021	19-01-2021	19-01-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product EMPAGEN 10mg & 25mg which was conducted on 24-08-2021 and was presented in 294th meeting of Registration Board held on 9th April , 2020. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML Registration. No. Liao20150233 issued by Food and Drug Administration of Liaoning Province-China valid till 20/12/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 6 , , DRAP acknowledgment for receiving of dapagliflozin ,form3, form 7 and invoice (invoice#HN200716-L) dated : 16-07-2020 specifying import of Dapagliflozin propanediol monohydrate 50gm (Batch# DG-20200107-D01-DG06-01).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.P.5.3	Protocols of analytical validation studies not submitted.	Protocols of analytical validation studies submitted
2.	3.2.P.5.4	In COA's Inhouse specifications mentioned while in section 1.5.6 Innovator specifications claimed. Clarification is required.	Revised COA's with Innovator's specifications are submitted.
3.	3.2.P.8	Submit Commercial invoice with approval from DRAP.	Drug substance was imported against form-6 and the DRAP-Peshawar office was also intimated regarding receiving of the same. Both Copy of form 6 , DRAP acknowledgment for receiving of dapagliflozin are attached. That's why commercial invoice with DRAP approval was not granted.

Decision:

Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

275.	Name, address of Applicant / Marketing Authorization Holder	Bryon Pharmaceuticals Pvt Ltd. 48-Indutiral estate Hayatabad Peshawar Pakistan
	Name, address of Manufacturing site.	Bryon Pharmaceuticals Pvt Ltd. 48-Indutiral estate Hayatabad Peshawar Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale

		☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25526 dated 14/09/2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 4766866794
	The proposed proprietary name / brand name	GLYCEM 500mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Metformin HCL …….500mg
	Pharmaceutical form of applied drug	White Film coated Oblong biconvex tablets having score on one side.
	Pharmacotherapeutic Group of (API)	Anti-diabetic ATC Code:A10BA02
	Reference to Finished product specifications	USP
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	GLUCOPHAGE Tablets 500 mg by M/s Martin Dow Marker Ltd, USFDA Approved.
	For generic drugs (me-too status)	NEOPHAGE 500 mg Tablets by M/s ABBOTT Laboratories Pakistan Ltd Reg. No. 025526
	GMP status of the Finished product manufacturer	Last GMP inspection conducted on 17-10-2019 and reports concludes that firm may be considered operating at satisfactory level of cGMP compliance
	Name and address of API manufacturer.	M/s Smruthi Organics Limited. Plot No: A-27, M.I.D.C. Chincholi, Taluka Mohol Solapur. - 413 255 Maharashtra. INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Metformin Hydrochloride is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity etc & related substances (impurity & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container

		closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MFH-001/07, MFH-002/07, MFH-003/07,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is GLUCOPHAGE 500mg Tablets by M/S Martin Dow Marker Ltd by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Glucophage 500mg tablet by M/S Martin Dow Marker Ltd in Acid media (pH 1.2, 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA

Manufacturer of API	M/s **Smruthi Organics Limited.** Plot No: A-27, M.I.D.C. Chincholi, Taluka Mohol Solapur 4 1 3 2 5 5 Maharashtra. INDIA.		
API Lot No.	MET-587/19		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's & 28's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 18 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2,3 & 6 (Months) Real Time: 0, 1,3, 6 ,9,12,18 (Months)		
Batch No.	TB-295	TB-296	TB-297
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	01-02-2020	01-02-2020	01-02-2020

No. of Batches	03	
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. NEW-WHO-GMP/CERT/PD/86368/2019/11/30111 issued by F&DA Maharashtra State INDIA valid till 13/11/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 5, form 3 form 7 & invoice (invoice# E-038) dated : 31-05-2019 cleared by DRAP Peshawar office dated 13.06-2019 specifying import of Metformin HCl (Batch# Met-587/19).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 s	Batch Manufacturing Record (BMR) for all the batches of drug product are submitted.
2.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product	Blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product is submitted.
3.	3.2.S.4.1	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is submitted.

		Drug substance & Drug Product manufacturer is required. • Specification claimed for drug substance are B.P while drug product specification claimed are USP. Clarification is required why B.P grade material is used.	• The drug substance specification is BP while Drug product is claimed USP. 1) The API manufacturer /Source claims its specification a per BP and DMF data provided as per BP specification. 2) Finished Product/ Drug product is available I both USP and BP As per DRAP guidelines if Drug product is available in various pharmacopeia priority order of Label claims specifications should be USP, BP, Eur and Japanese etc, so by following guidelines of DRAP we claim our Drug product as per USP.
4.	3.2.S.4.3	Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Shall be submitted.	Method Verification studies including performed by the Drug Product manufacturer for drug substance is submitted.
5.	3.2.S.4.5	COA of primary / secondary reference standard including source and lot number shall be provided	COA of primary / secondary reference standard is submitted.
6.	3.2.P.5.1	From specification of dissolution testing of drug product it is not evident which test of dissolution from USP monograph was adopted. Clarification is required.	Dissolution Test 1 applied.
7.	3.2.P.8	• Documents for the procurement of with approval from DRAP.	Submitted.

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

Case no. 02 Registration applications on Form 5 for local manufacturing of (Human) drugs

a. Deferred cases (Form 5)

276.	Name and address of manufacturer / Applicant	M/s Mediate Pharmaceutical Pvt Ltd. Plot No. 150-151, Sector 24, Korangi Industrial Area, Karchi, Pakistan
	Brand Name +Dosage Form + Strength	Medforge 5/80/12.5mg Tablet
	Composition	Each Film Coated Tablet Contains: Amlodipine as besylate…5mg Valsartan…80mg Hydrochlorothiazide…12.5mg
	Diary No. Date of R& I & fee	Dy.No. 9806 dated 04-03-2019 Rs.20,000/- Dated 04-02-2019
	Pharmacological Group	Anti-hypertension
	Type of Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status	Not found
	GMP status	Last GMP inspection conducted on 02-04-2019, and report concludes firm was considered to be operating at an acceptable level of good compliance with GMP guidelines
	Remarks of the Evaluator	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Previous decision	Deferred for following: • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board.(M-295)
	Evaluation by PEC: Now firm change formulations without submission of fee and also firm said that consider the same fee as for "Medforge 5/80/12.5mg Tablet". Formulation is as follows	
	Brand Name +Dosage Form + Strength	Medforge 5/160/12.5mg Tablet
	Composition	Each Film Coated Tablet Contains: Amlodipine as besylate…5mg Valsartan…160mg Hydrochlorothiazide…25mg
	Finished product Specifications	USP
	Approval status of product in Reference Regulatory Authorities	Exforge HCT 5/160/25 by Novartis (USFDA)

	Me-too status	Exforge HCT By Novartis (Reg. No. 069549)
	Previous Decision (M- 317): Deferred for clarification whether in applied formulation Hydrochlorthiazide is 25mg or 12.5mg.	
	Evaluation by PEC: Firm replied that they have registered product Alpertan Tablet 5/160/12.5mg so request for change of formulation without submission of fee as follows	
	Brand Name +Dosage Form + Strength	Medforge 5/80Tablet
	Composition	Each Film Coated Tablet Contains: Amlodipine as besylate…5mg Valsartan…80mg
	Finished product Specifications	USP
	Approval status of product in Reference Regulatory Authorities	Exforge 5/80 by Novartis (USFDA)
	Me-too status	Exforge By Novartis (Reg. No. 047569)
	Decision: Approved with USP specifications. • **Firm shall submit the fee of Rs. 30,000 for correction/pre-approval change in composition (correction/change Strength of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
277.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Dron 70mg Tablet
	Composition	Each Tablet Contains: Alendronate Sodium Eq. to Alendronic Acid…70mg
	Diary No. Date of R& I & fee	Dy.No. 14400 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Bisphosphonate (Antiosteoporotic)
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Alendronic Acid 70mg of MHRA approved
	Me-too status (with strength and dosage form)	Bonafide Tablets 70mg by M/s Medisure Labs.
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	Available in USP Pharmacopeia
	Decision: Approved with USP specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
278.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Aricure 50mg/5ml IV Injection
	Composition	Each 5ml Ampoule Contains: Atracurium Besylate…50mg

	Diary No. Date of R& I & fee	Dy.No. 14328 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Non depolarizing muscle relaxant
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Tracrium Injection10mg/ml of MHRA approved
	Me-too status (with strength and dosage form)	Atrium Injections by M/s Searle Pakistan, Karachi (Reg#053342)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications .	
279.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Aripine 1mg/ml Injection
	Composition	Each 1ml Ampoule Contains: Atropine Sulphate…1mg
	Diary No. Date of R& I & fee	Dy.No. 14385 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Anticholinergic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Atropine Sulfate Injection 1mg in 1 ml of MHRA approved
	Me-too status (with strength and dosage form)	Swiss Atropine 1mg/ml Injectionof M/s Swiss pharma, (Reg#044290**)**
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	Available in USP pharmacopeia
	Decision: Approved with USP Specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
280.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Bamral 20mg Tablet
	Composition	Each Tablet Contains: Bambuterol Hcl…20mg

	Diary No. Date of R& I & fee	Dy.No. 14367 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Long acting beta adrenoceptor agonist
	Type of Form	Form 5
	Finished product Specifications	Manufacturers specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Bambec Tablet of (MHRA Approved)
	Me-too status (with strength and dosage form)	Basthma tablet 10mg of M/s Polyfine Chempharma
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
281.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Clomix 75mg Tablet
	Composition	Each Film Coated Tablet Contains: Clomipramine HCl……75mg
	Diary No. Date of R& I & fee	Dy.No. 14402 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Antidepressant
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Clomipramine HCl by sandoz ANSM france Approved
	Me-too status (with strength and dosage form)	Clomipril Tablets of M/s Libra Reg# 027816
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
282.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Desatil 2.5mg/5ml Syrup

	Composition	Each 5ml contains: Desloratadine…2.5mg
	Diary No. Date of R& I & fee	Dy.No. 14360 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiallergic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Clarinex of (USFDA approved)
	Me-too status (with strength and dosage form)	Desora Syrup by M/s S.J &G. Fazul Ellahie
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
283.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Ibudex 200mg Tablet
	Composition	Each Film Coated Tablet Contains: Dexibuprofen…200mg
	Diary No. Date of R& I & fee	Dy.No. 14395 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	NSIADs
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	As Per SRO
	Approval status of product in Reference Regulatory Authorities	Dexibuprofen of (MHRA approved)
	Me-too status (with strength and dosage form)	Bekonil 200mg Tablet of M/s Martin Dow
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
284.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k

	Brand Name +Dosage Form + Strength	Arinate 50mg/ml Injection
	Composition	Each 1ml Ampoule Contains: Dimenhydrinate…50mg
	Diary No. Date of R& I & fee	Dy.No. 14374 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antihistamine
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	As Per SRO
	Approval status of product in Reference Regulatory Authorities	Dimenhydrinate Inj of Fresenius kabi, USFDA
	Me-too status (with strength and dosage form)	Dirinate Injection Each Ml Ampoule Contains:- Dime of M/s Elite Pharma
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	Available in USP Pharmacopeia
	Decision: Approved with USP specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
285.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Co-Besart 300/12.5 mg Tablet
	Composition	Each Film Coated Tablet Contains: Irbesartan…300mg Hydrochlorothiazide…12.5mg
	Diary No. Date of R& I & fee	Dy.No. 14380 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Angiotensin receptor blockers/diuretics
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	AVALIDE of (USFDA approved)
	Me-too status (with strength and dosage form)	Irbest Plus Tablets of M/s Highnoon Laboratories
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
286.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k

	Brand Name +Dosage Form + Strength	Ketalog 500mg/10ml Injection
	Composition	Each 10ml Ampoule Contains: Ketamine Hcl Eq. to Ketamine…500mg
	Diary No. Date of R& I & fee	Dy.No. 14392 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	General Anesthesic
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	2ml x 5's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Ketalar 50 mg/ml Injection, of MHRA approved 10ml
	Me-too status (with strength and dosage form)	Katafast 500mg Injection by M/s Vision
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
287.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Ketor 30mg/ml Injection
	Composition	Each 1ml ampoule contains: Ketorolac Tromethamine…30mg
	Diary No. Date of R& I & fee	Dy.No. 14394 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Analgesic
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Toradol 30mg/ml of TGA approved
	Me-too status (with strength and dosage form)	Ketopan Injection 30mg by M/s Welwrd Pharmaceuticals,
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
288.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Aricain 10mg/ml Injection
	Composition	Each 1ml Ampoule Contains: Lidocaine Hcl…10mg

	Diary No. Date of R& I & fee	Dy.No. 14373 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Local anaesthetic
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Lidocaine Injection 1% w/v (MHRA approved)
	Me-too status (with strength and dosage form)	Lacain 1% Injection of M/s. Pulse Pharmaceuticals
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
289.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Co-Locor 50/12.5 mg Tablet
	Composition	Each Film Coated Tablet Contains: Losartan Potassium…50mg Hydrochlorothiazide…12.5mg
	Diary No. Date of R& I & fee	Dy.No. 14359 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antihypertensive(Angiotensin II Receptor Antagonist,Thiazide Diuretic)
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Cozaar Comp 50 mg/12.5 mg of (MHRA Approved)
	Me-too status (with strength and dosage form)	Lotass Plus 50mg/12.5mg of M/S Getz pharma
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
290.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Prox 37.5mg CR Tablet
	Composition	Each Enteric Film Coated Controlled Release Tablet Contains: Paroxetine Hcl Eq. to Paroxetine…37.5mg

	Diary No. Date of R& I & fee	Dy.No. 14357 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Selective serotonin-reuptake inhibitors
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	PAXIL CR of (USFDA approved)
	Me-too status (with strength and dosage form)	Paraxyl CR M/s CCL Pharmaceuticals
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
291.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Arixicam IM 20mg/ml Injection
	Composition	Each 1ml Ampoule Contains: Piroxicam…20mg
	Diary No. Date of R& I & fee	Dy.No. 14393 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Anti-rheumatic
	Type of Form	Form -5
	Finished product Specifications	Manufacturers specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved by ANSM of France
	Me-too status (with strength and dosage form)	Salden 20mg Injection of M/s Danas Pharmaceutical(Reg.#080373)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
292.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Thioside 4mg/2ml Injection
	Composition	Each 2ml Ampoule Contains: Thiocolchicoside……4mg

	Diary No. Date of R& I & fee	Dy.No. 14382 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Skeletal Muscle Relaxant
	Type of Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Coltramyl Injection by M/s Sanofi Aventis ANSM France
	Me-too status (with strength and dosage form)	Myovi 4mg/2ml Injection by Macter International (Reg. No. 058692)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
293.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Aricure 30mg/3ml Injection
	Composition	Each 3ml Ampoule Contains: Atracurium Besylate…30mg
	Diary No. Date of R& I & fee	Dy.No. 14387 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Non-depolarizing skeletal muscle relaxant
	Type of Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	Not found
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	• Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Firm provided Atracurium 10mg/ml Solution for Injection or Infusion of MHRA approved. But 3ml volume not available in MHRA
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for following: • **Evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.**	

	• **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.**	
294.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Bamral 5mg/5ml Syrup
	Composition	Each 5ml Contains: Bambuterol Hcl…5mg
	Diary No. Date of R& I & fee	Dy.No. 14370 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Selective beta-2-adrenoreceptor agonists
	Type of Form	Form 5
	Finished product Specifications	Manufacturers specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Bambuterol juice 1mg/ml by AstraZaneca (Germany)
	Me-too status (with strength and dosage form)	Btno 5mg/5ml syrup by M/s Genix (Reg# 057873)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
295.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Dobicard 250mg/5ml IV Injection
	Composition	Each 5ml Ampoule Contains: Dobutamine Hcl…250mg
	Diary No. Date of R& I & fee	Dy.No. 14391 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	General anesthetic
	Type of Form	Form-5
	Finished product Specifications	USP Specs.
	Pack size & Demanded Price	As Per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	Botamin Injection by M/s Fynk Pharmaceuticals
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	Firm submitted fee of Rs: 5000/- Deposit slip No# 1984287,Dated: and Revise formulation as follows Dobicard 250mg/20ml IV Injection Each 20ml Contains: Dobutamine Hcl…250mg

		Dobutrex dobutamine 250mg/20ml injection solution of TGA approved Dobutamine Injection 250mg/20ml of Haji medicine (Reg # 027345)
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications as per following label claim: **Each 20ml Contains:** **Dobutamine HCl…250mg** • **Firm shall submit the remaining fee of Rs. 25,000 for correction/pre-approval change in composition (correction/change of strength of drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
296.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Levon 1.5mg Tablet
	Composition	Each Tablet Contains: Levonorgestrel…1.5mg
	Diary No. Date of R& I & fee	Dy.No. 14365 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Hormonal contraceptives for systemic use
	Type of Form	Form -5
	Finished product Specifications	BP
	Pack size & Demanded Price	1 x 10's , 1 x 20's, 1 x 30's:as per SRO
	Approval status of product in Reference Regulatory Authorities	Ezinelle 1.5 mg tablet of MHRA approved
	Me-too status (with strength and dosage form)	Emkit-DS tablet 1.5mg of Zafa Pharma Reg # 032543.
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	The firm change formulation from film coated to un coated with submission of fee of Rs: 5000/- Deposit slip No # 1984286, Dated : 07-08-2020.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with BP specifications. • **Firm shall submit the remaining fee of Rs. 2,500 for correction/pre-approval change in composition (correction/change of formulation from film-coated tablet to uncoated tablet), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
297.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Mebofac MR 200mg Capsule
	Composition	Each Capsule Contains: Enteric Coated Pellets Mebeverie Hcl 50% Eq. to Mebeverie Hcl…200mg
	Diary No. Date of R& I & fee	Dy.No. 14372 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Anti-spasmodic
	Type of Form	Form-5

	Finished product Specifications	Manufacturers
	Pack size & Demanded Price	10's, 30's & 40's & as per SRO
	Approval status of product in Reference Regulatory Authorities	MHRA Approved
	Me-too status (with strength and dosage form)	Mebever MR capsule of M/s Getz Pakistan (050747)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	Source of pellets : Vision pharmaceuticals
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator' specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
298.	Name and address of manufacturer / Applicant	M/s Aries Pharmaceuticals. 1-W, Industrial Estate, Hayatabad, Peshawar, k.p.k
	Brand Name +Dosage Form + Strength	Averon 4mg Tablet
	Composition	Each film coated Tablet Contains: Ondansetron Hcl Dihydrate Eq. to Ondansetron…….4mg
	Diary No. Date of R& I & fee	Dy.No. 14389 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Selective serotonin 5-HT3 receptor antagonist
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's, 20's, 30's,50's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZOFRAN Of (USFDA Approved)
	Me-too status (with strength and dosage form)	Ondonix 4mg Tablet M/s Genix Pharma
	GMP status	cGMP certificate on the basis of Evaluation conducted on 06-04-2022 and valid for two (02) Years.
	Previous remarks of the Evaluator.	• The firm change formulation from uncoated to film coated with submission of fee of Rs: 5000/- Deposit slip No # 1984285, Dated : 07-08-2020
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications. • **Firm shall submit the remaining fee of Rs. 2,500 for correction/pre-approval change in composition (correction/change of formulation from un coated tablet to film coated tablet), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
299.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Exor-H 5/160/12.5 mg Tablet
	Composition	Each Film Coated Tablet Contains:

		Amlodipine Besylate Eq. to Amlodipine…5mg Valsartan…160mg Hydrochlorothiazide…12.5mg
	Diary No. Date of R& I & fee	Dy.No. 14301 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Anti-hypertensive
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	14's, 28's : As per SRO
	Approval status of product in Reference Regulatory Authorities	Exforge Hct Of (USFDA Approved)
	Me-too status (with strength and dosage form)	Exforge Hct Of M/S Novartis Pharma
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	Available in USP Pharmacopeia
	Decision: Approved with USP specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
300.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Adzon Gel
	Composition	Each Gm Contains: Adapalene…1mg (0.1% w/w) Benzoyl Peroxide…25mg (2.5% w/w)
	Diary No. Date of R& I & fee	Dy.No. 14074 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Retinoids for topical use in acne
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	15gm, 30gm, 45gm, 60gm & 90gm ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Epiduo gel of (USFDA Approved)
	Me-too status (with strength and dosage form)	Adalen e-B Gel of M/s Pharmatec (Reg#076683)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications.	

	• **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
301.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	I Rot Tablet 5mg
	Composition	Each Tablet Contains: Folic Acid…5mg
	Diary No. Date of R& I & fee	Dy.No. 17447 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Vitamin B9
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's,20's, 30-'s, 100's: As per SRO
	Approval status of product in Reference Regulatory Authorities	MHRA Approved
	Me-too status (with strength and dosage form)	Zal 5mg Tablets of M/s Alsons Pharmaceuticals
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP Specifications.	
302.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Rogex 80mg Injection
	Composition	Each 2ml Contains: Gentamycin Sulphate Eq. to Gentamycin…80mg
	Diary No. Date of R& I & fee	Dy.No. 14295 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Aminoglycoside
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	2ml x 5's : As per SRO
	Approval status of product in Reference Regulatory Authorities	Gentamicin 40 mg/ml, solution for injection/infusion of MHRA approved
	Me-too status (with strength and dosage form)	Fengen Injection 80m of M/ Fynk Pharmaceuticals Reg # 065892
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	

	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
303.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Ketrox 2% w/v Lotion
	Composition	Each ml Contains: Ketoconazole…20mg
	Diary No. Date of R& I & fee	Dy.No. 14063 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Antifungal for topical use (Imidazole and triazole derivative)
	Type of Form	Form-5
	Finished product Specifications	JP
	Pack size & Demanded Price	60ml, 90ml :As per SRO
	Approval status of product in Reference Regulatory Authorities	Nizoral Anti-Dandruff Shampoo by M/s McNeil Products Limited (MHRA Approved)
	Me-too status (with strength and dosage form)	Ketonaz Lotion by M/s Sante (Reg#073453)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	Shampoo available in BP pharmacopeia
	Decision: Approved with BP specifications as per following brand name and label claim: **Ketrox 2% w/w Shampoo** **Each gram of shampoo contains:** **Ketoconazole……20mg** • **Firm shall submit the fee of Rs. 30,000 for correction/pre-approval change in composition (correction/change of salt form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
304.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Zefen 1mg Tablet
	Composition	Each Tablet Contains: Ketotifen Hydrogen Fumarate eq to Ketotifen……..1mg
	Diary No. Date of R& I & fee	Dy.No. 17454 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antihistamines
	Type of Form	Form-5
	Finished product Specifications	Manufacturer Specification
	Pack size & Demanded Price	20's, 30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZADITEN of (MHRA approved)

	Me-too status (with strength and dosage form)	Bronk 1 mg Tablet of Semos Pharmaceuticals
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
305.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Maxotex 10mg Tablet
	Composition	Each Tablet Contains: Metoclopramide HCl eq to Metoclopramide (Anhydrous)…10mg
	Diary No. Date of R& I & fee	Dy.No. 17430 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Anti-dopaminergic
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's, 100's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Maxolon 10mg Tablets of MHRA approved
	Me-too status (with strength and dosage form)	Faclomide 10mg Tablets of M/s Farm Aid Group
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications.	
306.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Dekzol 2% w/w Oral Gel
	Composition	Each Gm Contains: Miconazole…20mg
	Diary No. Date of R& I & fee	Dy.No. 14072 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Antiinfective/ Antiseptic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	20gm: As per SRO
	Approval status of product in	Daktarin Oral Gel of MHRA approved

	Reference Regulatory Authorities	
	Me-too status (with strength and dosage form)	Miconit Oral Gel 2% of M/s Bio-Labs (Reg. # 054776)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
307.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Rifapen Forte Tablet
	Composition	Each Film Coated Tablet Contains: Rifampicin…150mg Isoniazid…75mg Ethambutol Hcl…275mg Pyrazinamide…400mg
	Diary No. Date of R& I & fee	Dy.No. 14253 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Anti-tubercular drugs
	Type of Form	Form 5
	Finished product Specifications	IP
	Pack size & Demanded Price	50's, 80's, 100's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Rimstar, 150 mg/75 mg/400 mg/275 mg film-coated tablet. by M/s Sandoz (Swedish Medical Products Agency Approved)
	Me-too status (with strength and dosage form)	Myrin P Forte Tablets by M/s Wyeth, (Reg#027082)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	WHO prequalified
	Decision: Approved with International Pharmacopoeia specifications.	
308.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Rocept Injection 440mg/20ml
	Composition	Each Vial Contains: Trastuzumab…440mg
	Diary No. Date of R& I & fee	Dy.No. 14265 dated 07-03-2019 Rs.20,000/- Dated 07-02-2019
	Pharmacological Group	Monoclonal antibody

	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	20ml x 1's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	HERCEPTIN 440MG by M/s ROCHE
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board referred the case to biological division.	
309.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Warfix 5mg Tablet
	Composition	Each Tablet Contains: Warfarin Sodium…5mg
	Diary No. Date of R& I & fee	Dy.No. 17432 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Thromboembolic conditions
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	100's,: As per SRO
	Approval status of product in Reference Regulatory Authorities	COUMADIN of USFDA approved
	Me-too status (with strength and dosage form)	Coagurin 5mg Tablets of M/s Atco Laboratories
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications.	
310.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Clintop Gel
	Composition	Each gm Contains: Clindamycin as phosphate….10mg
	Diary No. Date of R& I & fee	Dy.No. 14073 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Anti-infective
	Type of Form	Form 5
	Finished product Specifications	USP

	Pack size & Demanded Price	10gm, 20gm : As per SRO
	Approval status of product in Reference Regulatory Authorities	RESIDERM 1%w/w GEL (MHRA approved)
	Me-too status (with strength and dosage form)	Sixil 10mg/g Gel of M/s Sigma Pharma (Reg # 079912)
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications.	
311.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Edoban 15mg Tablet
	Composition	Each Film Coated Tablet Contains: Edoxaban Tosilate Eq. to Edoxaban…15mg
	Diary No. Date of R& I & fee	Dy.No. 13933 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Antithrombotic agent
	Type of Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 20's, 30's : As per SRO
	Approval status of product in Reference Regulatory Authorities	Lixiana 15 mg film-coated tablets of MHRA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	Submit Stability studies along with requisite documents.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board deferred the case for submission of stability study data as per the guidelines provided in 293rd meeting of Registration Board.	
312.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Ercaf 1/100 mg Tablet
	Composition	Each Film Coated Tablet Contains: Ergotamine Tartrate…1mg Caffeine…100mg

	Diary No. Date of R& I & fee	Dy.No. 13936 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Ergot Alkaloid/ Xanthine
	Type of Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's, 20's, 30's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Cafergot of USFDA approved
	Me-too status (with strength and dosage form)	Cafergot TAB of M/s SANDOZ
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications.	
313.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Fidox 200mg Tablet
	Composition	Each Film Coated Tablet Contains: Fidaxomicin…200mg
	Diary No. Date of R& I & fee	Dy.No. 13931 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5D
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	10's,c 20's, 30's: As per SRO
	Approval status of product in Reference Regulatory Authorities	DIFICLIR 200 mg film-coated tablets of MHRA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	Submit Stability studies along with requisite documents.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board deferred the case for submission of stability study data as per the guidelines provided in 293rd meeting of Registration Board.	

314.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Verlin 1mg Tablet
	Composition	Each Film Coated Tablet Contains: Varenicline Tartrate Eq. to Varenicline…1mg
	Diary No. Date of R& I & fee	Dy.No. 13730 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Nicotinic acetylcholine receptor partial agonist/smoking cessation aid
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 20's, 30's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Prograf of USFDA approved
	Me-too status (with strength and dosage form)	Chantix 1.0mg Of M/S Parke Davis & Company (Reg.# 045698)
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
315.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Riocig 0.5mg Tablet
	Composition	Each Film Coated Tablet Contains: Riociguat…0.5mg
	Diary No. Date of R& I & fee	Dy.No. 13725 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Anti hypertensive
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	30's, 60's, :As per SRO
	Approval status of product in Reference Regulatory Authorities	Adempas of USFDA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and

		report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	Submit Stability studies along with requisite documents.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board deferred the case for submission of stability study data as per the guidelines provided in 293rd meeting of Registration Board.	
316.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Pirnix 534 mg Tablet
	Composition	Each Film Coated Tablet Contains: Pirfenidone…534mg
	Diary No. Date of R& I & fee	Dy.No. 13963 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Anti-fibrotic
	Type of Form	Form-5D
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	7's, 14, 21;s :As per SRO
	Approval status of product in Reference Regulatory Authorities	Esbriet 534 mg film-coated tablets of MHRA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	Submit Stability studies along with requisite documents.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board deferred the case for submission of stability study data as per the guidelines provided in 293rd meeting of Registration Board.	
317.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Obecol 10mg Tablet
	Composition	Each Film Coated Tablet Contains: Obeticholic Acid…10mg
	Diary No. Date of R& I & fee	Dy.No. 13928 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Bile acid prepartions
	Type of Form	Form-5D

	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	10's, 20, 30;s :As per SRO
	Approval status of product in Reference Regulatory Authorities	OCALIVA 5 mg film-coated tablets of MHRA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	Submit Stability studies along with requisite documents.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board deferred the case for submission of stability study data as per the guidelines provided in 293rd meeting of Registration Board.	
318.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Zovir 250mg/10ml Injection
	Composition	Each 10ml Vial Contains: Acyclovir…250mg
	Diary No. Date of R& I & fee	Dy.No. 14299 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiviral
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's (10ml); As per SRO
	Approval status of product in Reference Regulatory Authorities	Zovirax I.V. 250 mg of MHRA approved
	Me-too status (with strength and dosage form)	Aclovir 250mg Powder for infusion of Genix pharma Reg# 073690
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for confirmation of required manufacturing facility / section (lyophilized vial General section)	
319.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Zovir 500mg/20ml Injection
	Composition	Each 20ml vial Contains: Acyclovir…500mg

	Diary No. Date of R& I & fee	Dy.No. 14298 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiviral
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's (20ml) ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Zovirax I.V. 500 mg of MHRA approved
	Me-too status (with strength and dosage form)	Aclovir 500mg Powder for infusion of Genix pharma Reg# 073691
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for confirmation of required manufacturing facility / section (lyophilized vial General)	
320.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Beta One Lotion 0.1%
	Composition	Each ml contains: Betamethasone valerate…0.1% w/w
	Diary No. Date of R& I & fee	Dy.No. 17417 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Corticosteroids
	Type of Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	60ml, As per SRO
	Approval status of product in Reference Regulatory Authorities	Betnovate Lotion 0.1% w/w by (MHRA Approved
	Me-too status (with strength and dosage form)	Betamethasone Lotion by M/s Werrick Pharmaceuticals, (Reg# 051176)
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications.	
321.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Clintek Gel
	Composition	Each Gm Contains:

		Clindamycin Phosphate…12mg (1.2 % w/w) Tretinoin…0.25mg (0.025% w/w)
	Diary No. Date of R& I & fee	Dy.No. 14070 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Anti-Acne (Treatment of acne vulgaris)
	Type of Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	20gm ; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZIANA (Gel) of USFDA approved
	Me-too status (with strength and dosage form)	Clin Gel 20g Gel of M/s Linta pharmaceuticals
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
322.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Uric Tablet 120mg
	Composition	Each Film Coated Tablet Contains: Febuxostat…120mg
	Diary No. Date of R& I & fee	Dy.No. 17443 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antigout preparation(Non-purine xanthine oxidase Inhibitor)
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	20's: As per SRO
	Approval status of product in Reference Regulatory Authorities	ADENURIC 120 mg film-coated tablets of MHRA approved
	Me-too status (with strength and dosage form)	Gouric 120mg Tablet of M/s Pharmevo (Reg # 080284)
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

323.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Irofit Tablet 20mg/2.5mg
	Composition	Each Film Coated Tablet Contains: Iron protein succinylate 400mg eq to elemental iron …20mg Folic Acid……..2.5mg
	Diary No. Date of R& I & fee	Dy.No. 17427 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antianemic preparations
	Type of Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 14's, 20's , :As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	Eisen Tablets of Genome Pharmaceuticals
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: The Board deferred the case for submission of detail of specifications and complete analytical method for the applied product.	
324.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Methane 1% w/v Lotion
	Composition	Each ml Contains: Permethrin…10mg
	Diary No. Date of R& I & fee	Dy.No. 14296 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Pyrethroid insecticide
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	30ml: As per SRO
	Approval status of product in Reference Regulatory Authorities	Nix lotion of USFDA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status)

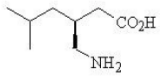
		along with registration number, brand name and name of firm.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
325.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Proman 10mg/ml Injection
	Composition	Each ml contains: Protamine sulphate…10mg
	Diary No. Date of R& I & fee	Dy.No. 14263 dated 07-03-2019 Rs.20,000/- Dated 07-02-2019
	Pharmacological Group	Antidote to heparin
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	5ml x 1's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Protamine Sulfate 10mg/ml Solution for Injection of MHRA approved
	Me-too status (with strength and dosage form)	Protamine Sulphate Injection of M/s Isman Drugs House Lahore. (Reg.# 008853)
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	Source: Biological
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Registration Board referred the case to Biological Division.	
326.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Rancol xr 1000mg
	Composition	Each film coated extended release tablet contains: Ranolazine…1000mg
	Diary No. Date of R& I & fee	Dy.No. 17435 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Anti-Anginal
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	14's :As per SRO
	Approval status of product in Reference Regulatory Authorities	RANEXA of USFDA Approved
	Me-too status (with strength and dosage form)	Ranoline SR 1000mg Tablet (Reg# 078790) by Searle IV Solutions
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022

	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
327.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Ilazole 10mg Tablet
	Composition	Each Enteric Coated Tablet Contains: Ilaprazole……10mg
	Diary No. Date of R& I & fee	Dy.No. 13960 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Proton pump inhibitor
	Type of Form	Form-5D
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	30's, 60's:As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	• Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for following: • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board.**	
328.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Ilazole 20mg Tablet
	Composition	Each Enteric Coated Tablet Contains: Ilaprazole……20mg

	Diary No. Date of R& I & fee	Dy.No. 13961 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Proton pump inhibitor
	Type of Form	Form-5D
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	30's, 60's:As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 12-02-2020 and report concludes that Based on the area inspected. The people met and the document reviewed and considering the findings of the inspection firm was considered to be operating at a good level of compliance with cGMP guideline as of today.
	Previous remarks of the Evaluator.	• Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for following: • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board.**	
329.	Name and address of manufacturer / Applicant	M/s Medimarker's Labortaries Pvt Ltd A-104, S.I.T.E Area, Hyderabad
	Brand Name +Dosage Form + Strength	Cefmark 250mg/Vial I.M Dry Powd
	Composition	Each Vial Contains: Ceftriaxone as Sodium…250mg
	Diary No. Date of R& I & fee	Dy.No. 17159 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Cephalosporin
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Rocephin I.M injection of (MHRA approved)
	Me-too status (with strength and dosage form)	Accucef 250 mg IM Injection M/s Wel Wink Pharmaceuticals,
	GMP status	Last GMP inspection of conducted on 16-10-2018 and the report concludes that the panel unanimously recommend the grant of renewal DML

	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications. Registration letter will be issued after submission of updated GMP status of the firm.	
330.	Name and address of manufacturer / Applicant	M/s Medimarker's Labortaries Pvt Ltd A-104, S.I.T.E Area, Hyderabad
	Brand Name +Dosage Form + Strength	Cefmark 500mg/Vial I.M Dry Powd
	Composition	Each Vial Contains: Ceftriaxone as Sodium…500mg
	Diary No. Date of R& I & fee	Dy.No. 17154 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Cephalosporin
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Rocephin I.M injection of (MHRA approved)
	Me-too status (with strength and dosage form)	Wixone 500 mg Injection IM M/s Wise Pharmaceuticals,
	GMP status	Last GMP inspection of conducted on 16-10-2018 and the report concludes that the panel unanimously recommend the grant of renewal DML
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications. Registration letter will be issued after submission of updated GMP status of the firm.	
331.	Name and address of manufacturer / Applicant	M/s Medimarker's Labortaries Pvt Ltd A-104, S.I.T.E Area, Hyderabad
	Brand Name +Dosage Form + Strength	Cefmark 1gm/Vial I.M Dry Powd
	Composition	Each Vial Contains: Ceftriaxone as Sodium…1gm
	Diary No. Date of R& I & fee	Dy.No. 17179 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Cephalosporin
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Rocephin I.M injection of (MHRA approved)
	Me-too status (with strength and dosage form)	Accucef 1gm IM Injection M/s Wel Wink Pharmaceuticals,
	GMP status	Last GMP inspection of conducted on 16-10-2018 and the report concludes that the panel unanimously recommend the grant of renewal DML

	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Approved with USP specifications. Registration letter will be issued after submission of updated GMP status of the firm.	
332.	Name and address of manufacturer / Applicant	M/s Medimarker's Labortaries Pvt Ltd A-104, S.I.T.E Area, Hyderabad
	Brand Name +Dosage Form + Strength	Medifik 2% Cream
	Composition	Each Gram Contains: Fusidic Acid…20mg
	Diary No. Date of R& I & fee	Dy.No. 17165 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Anti-bacterial
	Type of Form	Form-5
	Finished product Specifications	BP
	Pack size & Demanded Price	5gm, 15gm /As per SRO
	Approval status of product in Reference Regulatory Authorities	Fucidin of MHRA Approved
	Me-too status (with strength and dosage form)	Ucid 2% Cream by Ciba Pharma (Reg. No. 081566)
	GMP status	Last GMP inspection of conducted on 16-10-2018 and the report concludes that the panel unanimously recommend the grant of renewal DML
	Previous remarks of the Evaluator.	• Availability of Cream sections could not be confirmed.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision: Deferred for confirmation of required manufacturing facility / section (Cream sections)	
333.	Name and address of manufacturer / Applicant	M/s Genix Pharma Pvt Ltd. 44,45-B, Korangi Creek Road, Karachi, 75190, Pakistan
	Brand Name +Dosage Form + Strength	Seipil ER 330mg Tablet
	Composition	Each film coated Extended Release Tablet Contains: Pregabalin…330mg
	Diary No. Date of R& I & fee	Dy.No. 13930 dated 07-03-2019 Rs.50,000/- Dated 06-03-2019
	Pharmacological Group	Anti-epileptic
	Type of Form	Form-5D
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	10’s, 20’s, 30’s, 60’s, 100’s :As per SRO
	Approval status of product in Reference Regulatory Authorities	LYRICA CR of USFDA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	Last inspection was conducted on 10-04-2019 and report concludes that firm is operating at an

		acceptable level of cGMP compliance.
	Previous remarks of the Evaluator.	Submit Stability studies along with requisite documents.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	In USFDA description of product as follows: **11 DESCRIPTION** LYRICA CR (pregabalin extended-release) tablets are for oral use and contain pregabalin. Pregabalin is described chemically as (*S*)-3-(aminomethyl)-5-methylhexanoic acid. The molecular formula is $C_8H_{17}NO_2$ and the molecular weight is 159.23. The chemical structure of pregabalin is:  Pregabalin is a white to off-white, crystalline solid with a pK_{a1} of 4.2 and a pK_{a2} of 10.6. It is freely soluble in water and both basic and acidic aqueous solutions. The log of the partition coefficient (n-octanol/0.05M phosphate buffer) at pH 7.4 is – 1.35. LYRICA CR extended-release tablets are administered orally and contain 82.5, 165, or 330 mg of pregabalin, along with Kollidon SR (polyvinyl acetate, povidone, sodium lauryl sulphate, and silica), crospovidone, polyethylene oxide, carbomer, magnesium stearate, polyvinyl alcohol, titanium dioxide, talc, polyethylene glycol, and colorants as inactive ingredients.
	Decision: Registration Board deferred for submission of stability study data as per the guidelines provided in 293rd meeting of Registration Board.	

Case no. 02 Registration applications of newly granted DML or New section (Human)

a. New DML

M/s Swera Pharmaceuticals**. (New DML)**

CLB in its 282nd meeting held on 31st August 2021 has considered and approved the grant of Drug Manufacturing License by way of formulation with following six (06) sections to M/s Swera Pharmaceuticals

1	Tablet(General)	4	Cream/ Gel (General)
2	Capsule (General)	5	Lotion Section (General)
3	Sachet (General)	6	Dry Powder Injection (General)

Accordingly, firm has applied for following products for consideration by Drug Registration Board.

Capsule (General)
04 Molecules/ 06 Products

334.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4, National Industrial Zone, Rawat, Islamabad
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4 National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 2365 dated 25-01-2022

	Details of fee submitted	PKR 30,000/-: Deposit Slip No# 64944411
	The proposed proprietary name / brand name	Login 50mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Diclofenac Sodium (as 32% Enteric coated pellets)…50mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Non steroidal anti inflammatory Drugs
	Reference to Finished product specifications	Innovator specifications
	Proposed Pack size	2 x 10's , 3 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Difene 50mg Capsules of Ireland approved
	For generic drugs (me-too status)	Diclogesic 50mg Capsule by Wilson Pharmaceuticals Reg. No. 011892
	GMP status of the Finished product manufacturer	New DML letter issued dated; 16-09-2021
	Name and address of API manufacturer.	Vision Pharmaceuticals (pvt) Ltd Plot3 22-23, Industrial Triangle, Kahutta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Mobikare 50mg Capsule. By M/s Barret Hodgson by performing quality tests (Identification, Assay, and dissolution). Firm has performed comparative dissolution profile against the product i.e Mobikare by M/s Barret Hodgson Batch No# C8862, Pakistan in Acid media (pH 1.2) & Phosphate Buffer (pH 6.8). and the results are within acceptable limit
	Analytical method validation/verification of product	Method Validation have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA		
Manufacturer of API	Vision Pharmaceuticals (Pvt) Ltd Plot# 22-23, Industrial Triangle, Kahutta road, Islamabad.	
API Lot No.	DE931	
Description of Pack (Container closure system)	PVC Blistering	
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH	
Time Period	Real time: 6 months Accelerated: 6 months	
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)	
Batch No.	TB-C001	TB-C002
Batch Size	5000 Capsules	5000 Capsules
Manufacturing Date	10-2021	10-2021
Date of Initiation	08-10-2021	08-10-2021
No. of Batches	02	

Administrative Portion		
19.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
20.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
21.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No # 801689 dated: 16-09-2021 specifying 2 Kg of Diclofenac sodium 32% EC pellets batch no # DE931
22.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches have been submitted by UV method along with respective documents like COA, summary data, sheets.
23.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has performed testing of Login 50mg capsule on UV spectrophotometer

24.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Quantity of Pellets subject to assay and moisture content not calculated, clarification is required	Assay is done on 'as is basis' so there is no need of calculation of moisture content.
2.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted
3.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator product and results of all the quality tests of the developed formulation and the innovator product shall be submitted and discussed.	We were unable to arrange the innovator product that's why we couldn't perform Pharmaceutical equivalence against the innovator product. Pharmaceutical equivalence of Login capsules has been performed against Mobikare capsules prepared by Barret Hodgson as per available guidance document on DRA website i.e Pharmaceutical equivalence may also be carried out against reference/comparator product.
4.	3.2.P.5.2	• Justification is required for performing assay testing by UV method instead of HPLC method. • Justification is required for setting dissolution limit in phosphate buffer stage as NLT 75% in 45 min which is different from that mentioned in Specifications i.e., NLT 75% in 30 min.	• The assay was performed on UV Spectrophotometer as the method provided by the Diclofenac sodium pellets manufacturer was also on UV, moreover complete method validation has been performed and submitted for your kind consideration. • The dissolution time limit is 45 minutes, the time 30 minutes is typographical error.
5.	3.2.P.5.3	Submit protocols of analytical method validation.	Submitted
6.	3.2.P.8	• Documents for the procurement of the API including purchase invoice from M/s Vision Pharmaceuticals (Pvt.) Ltd. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• Submitted • Submitted

Decision: The Board deferred the case for scientific justification of performance of assay testing by using UV-spectrophotometer instead of using HPLC method as performed by the reference product.		
335.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4, National Industrial Zone, Rawat, Islamabad
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4 National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7360 dated 16-03-2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip No# 9636146182
	The proposed proprietary name / brand name	Emozol 20mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains:- Esomeprazole magnesium Trihydrate enteric coated pellets 22.5% equivalent to 20mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexium 20mg Capsule of USFDA approved
	For generic drugs (me-too status)	Es0-DEW 20mg Capsule by Dew-maxPharma Reg. No. 09505
	GMP status of the Finished product manufacturer	New DML letter issued dated; 16-09-2021
	Name and address of API manufacturer.	Vision Pharmaceuticals (pvt) Ltd Plot3 22-23, Industrial Triangle, Kahutta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against against the brand leader that is Nexum 20mg Capsules Getz Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). Firm has performed comparative dissolution profile against the Nexum 20mg Capsules by Getz Pharma in Acid media (pH 1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals (Pvt) Ltd Plot# 22-23, Industrial Triangle, Kahutta road, Islamabad.	
API Lot No.	EMZ046402	
Description of Pack (Container closure system)	Alu-Alu blister	
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH	
Time Period	Real time: 6 months Accelerated: 6 months	
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)	
Batch No.	RD-C007	RD-C008
Batch Size	5000 cap	5000 cap
Manufacturing Date	11-2021	11-2021

Date of Initiation	17-11-2021	17-11-2021
No. of Batches	02	

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No # 801173 dated: 10-11-2021 specifying 2 Kg of Esomeprazole Magnesium 22.5% EC pellets batch no # EMZ046402
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2	Revise label claim with salt form with submission of RS: 30000/- fee.	In section 1.5.2 there is typographical error, the same label claim has been written in correct form as in section: 2.3.P.1 2.3.P.2.2.1 3.2.P.2.2.1 3.2.P.3.5
2.	2.3.R.1.1	• Justify the quantity of 92.46mg of Esomeprazole magnesium Pellets 22.5% equivalent to 20mg of Esomeprazole. • Salt factor is not adjusted in the product development. Justification is required	Molecular weight of Esomeprazole Mg: 713.1 Molecular weight of Mg: 24.305 Factor for Mg: 1.035 As the pellets contain Esomeprazole Mg Label claim for 20mg: 100/22.39 *20=89.33mg For Mg adjustment multiply the factor of Mg with 89.33=92.46 Salt factor already adjusted for Mg as above.
3.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted
4.	3.2.P.1	Justify the quantity of 92.46mg of Esomeprazole magnesium	Please refer to the reply of 2.3.R.1.1 as already discussed above.

		Pellets 22.5% equivalent to 20mg of Esomeprazole	
5.	3.2.P.2.2.1	• Justify the quantity of 92.46mg of Esomeprazole magnesium Pellets 22.5% equivalent to 20mg of Esomeprazole. • Salt factor is not adjusted in the product development. Justification is required	• We were unable to arrange the innovator product that's why we couldn't perform Pharmaceutical equivalence against the innovator product. • Pharmaceutical equivalence of Emozol 20mg capsules has been performed against Nexum 20mg capsules prepared by Getz Pharma as per available guidance document on dra website i.e Pharmaceutical equivalence may also be carried out against reference/comparator product.
6.	3.2.P.5.2	• For Dissolution which test of USP was adopted. • In USP dissolution is conducted by HPLC while Your method is by U.V. Clarification is required.	• For Dissolution Test 1 was adopted. • Dissolution was performed on HPLC for raw material i.e pellets and the same pellets has been used for filling, so due to convenience of UV the dissolution has been performed on UV as the dissolution of the same pellets has been performed on HPLC in case of Raw material. Furthermore it is committed that Dissolution will be performed on HPLC in coming commercial batches.
7.	3.2.P.5.3	Submit protocols of analytical method validation.	Submitted
8.	3.2.P.8	• Documents for the procurement of the API including purchase invoice from M/s Vision Pharmaceuticals (Pvt.) Ltd. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• Submitted • Submitted.

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 30,000 for correction/pre-approval change in label claim, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

• **Registration letter will be issued after submission of revised method for dissolution testing on HPLC method according to USP pharmacopeia monograph and performance of dissolution testing on HPLC method on next time point.**		
336.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4, National Industrial Zone, Rawat, Islamabad
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4 National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.6646 dated 10-03-2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip No# 57881708408
	The proposed proprietary name / brand name	Emozol 40mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains:- Esomeprazole magnesium Trihydrate enteric coated pellets 22.5% equivalent to 40mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexium 40mg Capsule of USFDA approved
	For generic drugs (me-too status)	Eso-Dew 40mg Capsules by M/s Dew-Max Pharma, Reg. No. 09506
	GMP status of the Finished product manufacturer	New DML letter issued dated; 16-09-2021
	Name and address of API manufacturer.	Vision Pharmaceuticals (pvt) Ltd Plot3 22-23, Industrial Triangle, Kahutta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against against the brand leader that is Nexum 40mg Capsules Getz Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). Firm has performed comparative dissolution profile against the Nexum 40mg Capsules by Getz Pharma in Acid media (pH 1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals (Pvt) Ltd Plot# 22-23, Industrial Triangle, Kahutta road, Islamabad.		
API Lot No.	EMZ046402		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-C009	RD-C010	RD-C011
Batch Size	1500 cap	1500 cap	1500 cap
Manufacturing Date	11-2021	11-2021	11-2021

Date of Initiation	18-11-2021	18-11-2021	18-11-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No # 801173 dated: 10-11-2021 specifying 2 Kg of Esomeprazole Magnesium 22.5% EC pellets batch no # EMZ046402
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2	Revise label claim with salt form with submission of RS: 30000/- fee.	In section 1.5.2 there is typographical error, the same label claim has been written in correct form as in section: 2.3.P.1 2.3.P.2.2.1 3.2.P.2.2.1 3.2.P.3.5
2.	2.3.R.1.1	• Justify the quantity of 184.920mg of Esomeprazole magnesium Pellets 22.5% equivalent to 40mg of Esomeprazole. • Salt factor is not adjusted in the product development. Justification is required	Molecular weight of Esomeprazole Mg: 713.1 Molecular weight of Mg: 24.305 Factor for Mg: 1.035 As the pellets contain Esomeprazole Mg Label claim for 20mg: 100/22.39 *40=178.65mg For Mg adjustment multiply the factor of Mg with 178.65=184.9 Salt factor already adjusted for Mg as above.
3.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted
4.	3.2.P.1	Justify the quantity of 184.920mg of Esomeprazole magnesium	Please refer to the reply of 2.3.R.1.1 as already discussed above.

		Pellets 22.5% equivalent to 40mg of Esomeprazole	
5.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator product and results of all the quality tests of the developed formulation and the innovator product shall be submitted and discussed.	• We were unable to arrange the innovator product that's why we couldn't perform Pharmaceutical equivalence against the innovator product. • Pharmaceutical equivalence of Emozol 40mg capsules has been performed against Nexum 40mg capsules prepared by Getz Pharma as per available guidance document on dra website i.e Pharmaceutical equivalence may also be carried out against reference/comparator product.
6.	3.2.P.5.2	• For Dissolution which test of USP was adopted. • In USP dissolution is conducted by HPLC while Your method is by U.V. Clarification is required.	• For Dissolution Test 1 was adopted. • Dissolution was performed on HPLC for raw material i.e pellets and the same pellets has been used for filling, so due to convenience of UV the dissolution has been performed on UV as the dissolution of the same pellets has been performed on HPLC in case of Raw material. Furthermore it is committed that Dissolution will be performed on HPLC in coming commercial batches.
7.	3.2.P.5.3	Submit protocols of analytical method validation.	Submitted
8.	3.2.P.8	• Documents for the procurement of the API including purchase invoice from M/s Vision Pharmaceuticals (Pvt.) Ltd. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• Submitted • Submitted.

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 30,000 for correction/pre-approval change in label claim, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

• **Registration letter will be issued after submission of revised method for dissolution testing on HPLC method according to USP pharmacopeia monograph and performance of dissolution testing on HPLC method on next time point.**		
337.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4, National Industrial Zone, Rawat, Islamabad
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4 National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.6646 dated 10-03-2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip No# 743786744475
	The proposed proprietary name / brand name	Sevodex 30mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin Capsule contains: DDR Pellets of Dexlansoprazole Eq. to Dexlansoprazole……. 30mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	3 x 10’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	DEXILANT delayed-release capsules of USFDA approved
	For generic drugs (me-too status)	Dexxoo 30mg Capsules by M/s Horizon Pharma, Reg. No. 088381
	GMP status of the Finished product manufacturer	New DML letter issued dated; 16-09-2021
	Name and address of API manufacturer.	Vision Pharmaceuticals (pvt) Ltd Plot3 22-23, Industrial Triangle, Kahutta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product. Firm submitted dissolution of drug product in 3 pH: Acid stage 0.1N HCl and Buffer stage pH 5.5 and pH 7.0
	Pharmaceutical equivalence and comparative dissolution profile	established against the brand leader that is Razodex 30mg Capsules Getz Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Razodex 30mg Capsules by Getz Pharma in Acid media (pH 1.2) & Phosphate Buffer (pH 7.0). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals (Pvt) Ltd Plot# 22-23, Industrial Triangle, Kahutta road, Islamabad.		
API Lot No.	DLP756		
Description of Pack (Container closure system)	Alu-Alu Blistering		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-C001	RD-C002	RD-C003
Batch Size	1500 cap	1500 cap	1500 cap
Manufacturing Date	11-2021	11-2021	11-2021

Date of Initiation	08-11-2021	08-11-2021	09-11-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No # 801084 dated: 01-11-2021 specifying 2 Kg of DDR Pellets of Dexlansoprazole 22.5% EC pellets batch no # DLP756
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Quantity of Pellets subject to assay and moisture content not calculated, clarification is required	Assay is done on 'as is basis' so there is no need of calculation of moisture content.
2.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted
3.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be established with the innovator product and results of all the quality tests of the developed formulation and the innovator product shall be submitted and discussed.	We were unable to arrange the innovator product that's why we couldn't perform Pharmaceutical equivalence against the innovator product. Pharmaceutical equivalence of Sevodex 30mg capsules has been performed against Razodex 30mg capsules prepared by Getz Pharma as per available guidance document on dra website i.e Pharmaceutical equivalence may also be carried out against reference/comparator product.
4.	3.2.P.5.3	Submit protocols of analytical method validation.	Submitted
5.	3.2.P.8	• Documents for the procurement of the API	• Submitted • Submitted.

		including purchase invoice from M/s Vision Pharmaceuticals (Pvt.) Ltd. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Decision: Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **The firm will perform Comparatice Dissolution Profile and Pharmaceutical Equivalence studies against the innovator's product before issuance of registration letter.**

338.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4, National Industrial Zone, Rawat, Islamabad
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals. Plot No. 27, Street No. S-4 National Industrial Zone, Rawat, Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.6645 dated 10-03-2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip No# 297215193414
	The proposed proprietary name / brand name	Sevodex 60mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin Capsule contains: DDR Pellets of Dexlansoprazole Eq. to Dexlansoprazole……. 60mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	3 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	DEXILANT delayed-release capsules of USFDA approved

	For generic drugs (me-too status)	Dexxoo 60mg Capsules by M/s Horizon Pharma, Reg. No. 088380
	GMP status of the Finished product manufacturer	New DML letter issued dated; 16-09-2021
	Name and address of API manufacturer.	Vision Pharmaceuticals (pvt) Ltd Plot3 22-23, Industrial Triangle, Kahutta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product. Firm submitted dissolution of drug product in 3 pH: Acid stage 0.1N HCl and Buffer stage pH 5.5 and pH 7.0
	Pharmaceutical equivalence and comparative dissolution profile	established against the brand leader that is Razodex 60mg Capsules Getz Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Razodex 60mg Capsules by Getz Pharma in Acid media (pH 1.2) & Phosphate Buffer (pH 7.0). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	Vision Pharmaceuticals (Pvt) Ltd Plot# 22-23, Industrial Triangle, Kahutta road, Islamabad.	

API Lot No.	DLP756		
Description of Pack (Container closure system)	Alu-Alu Blistering		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-C004	RD-C005	RD-C006
Batch Size	1500 cap	1500 cap	1500 cap
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	09-11-2021	09-11-2021	09-11-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No # 801084 dated: 01-11-2021 specifying 2 Kg of DDR Pellets of Dexlansoprazole 22.5% EC pellets batch no # DLP756
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Quantity of Pellets subject to assay and moisture content not calculated, clarification is required	Assay is done on 'as is basis' so there is no need of calculation of moisture content.
2.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted
3.	3.2.P.2.2.1	Pharmaceutical equivalence of the applied drug shall be	We were unable to arrange the innovator product that's why we couldn't perform

		established with the innovator product and results of all the quality tests of the developed formulation and the innovator product shall be submitted and discussed.	Pharmaceutical equivalence against the innovator product. Pharmaceutical equivalence of Sevodex 60mg capsules has been performed against Razodex 60mg capsules prepared by Getz Pharma as per available guidance document on dra website i.e Pharmaceutical equivalence may also be carried out against reference/comparator product.
4.	3.2.P.5.3	Submit protocols of analytical method validation.	Submitted
5.	3.2.P.8	• Documents for the procurement of the API including purchase invoice from M/s Vision Pharmaceuticals (Pvt.) Ltd. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• Submitted • Submitted.

Decision: Approved with innovator's specification.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **The firm will perform Comparatice Dissolution Profile and Pharmaceutical Equivalence studies against the innovator's product before issuance of registration letter.**

339.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals Islamabad
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals Plot 27, Street S-4, Industrial Area Rawat Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 9553 dated 14/04/2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip No# 5777421391
	The proposed proprietary name / brand name	Itrora 100mg Capsules

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin Capsule contains: Immediate Release pellets of Itraconazole eq. to Itraconazole USP ……. 100mg (Product Specs: USP)
	Pharmaceutical form of applied drug	White to off white enteric coated pellets filled in green/white hard gelatin capsule shells
	Pharmacotherapeutic Group of (API)	Anti-fungal (Triazoles)
	Reference to Finished product specifications	USP specs
	Proposed Pack size	1×4's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Sporanox Capsule of Janseen Pharmaceuticals Horsham USFDA
	For generic drugs (me-too status)	ICON 100mg Capsule of M/s Ferozsons, Nowshehra Reg No: 026877
	GMP status of the Finished product manufacturer	New DML letter issued dated; 16-09-2021
	Name and address of API manufacturer.	Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial Triangle, Kahutta Road, Islamabad-Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted
	Module III (Drug Substance)	Monograph of Itraconazole pellets is USP Monograph. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 18 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ICZ1465, ICZ1466, ICZ1467)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing) and its verification studies, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the Innovator product that is Sporanox 100mg Capsules TM of Janseen Pharmaceutica, Beerse, Belgium manufactured in Pak by Aspin Pharma, by performing quality tests (Identification, Assay, Dissolution and Uniformity of dosage form). CDP has been performed against the same brand that is Sporanox 100mg Capsules by Aspin Pharma in Acid media (pH 1.0-1.2) & in media of pH 4.5 & 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision and specificity.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial Triangle, Kahutta Road, Islamabad-Pakistan.		
API Lot No.	ICZ1497		
Description of Pack (Container closure system)	PVC blister packed in unit carton (1×4's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-C012	RD-C013	RD-C014
Batch Size	700 cap	700 cap	700 cap
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	25-11-2021	25-11-2021	25-11-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice No # 801933 dated: 16-09-2021 specifying 1 Kg of Itraconazole 22% IR pellets batch no # ICZ1497
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches have been submitted by UV method along with respective documents like COA, summary data, sheets.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Manual audit trail report submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Quantity of Pellets subject to assay and moisture content not calculated, clarification is required	Assay is done on 'as is basis' so there is no need of calculation of moisture content.
2.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted
3.	3.2.P.5.2	• Justification is required for setting dissolution limit in 0.25% W/v SLS in 0.1N HCl as NLT 80% in 45 min which is different from that mentioned in Specifications i.e., NLT 80% in 30 min.	The dissolution time limit is 45 minutes, the time 30 minutes is typographical error.
4.	3.2.P.8	• Documents for the procurement of the API including purchase invoice from M/s Vision Pharmaceuticals (Pvt.) Ltd. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• Submitted • Submitted

Decision: Approved with USP specification..

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

b. New/Additional section(s)

M/s News Pharma Lahore**. (New Section)**

CLB in its 283rd meeting held on 28th October 2021 has considered and approved the grant One (01) Additional section to M/s News Pharma Lahore. Accordingly, firm has applied for following products for consideration by Drug Registration Board.

Oral Liquid General section
09 Molecules/ 10 Products

340.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.6140 dated: 07-03-2022
	Details of fee submitted	PKR 30,000/-: dated : 03-03-2022
	The proposed proprietary name / brand name	Newmol 120 mg / 5 mL Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 mL contains: Paracetamol (BP).... 120 mg
	Pharmaceutical form of applied drug	Pink colour sweet homogeneous strawberry flavored oral suspension
	Pharmacotherapeutic Group of (API)	Paracetamol is part of the class of drugs known as "aniline **analgesics**"
	Reference to Finished product specifications	BP
	Proposed Pack size	60 mL, 120 mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Paracetamol 120 mg/5 ml Oral Suspension by M/s Pinewood healthcare UK (MHRA Approved)
	For generic drugs (me-too status)	Febrol 120 mg/5 ml Suspension by Barret Hodgson Reg. No. 023532
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	Pharmagen Limited. 34-Km, Ferozepur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Paracetamol is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Calpol 120 mg/5 mL Susp. By M/s GSK by performing quality tests (Identification, Assay, and determination of Impurity (4-Aminophenol). CDP – Not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Pharmagen Limited. 34-Km, Ferozepur Road, Lahore, Pakistan.		
API Lot No.	00510921/040/2021		
Description of Pack (Container closure system)	Amber glass bottle sealed with aluminium cap and packed in printed unit cartons.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	10-09-2021	10-09-2021	10-09-2021
No. of Batches	03		
Administrative Portion			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate dated 22-05-2019 issued by DRAP
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local source
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit Trail submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1 and 2.3.R.1.1	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	BMR's, 3.2.P.2.3 and 3.2.P.3.5. have been revised and same method is adopted. Documents attached
2.	3.2.S.4.2	• Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required. • Submitted assay method is different than B.P monograph. Clarification is required.	• Analytical Procedures used for routine testing of the drug substance / Active Pharmaceutical Ingredient by Drug Substance are attached. • It is a typographical mistake. Actual method is submitted.
3.	3.2.S.4.3	In B.P and as per your , method Assay is carried out by titration method while Verification studies are conducted by HPLC. Clarification is required.	Revised Verification studies were conducted by titration method. Copy of reports is attached.
4.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia) shall be provided	Preservative effectiveness studies performed as per recommendations of Pharmacopoeia.
5.	3.2.P.5.4	The copies of complete analysis of at least two batches shall be provided.	The copies of complete analysis of at least two batches.

Decision: Approved with BP specifications.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
341.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.6141 dated: 07-03-2022
	Details of fee submitted	PKR 30,000/-: dated : 03-03-2022
	The proposed proprietary name / brand name	Newmol 6 Plus 250 mg / 5 mL Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 mL contains: Paracetamol (BP).... 250 mg
	Pharmaceutical form of applied drug	Pink colour sweet homogeneous strawberry flavored oral suspension
	Pharmacotherapeutic Group of (API)	Paracetamol is part of the class of drugs known as "aniline **analgesics**"
	Reference to Finished product specifications	BP
	Proposed Pack size	60 mL, 120 mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Paracetamol 250 mg/5 ml Oral Suspension by M/s Pinewood healthcare UK (MHRA Approved)
	For generic drugs (me-too status)	Febrol 250 mg/5 ml Suspension by Barret Hodgson Reg. No. 023533
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	Pharmagen Limited. 34-Km, Ferozepur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Paracetamol is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Calpol 6 Plus 250 mg/5 mL Susp. By M/s GSK by performing quality tests (Identification, Assay, and determination of Impurity (4-Aminophenol). CDP – Not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited. 34-Km, Ferozepur Road, Lahore, Pakistan.		
API Lot No.	00510921/040/2021		
Description of Pack (Container closure system)	Amber glass bottle sealed with aluminium cap and packed in printed unit cartons.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021

Date of Initiation	10-09-2021	10-09-2021	10-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate dated 22-05-2019 issued by DRAP
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local source
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit Trail submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	• Manufacturing method mentioned in BMR's is not same mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required. • Justification of overages in the formulation(s) shall be submitted. • Batch size 100 bottles mentioned while in stability sheets and COA's 45 bottles mentioned.	• BMR's, 3.2.P.2.3 and 3.2.P.3.5. have been revised and same method is adopted. Documents attached. • No overage was added in the formulation. There was human error in calculation of material which has been corrected in BMR's attached. • Actual batch size is 45 bottles according to which all calculations done. 100 bottles was mentioned by clerical mistake.
2.	2.3.R.1.2	• Manufacturing method mentioned in BMR's is not same mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	BMR's, 3.2.P.2.3 and 3.2.P.3.5. have been revised and same method is adopted. Documents attached.
3.	3.2.S.4.2	• Analytical procedures used for routine testing of the Drug substance /Active	• Analytical Procedures used for routine testing of the drug substance / Active Pharmaceutical Ingredient by Drug Substance are attached.

		Pharmaceutical Ingredient by Drug substance is required. • Submitted assay method is different than B.P monograph. Clarification is required.	• It is a typographical mistake. Actual method is submitted.
4.	3.2.S.4.3	In B.P and as per your ,method Assay is carried out by titration method while Verification studies are conducted by HPLC. Clarification is required.	Revised Verification studies were conducted by titration method. Copy of reports is attached.
5.	3.2.P.2.2.2	Justification of overages in the formulation(s) shall be submitted.	No overage was added in the formulation. There was human error in calculation of material which has been corrected in BMR's attached.
6.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia) shall be provided	Preservative effectiveness studies performed as per recommendations of Pharmacopoeia.
7.	3.2.P.5.4	The copies of complete analysis of at least two batches shall be provided.	The copies of complete analysis of at least two batches.

Decision: Approved with BP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of Pharmaceutical Equivalence with Innovator product.**

342.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.6137 dated: 07-03-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 65511595005
	The proposed proprietary name / brand name	Newzine 5mg/5ml oral solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 mL contains: Cetirizine Dihydrochloride…..5 mg

	Pharmaceutical form of applied drug	Clear & transparent, sweet with characteric flavor solution filled in 60 mL amber pet bottle sealed wit pilfer proof aluminium caps
	Pharmacotherapeutic Group of (API)	Anti-histamine
	Reference to Finished product specifications	BP
	Proposed Pack size	1 ×60 mL, 1 x 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zirtek Allergy Solution 1 mg/ml oral solution by M/s UCB Pharma, MHRA Approved.
	For generic drugs (me-too status)	Avec 5 mg/ 5 mL oral solution by M/s Platinum Pharma, Reg. No. 025507
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	Karunesh Remedies Plot # 417/2, Phase-II, G.I.D.C., Estate Panoli-394116. Ta. Ankleshwar, District Bharuch, Gujarat (India)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cetirizine Dihydrochloride is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, Identification, Assay and tests for related substances (impurity A, B, C, D, E,F & unspecified and total impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(SLL/CTR/0309047, SLL/CTR/0309048, SLL/CTR/0309047)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls,

		specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.	
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is ***Zyrtec oral solution*** by GSK Pharma by performing quality tests (Identification, Assay, pH, Uniformity of dosage form & related substances). CDP – Not applicable	
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.	
STABILITY STUDY DATA			
Manufacturer of API	Karunesh Remedies Plot # 417/2, Phase-II, G.I.D.C., Estate Panoli-394116. Ta. Ankleshwar, District Bharuch, Gujarat (India)		
API Lot No.	CTZ/028/21-22		
Description of Pack (Container closure system)	Amber glass bottle sealed with aluminium cap and packed in printed unit cartons.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	08-09-2021	08-09-2021	08-09-2021
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No.S-GMP-20102293 issued by Food and Drug Administration (Gujrat Estate) India valid till 25/10/2022.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Cetirizine Dihydrochloride for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, form 7 & invoice (invoice# EXP/80(20-21) specifying import 1Kg Cetirizine Dihydrochloride (Batch#	

		CTZ/028/21-22).However not attested by DRAP. Copy of DHL is provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit Trail submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	Short method was mentioned in BMR. Now Revise BMR (s) are submitted as with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5
2.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product	Blank Batch Manufacturing Record is attached
3.	3.2.S.4.2	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required.	Analytical Procedures used for routine testing of the drug substance / Active Pharmaceutical Ingredient by Drug Substance is attached.
4.	3.2.S.4.3	In analytical method verifications in accuracy Volume of 0.1M Sodium nitrile used mentioned while in assay 0.1M Sodium Hydroxide used. Clarification is required.	It is clarified that 0.1M Sodium Nitrite is a typing mistake, 0.1M Sodium Hydroxide is correct
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia) shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.
6.	3.2.P.5.4	Batch size mentioned in this section is 100 bottles while in section 3.2.P.8 mentioned as 45 bottles. Clarification is required.	It is clarified that actual batch size is 45 bottles and in 3.2.P.5.4 100 bottles mentioned mistakenly. Revised COA (s) are attached
7.	3.2.P.8	Commercial invoice with approval from DRAP. Submit Calculations of Assay with details of dilutions.	Copy of DHL is provided. Calculations of Assay.

Decision: Approved with BP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
343.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10564 dated: 27-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 7165597263
	The proposed proprietary name / brand name	Newzol 200 mg / 5 mL Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 mL suspension contains: Metronidazole Benzoate eq to Metronidazole .... 200 mg
	Pharmaceutical form of applied drug	Liquid suspension filled in amber glass bottle seale with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Anti-Protozoal (Antimicrobial)
	Reference to Finished product specifications	BP Specs.
	Proposed Pack size	60 mL , 120 mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Metronidazole 200mg/5ml Oral Suspension by Rosemont House, York dale Industrial Park, Braithwaite Street, Leeds, Yorkshire, LS11 9XE Approved by MHRA
	For generic drugs (me-too status)	Diagyl 200 mg/5 ml Suspension by M/S Swiss Pharma , Reg. No. 020229
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	M/S Hubei Hongyuan Pharmaceutical Technology Co., Ltd. Address: No. 126, Dabieshan Aveneu, Economic Development Zone, Luotian, Hubei, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls,

		specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MTZ/001/2015, MTZ/002/2015, MTZ/003/2015)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of the developed formulation Newzol Suspension 200 mg/5mL with brand leader product Flagyl 200 mg/5ml Susp. (Sanofi-Aventis).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/S Hubei Hongyuan Pharmaceutical Technology Co., Ltd. Address: No. 126, Dabieshan Aveneu, Economic Development Zone, Luotian, Hubei, China.		
API Lot No.	02120190993		
Description of Pack (Container closure system)	Oral Suspension filled in amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03

Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	14-09-2021	14-09-2021	14-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate # HB20180424 for M/S Hubei Hongyuan Pharmaceutical Technology Co., Ltd. issued by China Food and Drug administration. It is valid till 03-07-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Metronidazole Benzoate for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3,form 7 & invoice (invoice# EXP/0109SLT2110(20-21) dated: 05-09-2021 specifying import 1Kg Metronidazole Benzoate (Batch# 02120190993). However not attested by DRAP. Copy of DHL is provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit Trail submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	• Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required. • Batch size mentioned is 100 bottles while in 3.2.P.5.4 and 3.2.P.8 batch size mentioned is 45 bottles mentioned . Clarification is required.	Short method was mentioned in BMR. Now Revise BMR (s) & 3.2.P.2.3 are submitted as with detailed method as mentioned in 3.2.P.3.5 It is clarified that actual batch size is 45 bottles and 100 bottles mentioned mistakenly.
2.	2.3.R.1.2	Manufacturing method mentioned in BMR's is not same as	Short method was mentioned in BMR. Now Revise BMR is submitted with

		mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5
3.	3.2.S.4.2	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is attached.
4.	3.2.S.4.3	In B.P and as per your ,method Assay is carried out by titration method while Verification studies are conducted by HPLC. Clarification is required.	It is clarified that Titration method is used for Verification studies. Revised Verification reports with Titration method is attached.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.
6.	3.2.P.5.1	In B.P monograph test for metronidazole included which is not performed. Clarification is required.	Revised reports including test of metronidazole are attached
7.	3.2.P.5.3	Submit protocols for analytical method verifications.	Protocols for analytical method verifications are submitted.
8.	3.2.P.6	COA of metronidazole reference standard including source and lot number shall be provided	COA of Metronidazole reference standard including source and lot number is attached.
9.	3.2.P.8	Commercial invoice with approval from DRAP. Submit Calculations of Assay with details of dilutions.	Copy of DHL is provided. Calculations of Assay.

Decision: Approved with BP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

344.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10565 dated: 27-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 6679601472

	The proposed proprietary name / brand name	Newsal Oral Solution 2 mg / 5 mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 mL contains: Salbutamol (as Sulphate).... 2mg
	Pharmaceutical form of applied drug	Oral solution filled in amber glass bottle sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	B2-Agonist
	Reference to Finished product specifications	B.P Specs.
	Proposed Pack size	60 mL, 120mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Salbutamol syrup 2mg/5ml by M/S Pinewood Healthcare Approved by MHRA
	For generic drugs (me-too status)	Ventolin 2 mg/ 5mL M/s GSK, Reg. No. 000287
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	M/S Vamsi Labs Ltd. Address: A-14/15,M.I.D.C.area,, CHINCHOLL, SOLAPUR, DIST- SOLAPUR, INDIA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (SS-0010610, SS-0020610&SS-0030610)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls,

		specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation Newsal Syrup with brand leader product Ventolin Syrup of M/s GSK
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/S Vamsi Labs Ltd. Address: A-14/15,M.I.D.C.area,, CHINCHOLL, SOLAPUR-413255, DIST- SOLAPUR, INDIA		
API Lot No.	SS-0070721		
Description of Pack (Container closure system)	Oral solution filled in amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	17-09-2021	17-09-2021	17-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate No # 6100529 for M/s Vamsi Labs. Ltd, India issued by food and drugs administration (Maharashtra State) India. It is valid till 07-07-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Salbutamol Sulphate for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, form 7 & invoice (invoice# EXP/VAM/186 dated: 06-09-2021 specifying import 1Kg Salbutamol Sulphate

		(Batch# SS-0070721). However not attested by DRAP. Copy of DHL is provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit Trail submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	• Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required. • Batch size mentioned is 100 bottles while in 3.2.P.5.4 and 3.2.P.8 45 bottles mentioned . Clarification is required.	Short method was mentioned in BMR. Now Revise BMR (s) & 3.2.P.2.3 are submitted as with detailed method as mentioned in 3.2.P.3.5 It is clarified that actual batch size is 45 bottles and 100 bottles mentioned mistakenly.
2.	2.3.R.1.2	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	Short method was mentioned in BMR. Now Revise BMR is submitted with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5
3.	3.2.S.4.2	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is attached.
4.	3.2.S.4.3	In verification studies Sodium hydroxide and sodium nitrile mentioned. Clarification is required.	Titration is performed with 01M Perchloric acid and not with sodium hydroxide or sodium nitrile.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia) is provided.
6.	3.2.P.5.3	Submit protocols for analytical method verifications.	Protocols for analytical method verifications are submitted
7.	3.2.P.8	Commercial invoice with approval from DRAP. Submit Calculations of Assay with details of dilutions.	Copy of DHL is provided. Calculations of Assay.

Decision: Approved with BP specifications.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
345.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10573 dated: 27-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 53255466
	The proposed proprietary name / brand name	Newdom Suspension 5mg/5ml.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 ml Suspension contains: Domperidone ……..5 mg
	Pharmaceutical form of applied drug	Oral suspension filled in amber glass bottle sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Dopamine Antagonist
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	60 ml, 90 mL, 120 mL & 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Domperidone 1 mg/mL Suspension. MHRA approved
	For generic drugs (me-too status)	Motilium Suspension 5 mg /5 mL Reg # 006527
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	M/S Vasudha Pharma Chem Limited. Address: Unit-II, Plot No. 79Jawaharlal Nehru Pharma City Thanam(V), Parawada(M), Visakhapatnam District-531019, Andhra Pradesh, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DN-01T15, DN-02T15, DN-03T15)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation Newdom Suspension with comparator product Motilium Susp. 5 mg/5ml Susp. By M/s Aspin Pharma.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/S Vasudha Pharma Chem Limited Unit-II, Plot No. 79 Jawaharlal Nehru Pharma City Thanam (V), Parawada(M), Visakhapatnam District-531019, Andhra Pradesh, India.
API Lot No.	EDOM/2110097
Description of Pack (Container closure system)	Oral Suspension filled in Amber glass bottle sealed with pilfer pr aluminium caps.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	17-09-2021	17-09-2021	17-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Vasudha Pharma Chem Ltd, India issued by food and drugs administration (Andhra Pradesh) India. It is valid till 20-11-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Domperidone for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, form 7 & invoice (invoice# EXP/6994 (20-21) dated: 06-09-2021 specifying import 1Kg Domperidone (Batch# EDOM/2110097). However not attested by DRAP. Copy of DHL is provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	• Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required.	Short method was mentioned in BMR. Now Revise BMR (s) & 3.2.P.2.3 are submitted as with detailed method as mentioned in 3.2.P.3.5 It is clarified that actual batch size is 45 bottles and 100 bottles mentioned mistakenly.
2.	2.3.R.1.2	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	Short method was mentioned in BMR. Now Revise BMR is submitted with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5

3.	3.2.S.4.2	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required	Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is attached.
4.	3.2.S.4.3	Verification studies are conducted by HPLC while assay method is by titrimetry. Clarification is required.	Revised verification reports are attached conducted by Titrimetry.
5.	3.2.S.4.4	Specification claimed are USP while it is not available in USP. Clarification is required.	Domperidone is not present in USP . USP was mentioned by mistakenly.
6.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.
7.	3.2.P.5.1	Specification claimed are B.P. Provide evidence of B.P specifications.	The product is not available in any pharmacopeia and B.P is mentioned by mistake.
8.	3.2.P.5.2	Justification is required for performing assay testing by UV method	The product is not available in any pharmacopeia so we have test from in-house testing method. The validation of testing method is attached in Dossier.
9.	3.2.P.8	Commercial invoice with approval from DRAP..	Copy of DHL is provided. Calculations of Assay.

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

346.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10881 dated: 29-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 70380326443
	The proposed proprietary name / brand name	New-tran Paediatric Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 mL suspension contains: Trimethprim ..... 40 mg Sulfamethoxazole ..... 200 mg

	Pharmaceutical form of applied drug	Clear sweet strawberry flavored homogeneous suspension filled in amber glass bottle sealed with aluminium cap.
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	BP
	Proposed Pack size	50 mL, 400 ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Bactrim Suspension by M/S Sun Pharm industries, USFDA Approved.
	For generic drugs (me-too status)	Septran Paediatric Suspension by M/s GSK Pharma Reg. No. 000384
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	Shouguang Fukang Pharmaceutical company Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang City, Shandong Province, People's Republic of China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Trimethoprim and Sulfamethoxazole is present in BP. **Trimethoprim:** The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, Identification, Assay and tests for related substances, impurity K, heavy metals, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance **Sulfamethoxazole:** The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, Identification, Assay and tests for related substances (impurities A, C, D, E) & impurity B, impurity F, unspecified impurities and total impurities, specifications, analytical procedures and its verification, batch analysis and

		justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Batches of Trimethoprim**: (201103504,201103505, 201103506) **Batches of Sulfamethoxazole**: Accelerated: (200604001,200604002, 200604003 Real Time: (2007706001, 2007706002, 2007706003))
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Septran Paediatric Suspension by GSK Pharma by performing quality tests (Identification, Assay, pH, Uniformity of dosage unit). CDP – Not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Shouguang Fukang Pharmaceutical company Ltd. North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shouguang City, Shandong Province, People's Republic of China		
API Lot No.	Trimethoprim = A-50112007004-0500 Sulfamethoxazole = A-50212005029		
Description of Pack (Container closure system)	Oral Suspension filled in Amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	100 Bottles	100 Bottles	100 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	11-09-2021	11-09-2021	11-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD 20190888 issued by China Food and Drug Administration valid till 12/03/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Trimethoprim & Sulfamethoxazole for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of invoice (invoice# 21FK08Z814M dated: 12-08-2021 specifying import 1Kg Sulfamethoxazle (Batch# A-50212005029) and 0.50 Kg of Trimethoprim (Batch# A-50112007004-0500). However not attested by DRAP. Copy of DHL is provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has performed testing on UV Spectrophotometer
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.	GMP Certificate is attached.
2.	3.2.S.4.2	Analytical procedures used for routine testing of the both Drug substance /Active Pharmaceutical Ingredient (Trimethoprim & Sulfamethoxazole) by Drug substance is required	Analytical Procedures used for routine testing of the drug substance / Active Pharmaceutical Ingredient by Drug Substance is attached.
3.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.

4.	3.2.P.8	• Commercial invoice with approval from DRAP. • Batch size mentioned is 45 bottles while in 3.2.P.5.4 and in BMR's 100 bottles mentioned.	• Copy of DHL is provided. • Actual batch size is 45 bottles for each batch. 100 bottles is mentioned by typographic mistake.

Decision: Approved with BP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

347.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10562 dated: 27-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 5820244638
	The proposed proprietary name / brand name	Newfate 1 g / 10 mL Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 10 mL contains: Sucralfate ……..1 g
	Pharmaceutical form of applied drug	Liquid suspension filled in amber glass bottle seale with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Cytoprotective agent (Drugs for Peptic Ulcer and Gastro-Oesophageal Reflux Disease -GORD) ATC Code: A02BX02
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	60 mL , 120 mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Carafate 1 g / 10 mL Suspension by M/s Allergan Pharmaceuticals Approved by USFDA
	For generic drugs (me-too status)	Ulsanic 500 mg/5 ml Suspension M/s Highnoon Laboratories, Reg. No. 032072
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on:

		12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	M/S Northeast Pharmaceutical group Co. Ltd. No. 29 Shenxiliu dong road, Economic Technological Development District SHENGYANG. P.R. CHINA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DY0011500185, DY0011500186 & DY0011500187)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation New-fate Suspension with comparator product Ulsanic Suspension of Highnoon Laboratories.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	M/S Northeast Pharmaceutical group Co. Ltd. No. 29 Shenxiliu dong road, Economic Technological Development District SHENGYANG. P.R. CHINA.	

API Lot No.	DY0011900195		
Description of Pack (Container closure system)	Oral Suspension filled in amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	15-09-2021	15-09-2021	15-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate No # LN20190041 for M/S Northeast Pharmaceutical group Co. Ltd. No. 29 Shenxiliu dong road, Economic Technological Development District SHENGYANG. P.R. CHINA issued by China Food and Drug administration. It is valid till 15-07-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Sucralfate USP for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3,form 7 & invoice (invoice# EXP/71221(20-21) dated: 06-09-2021 specifying import 400g Sucralfate USP (Batch# DY0011900195) however not attested by DRAP. Copy of DHL provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	UV method was used.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply

1.	3.2.S.4.2	• Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required. • Specification claimed USP while Submitted analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug product manufacturer are according to B.P. Clarify which monograph have been used among USP or B.P Pharmacopeia monograph for drug substance.	• Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance are attached. • It is clarified that USP monograph has been used for routine testing of drug substance.
2.	3.2.S.4.3	If USP Pharmacopeia followed than Analytical verification of sucrose octasulfate by drug product manufacturer should be submitted. If B.P pharmacopeia followed than Analytical verification of sucrose octasulfate and aluminium by drug product manufacturer should be submitted	Analytical verification of Sucrose Octasulfate by drug product manufacturer is attached.
3.	3.2.S.5	Reference standard according to USP and B.P is Potassium sucrose octasulfate while submitted COA of working standard of Sucralfate USP. Clarification is required.	COA of Potassium Sucrose Octasulfate is attached.
4.	3.2.P.2.2.1	• Pharmaceutical equivalence of the applied drug shall be established with the innovator product and results of all the quality tests of the developed formulation and the innovator product shall be submitted and discussed. • B.P specification mentioned in Pharmaceutical equivalence . Clarification is required**.**	• Pharmaceutical Equivalence had been performed with market brand leader as Innovator product is not available in the country. I had be done according to ***WHO_TRS_902_ANNEX11*** report which is attached • Actual Specification is Innovator, BP mentioned mistakenly.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia) shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.
6.	3.2.P.5.2	• In assay Content of Aluminium and sucrose octasulfate separate are not	• Revised method is attached • Due to non-Pharmacopeial product, in-house method had been developed

		detected. Clarification should be submitted in this regard. • In Monograph of Drug substance assay is conducted by HPLC while drug product assay was conducted by U.V. Clarification is required from where you have adopted U.V method for assay.	on UV. Method validation is provided in 3.2. P.5.3.
7.	3.2.P.5.3	Analytical method validation of sucrose octasulfate not conducted. Clarification is required	Analytical method validation of sucrose octasulfate is attached.
8.	3.2.P.8	Commercial invoice with approval from DRAP.	Copy of DHL provided.

Decision: Registration Board deferred the case for following:

- **Justification of assay of drug product conducted by UV method while drug substance assay is conducted by HPLC as per USP monograph.**
- **Performance of assay of drug product as per Revised method.**

348.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10883 dated: 29-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 52967004840
	The proposed proprietary name / brand name	Newfer Syrup 50 mg/5mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Iron (III) Hydroxide Polymaltose Complex Eq. to Elemental Iron -----50 mg Folic Acid …….. 0.35mg
	Pharmaceutical form of applied drug	Liquid Syrup filled in amber glass bottle sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Iron Supplement
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	60 mL , 120 mL, 400 mL
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	……
	For generic drugs (me-too status)	Ferosoft-FA Syrup by M/S Hilton Pharma , Reg. No. 045110
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	**Iron Polymaltose Complex:** Chemiworld Pvt. Ltd. Plot No. 97, J- Industrial Estate Jamrud Peshawar Pakistan. **Folic Acid:** Hebei Jiheng Pharmaceutical Co., Ltd, 1 Weiwu Street, Hengshui City, Hebei Province, P.R. China 053000
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of both drug substances (i.e. Iron Polymaltose Complex and Folic acid).
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Batches of Iron Polymaltose Complex :** (BPS-0405118, BPS-0405119, BPS-0405120) **Folic acid :** (021702001, 021702002, 021702003)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of

		specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of the developed formulation Newfer Syrup 50 mg/5mL with comparator product ***Ferosoft-FA Syrup*** by ***Hilton Pharma.***
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Iron Polymaltose Complex:** Chemiworld Pvt. Ltd. Plot No. 97, J-Industrial Estate Jamrud Peshawar Pakistan. **Folic Acid:** Hebei Jiheng Pharmaceutical Co., Ltd, 1 Weiwu Street, Hengshui City, Hebei Province, P.R. China 053000		
API Lot No.	**Iron Polymaltose Complex:** K20-IPC-420 **Folic Acid:** 022004010		
Description of Pack (Container closure system)	Oral Suspension filled in Amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	21-09-2021	21-09-2021	21-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**IPC:** The firm has submitted copy of GMP Certificate # F.3-20/2017-DRAP-90 on the basis of inspection conducted on 29-11-2016 for M/S Chemiworld Pvt. Ltd. issued by DRAP. The firm has submitted application for issuance of new GMP certificate. **Folic Acid :** Copy of GMP certificate No. HE20170030 issued by China Food and Drug Administration valid till 26/05/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs Folic acid for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, form 7 & invoice (invoice# HJG/EXP/0124) dated: 07-09-

		2021 specifying import 100g Folic acid (Batch# 022004010) however not attested by DRAP. Copy of DHL provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	UV method used
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin for Iron Polymaltose Complex.	Firm submitted copy of request to federal inspector of Drugs, Peshawar for issuance of GMP certificate.
2.	3.2.S.4.1	Drug substance manufacturer and Drug product manufacturer did not mentioned Which specifications followed for Iron Polymaltose Complex. Please clarify.	It is clarified that Iron Polymaltose Complex is not present in any Pharmacopeia and manufacturer has developed an in-house method. Drug Product manufacturer also followed the Drug Substance manufacturer's method for testing
3.	3.2.S.4.2	Analytical procedures used for routine testing of the both Drug substance /Active Pharmaceutical Ingredient (Iron Polymaltose Complex &Folic Acid) by Drug substance is required	Analytical Procedures used for routine testing of the drug substance / Active Pharmaceutical Ingredient by Drug Substance is attached.
4.	3.2.S.4.3	• In analytical method verification of Iron polymaltose complex Sodium nitrile mentioned . clarification is required. • Submit analytical method verification according to analytical testing method of Iron polymaltose complex • Analytical verification is done by titration while analytical testing method of folic acid is by HPLC. Clarification is required.	• It is clarified that sodium nitrile is a clerical mistake. • Analytical verification according to analytical testing method of Iron Polymaltose Complex. Is attached. • Revised Verification by HPLC is attached.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.

6.	3.2.P.5.1	Specifications claimed are B.P. provide evidence.	Revised specification with in-house specs is attached.
7.	3.2.P.5.2	• Clarification is required that how drug product analytical testing method developed. • In Drug substance Iron polymaltose complex assay of iron contents and polymaltose contents are separately conducted. While in your analytical testing method assay of Iron polymaltose is conducted. Justify how quantity of elemental Iron is equivalent to 50mg deducted.	• The Product is not available in any Pharmacopeia we have test the product with in-house testing method. The standard & sample solutions scan on UV Spectrophotometer pick absorbance on maximum nm. After scanning this solution we have scan sample solution placebo for the conformation of method absorbance and wavelength. • In Drug substance iron Polymaltose complex assay of iron contents and Polymaltose contents are separately conducted but in syrup have many other excipients which disturbed in testing so that we use factor calculation for the equivalence of Iron Polymaltose complex to iron. 1mg of Iron is equivalent to 1.1243mg of Iron Polymaltose complex
8.	3.2.P.8	• Purchase documents for iron hydroxide polymaltose • Commercial invoice with approval from DRAP.	• Iron Polymaltose Complex was purchased locally. • Copy of DHL is provided.

Decision: The Board deferred the case for scientific justification of performance of assay testing by using UV-spectrophotometer instead of using potentiometric titration or atomic absorption spectrophotometer.

349.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10882 dated: 29-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 4481928067
	The proposed proprietary name / brand name	New-Deslor Syrup 2.5 mg / 5 mL

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each mL contains: Desloratadine .... 0.5 mg
	Pharmaceutical form of applied drug	Oral solution filled in amber glass bottle sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Anti-histamine
	Reference to Finished product specifications	Inhouse
	Proposed Pack size	60 mL / 120 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	New-Clarityn by Merck Sharp and Dhome Ltd. Approved by AEPMS (Spanish Agency for Medicine and Health Products.)
	For generic drugs (me-too status)	Desora 0.5 mg/mL M/s Continental Pharma, Reg. No. 055192
	GMP status of the Finished product manufacturer	New Section granted on 12/11/2021 Oral Liquid General Section approved.
	Name and address of API manufacturer.	M/s Morepen Laboratories Ltd. Address: Village-Masulkhana, Parwanoo, District, Solan, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DH-1501, DH-1502, DH-1503)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development,

		manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation New-Deslor Syrup with comparator product Clarinex Syrup of M/s Merck & Co.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s M/s Morepen Laboratories Ltd. Village-Masulkhana, Parwanoo, Distt. Solan India.		
API Lot No.	DH-0106		
Description of Pack (Container closure system)	Oral solution filled in amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	24-09-2021	24-09-2021	24-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Morepen Laboratories Ltd, India issued by State Drugs Controller, Controlling cum Licensing Authority, Baddi, District Solan. It is valid till 30-04-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs Folic acid for the purpose of test/analysis and stability studies is granted.

		Firm has submitted copy of Form 3, form 7 & invoice (invoice# MME202100508) dated: 14-09-2021 specifying import 0.5Kg Desloratadine (Batch# DH-0106).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Manual audit trail report submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
5.	2.3.R.1.1	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required.	Short method was mentioned in BMR. Now Revise BMR (s) are submitted as with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5.
6.	2.3.R.1.2	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2.P.3.5. Clarification is required	Short method was mentioned in BMR. Now Revise BMR (s) are submitted as with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5
7.	3.2.S.4.3	Testing method of desloratadine is by HPLC while verification is done by U.V method. Clarification is required.	Revised verification by HPLC method is submitted
8.	3.2.S.7	Accelerated stability studies of drug substance not submitted.	Accelerated stability studies of drug substance submitted.
9.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia are provided
10.	3.2.P.5.1	Specifications claimed for drug product are B.P. provide evidence.	Revised Specification are attached (Inhouse)
11.	3.2.P.5.2	Justification is required for performing assay testing by UV method	The Product is not available in any pharmacopeia so we have test from inhouse testing method. The validation of testing method is attached in dossier
12.	3.2.P.8	Commercial invoice with approval from DRAP.	Copy of DHL provided.

Decision: Registration Board deferred the case for Justification of assay of drug product conducted by UV method while drug substance assay is conducted by HPLC as per BP monograph.

M/s Hudson Pharma Private Limited, Karachi (**New Section)**

CLB in its 283rd meeting held on 28th October 2021 has considered and approved the grant Two (02) Additional section/Revised Section to M/s Hudson Pharma Karachi.

Sr.No	Name of Section
1.	Injection Ampoule BF (Steroid)
2.	Capsule (General) Section

Accordingly, firm has applied for following products for consideration by Drug Registration Board.

Injection Ampoule BF (Steroid)
02 Molecules/02 Products

350.	Name, address of Applicant / Marketing Authorization Holder	M/s Hudson Pharma Private Limited D-93, North Western Industrial Zone, Port Qasim, Karachi, Sindh 75350, Pakistan.
	Name, address of Manufacturing site.	M/s Hudson Pharma Private Limited D-93, North Western Industrial Zone, Port Qasim, Karachi, Sindh 75350, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10868 dated 29/04/2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 346815315617
	The proposed proprietary name / brand name	Becloson Suspension for Nebulisation 0.8mg/2ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml of suspension contains: Beclomethasone dipropionate….. 0.8mg
	Pharmaceutical form of applied drug	Suspension for Nebulisation
	Pharmacotherapeutic Group of (API)	Corticosteroid
	Reference to Finished product specifications	In-house
	Proposed Pack size	2ml × 1's, 5's & 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product is registered in Italian Medicine Agency (AIFA), with the brand name "Clenil" by Chiesi Farmaceutici, Italy.
	For generic drugs (me-too status)	Manufacturer name: Chiesi Farmaceutici, Italy. Importer: Chiesi Pharmaceutical (Pvt.) Ltd. Brand name: Clenil, Strength: 0.8mg/2ml, Registration number: 014091

	GMP status of the Finished product manufacturer	New section granted on 24/11/2021 Injectable Ampoule BF (steroid) - New
	Name and address of API manufacturer.	FARMABIOS S.p.A.Via Pavia, 1 27027 Gropello Cairoli, (PV) Italy.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Beclomethasone dipropionate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Batches: (0081300, 0091300, B0111322) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (0031130, 0101515, 0111515,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product that is Clenil Suspension for Nebulisation 0.8mg/2ml Batch - 1134222 by Chiesi Farmaceutici, Italy
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, Limit of Quantitation (LOQ), specificity, accuracy, precision (repeatability and intermediate), robustness and range.

STABILITY STUDY DATA	
Manufacturer of API	M/s FARMABIOS S.p.A. Via Pavia, 1 27027 Gropello Cairoli, (PV) Italy
API Lot No.	2106DM4
Description of Pack	Two aluminium pouches present in a unit carton with leaflet. Each

(Container closure system)	aluminium pouch contain 2ml x 5s product filled in plastic Ampoule (LDPE) 10 mono dose vials		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	SB-BD-NU-04	SB-BD-NU-05	SB-BD-NU-06
Batch Size	2 Liters	2 Liters	2 Liters
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	03-01-2022	03-01-2022	03-01-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No.IT-API/167/H/2020 issued by Italian Medicine Agency valid till 12/06/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 invoice (invoice# 380) Dated 19-11-2021 cleared by DRAP Karachi office dated 10-12-2021 specifying import 0.2g Beclomethasone dipropionate (Batch# 2106DM4).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail reports on product testing
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.7	Aerosol for Nebulization mentioned in this section. Clarification is required about applied formulation	Our applied formulation is in suspension form which is used as nebulisation for aerosol. So, our formulation route of administration is Suspension for nebulisation for aerosol, and the same has been mentioned on the innovator (Clenil) pack.
2.	3.2.P.5.3	Analytical Method Verification studies including specificity, accuracy and repeatability	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision)

		(method precision) performed by the Drug Product manufacturer drug substance(s) shall be submitted.	performed by the Drug Product manufacturer drug substance(s) submitted.
3.	3.2.S.5	COA of primary / secondary reference standard Testosteron Propionate including source and lot number shall be provided.	With reference to this query we would like to inform you that at the time of initial testing of Beclomethasone Dipropionate, the internal standard testosterone propionate was not available to us due to import constraints of the USP primary reference standard. Hence, we have used the same method as per USP without internal standard and complete validation has been performed to validate our results and also compare it with manufacturer results as well. Furthermore, we have ordered for working standard of Testosterone propionate from Merck, Same will be used for the release testing in future consignment. The complete method of validation is already submitted.
4.	3.2.P.5.4	The copies of complete analysis of at least two batches shall be provided.	CoA's attached
5.	3.2.P.8	• Sterility testing and Uniformity of dose units not included in initial testing. • Manufacturing date on summary sheets of stability studies for batch SB-BD-NU-05 & SB-BD-NU-06 is 12-2021 while in BMR manufactured on 03-01-2022. • Details of Water loss test for 6 months not submitted.	• We have performed the Sterility testing and Uniformity of dose on all stability batches and results are within range. CoA' are attached. • There is a Typo-graphical error in the stability sheets of both batches but the actual manufacturing date was 03-01-2022 as per BMR's. • Details of Water loss test for 6 months submitted.

Decision: Approved with innovator's specification..

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

351.	Name, address of Applicant / Marketing Authorization Holder	M/s Hudson Pharma Private Limited D-93, North Western Industrial Zone, Port Qasim, Karachi, Sindh 75350, Pakistan.
	Name, address of Manufacturing site.	M/s Hudson Pharma Private Limited D-93, North Western Industrial Zone, Port Qasim, Karachi, Sindh 75350,

		Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11038 dated 06/05/2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 40017019
	The proposed proprietary name / brand name	Becloson S Suspension for Nebulisation 0.8mg + 1.6mg/2ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml of suspension contains: Beclometasone dipropionate…….. 0.8mg Salbutamol sulphate 1.928mg equivalent to salbutamol …….1.6mg
	Pharmaceutical form of applied drug	Suspension for Nebulisation
	Pharmacotherapeutic Group of (API)	Corticosteroid and Selective beta-2-adrenoreceptor agonists
	Reference to Finished product specifications	In-house
	Proposed Pack size	2ml × 1's, 5's & 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product is registered in Italian Medicine Agency (AIFA), with the brand name "Clenil Compositum" by Chiesi Farmaceutici, Italy.
	For generic drugs (me-too status)	Manufacturer name: Chiesi Farmaceutici, Italy. Importer: Chiesi Pharmaceutical (Pvt.) Ltd. Brand name: Clenil Compositum, Strength: 0.8mg+1.6mg/2ml, Registration number: 021199
	GMP status of the Finished product manufacturer	New section granted on 24/11/2021 Injectable Ampoule BF (steroid) - New
	Name and address of API manufacturer.	**Beclomethasone dipropionate:** FARMABIOS S.p.A.Via Pavia, 1 27027 Gropello Cairoli, (PV) Italy. **Salbutamol sulphate:** LUSOCHIMICA SpA – Via Giotto 9 – 23871 Lomagna (LC) – ITALY
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification

		of specification, reference standard, container closure system and stability studies of drug substances. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Official monograph of Beclomethasone dipropionate is present in USP and Salbutamol sulphate is present in BP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	**Beclomethasone dipropionate**: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Batches: (0081300, 0091300, B0111322) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (0031130, 0101515, 0111515,) **Salbutamol sulphate:** Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (SAL 104, SAL 204, SAL 304)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product that is Clenil Compositum Suspension for Nebulisation 0.8mg+1.6mg/2ml Batch - 1136521 by Chiesi Farmaceutici, Italy
	Analytical method validation/verification of product	Method validation studies have submitted including specificity, linearity/range, accuracy, precision (repeatability and intermediate), Limit of

		Quantitation (LOQ), Limit of Detection (LOD) and robustness.		
STABILITY STUDY DATA				
Manufacturer of API		Beclomethasone dipropionate: M/s FARMABIOS S.p.A.Via Pavia, 1 27027 Gropello Cairoli, (PV) Italy. Salbutamol sulphate: M/s LUSOCHIMICA SpA – Via Giotto 9 – 23871 Lomagna (LC) – ITALY		
API Lot No.		Beclomethasone dipropionate: 2106DM4 Salbutamol sulphate: SALM119		
Description of Pack (Container closure system)		Two aluminium pouches present in a unit carton with leaflet. Each aluminium pouch contain 2ml x 5s product filled in plastic Ampoule (LDPE) 10 mono dose vials		
Stability Storage Condition		Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		SB-BS-NU-01	SB-BS-NU-02	SB-BS-NU-03
Batch Size		2 Liters	2 Liters	2 Liters
Manufacturing Date		01-2022	01-2022	01-2022
Date of Initiation		14-01-2022	14-01-2022	14-01-2022
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Beclomethasone dipropionate: Copy of GMP certificate No.IT-API/167/H/2020 issued by Italian Medicine Agency valid till 12/06/2023. Salbutamol sulphate: Copy of GMP certificate No.IT-API/69/H/2019 issued by Italian Medicine Agency valid till 03/08/2022.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Beclomethasone dipropionate : Firm has submitted copy of invoice (invoice# 380) Dated 19-11-2021 cleared by DRAP Karachi office dated 10-12-2021 specifying import 0.2g Beclomethasone dipropionate (Batch# 2106DM4). Salbutamol sulphate: Firm has submitted copy of invoice (invoice# 112) Dated 27-03-2020 cleared by DRAP Karachi office dated 23-04-2022 specifying import 5kg Salbutamol Sulphate (Batch# SALM119).		

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2	Specify the equivalent strength of the base for Salbutamol sulfate	Each 2ml of suspension contains: Beclometasone dipropionate 0.8mg Salbutamol sulphate 1.928mg equivalent to salbutamol 1.6mg
2.	1.5.7	Aerosol for Nebulization mentioned in this section. Clarification is required about applied formulation	Our applied formulation is in suspension form which is used as nebulisation for aerosol. So, our formulation route of administration is Suspension for nebulisation for aerosol, and the same has been mentioned on the innovator (Clenil Compositum) pack.
3.	2.3.R.1.1	Source of Salbutamol Sulfate in BMR's is from Cipla. Clarification is required.	A typographical error in the BMR and we have used the salbutamol sulfate manufactured by Lusochimica and it can be verified from the CoA of FPP manufacturer for the same lot number.
4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer of both drug substances (Beclomethasone dipropionate &Salbutamol sulphate shall be submitted..	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer of both drug substances (Beclometasone dipropionate & Salbutamol sulphate) shall be submitted.
5.	3.2.S.5	COA of primary / secondary reference standard Testosteron Propionate including source and lot number shall be provided.	With reference to this query we would like to inform you that at the time of initial testing of Beclomethasone Dipropionate, the internal standard testosterone propionate was not available to us due to import constraints of the USP primary reference standard. Hence, we have used the same method as per USP without internal standard and complete validation has been performed to validate our results and also compare it with manufacturer results as well.

			Furthermore, we have ordered for working standard of Testosterone propionate from Merck, Same will be used for the release testing in future consignment. The complete method of validation is already submitted.
6.	3.2.P.8	• Sterility testing and Uniformity of dose units not included in initial testing. • Details of Water loss test for 6 months not submitted.	• We have performed the Sterility testing and Uniformity of dose on all stability batches and the results are within range. • Details of Water loss test for 6 months submitted.

Decision: Registration Board deferred the case for further deliberation regarding manufacturing requirement of products containing steroidal and non-steroidal drug substance in one formulation.

Variant Pharmaceuticals (Pvt.) Ltd (New Section)

CLB in its 282nd meeting held on 31st September 2021 has considered and approved the grant One (01) Additional section to Variant Pharmaceuticals (Pvt.) Ltd

Sr.No	Name of Section
1.	Liquid Injectable -Ampoule & Vial (General)

Accordingly, firm has applied for following products for consideration by Drug Registration Board.

Liquid Injectable -Ampoule & Vial (General)
01 Molecules/02 Products

352.	Name, address of Applicant / Marketing Authorization Holder	Variant Pharmaceuticals (Pvt.) Ltd
	Name, address of Manufacturing site.	Variant Pharmaceuticals (Pvt.) Ltd Plot # 5, M-2, Pharmazone, 26 Km Main Sharaqpur Road District Sheikhupura.Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17403 dated 14/06/2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip # 561999878
	The proposed proprietary name / brand name	VARISOL 5ML STERILE WATER FOR INJECTION
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains sterile water for injection ….5ml
	Pharmaceutical form of applied drug	Intravenous injection
	Pharmacotherapeutic Group of (API)	Diluent

	Reference to Finished product specifications	USP specifications
	Proposed Pack size	5ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Sterile Water for injection 5ml by MEDEFIL INC., USFDA Approved.
	For generic drugs (me-too status)	Sterile water for injection 5ml by M/s Getz pharma (Pvt.) Ltd. (Pvt.) Ltd., Reg. No. 053043
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020 General Tablet, General Capsule, General Sachet and General dry powder injectable (pre-lyophilized), General ampoule and vial section
	Name and address of API manufacturer.	Variant Pharmaceuticals Pvt. Limited. Plot # 5, M-2, pharma zone, 26 km main sharaqpur road district Sheikhupura. Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of water for injection is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	NA
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sterile water for injection 5ml by M/s GSK pakistan Batch # SJ4PO by performing quality tests
	Analytical method validation/verification of product	NA

STABILITY STUDY DATA			
Manufacturer of API	Variant Pharmaceuticals Pvt. Limited. Plot # 5, m-2, pharma zone, 26 km main sharaqpur road district Sheikhupura. Pakistan		
API Lot No.	Lab21-001		
Description of Pack (Container closure system)	5ml glass ampoule		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 Ampoules	2000 Ampoules	2000 Ampoules
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	18-06-2021	18-06-2021	18-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	NA
3.	Documents for the procurement of API with approval from DRAP (in case of import).	NA
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.2	Explain by which method bulk water (water for injection) prepared..	By distillation method bulk water (water for injection) prepared. Complete method is attached.
2.	3.2.S.4.4	Submit certificate of analysis for batch no # Lab21-002 and Lab21-003.	Certificate of analysis for batch no # Lab21-002 and Lab21-003 submitted

3.	3.2.P.2.3 and 3.2.P.3.3	In manufacturing method no step for sterilization of water for injection included than how the product is Sterile water for injection.	Revised manufacturing method with step for terminal sterilization submitted.
4.	3.2.P.5,4	On certificate of analysis water for injection mentioned. Clarification is required..	Revise certificate of analysis with sterile water for injection are submitted.

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

353.	Name, address of Applicant / Marketing Authorization Holder	Variant Pharmaceuticals (Pvt.) Ltd
	Name, address of Manufacturing site.	Variant Pharmaceuticals (Pvt.) Ltd Plot # 5, M-2, Pharmazone, 26 Km Main Sharaqpur Road District Sheikhupura.Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17404 dated 14/06/2022
	Details of fee submitted	PKR 30,000/-: Deposit Slip # 96273520421
	The proposed proprietary name / brand name	VARISOL 10ML STERILE WATER FOR INJECTION
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains sterile water for injection ….10ml
	Pharmaceutical form of applied drug	Intravenous injection
	Pharmacotherapeutic Group of (API)	Diluent
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	10ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Sterile Water for injection 10ml by MEDEFIL INC., USFDA Approved.
	For generic drugs (me-too status)	Sterile water for injection 10ml by M/s Barrett Hodgson., Reg. No. 024637
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020

		General Tablet, General Capsule, General Sachet and General dry powder injectable (pre-lyophilized), General ampoule and vial section
	Name and address of API manufacturer.	Variant Pharmaceuticals Pvt. Limited. Plot # 5, M-2, pharma zone, 26 km main sharaqpur road district Sheikhupura. Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of water for injection is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	NA
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sterile water for injection 10ml by M/s Barrett Hodgson Reg. No. 024637 by performing quality tests
	Analytical method validation/verification of product	NA

STABILITY STUDY DATA	
Manufacturer of API	Variant Pharmaceuticals Pvt. Limited. Plot # 5, m-2, pharma zone, 26 km main sharaqpur road district Sheikhupura. Pakistan
API Lot No.	Lab21-004
Description of Pack (Container closure system)	10ml glass ampoule
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 Ampoules	2000 Ampoules	2000 Ampoules
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	19-06-2021	19-06-2021	19-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	NA
3.	Documents for the procurement of API with approval from DRAP (in case of import).	NA
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
5.	3.2.S.2	Explain by which method bulk water (water for injection prepared.)	By distillation method bulk water (water for injection) prepared. Complete method is attached.
6.	3.2.S.4.4	• Submit certificate of analysis for batch no # Lab21-005 and Lab21-006. • Batch size on COA of Batch No # Lab21-004,,mentioned 2000 Ampoules ,however it is bulk water. Clarification is required.	• Certificate of analysis for batch no # Lab21-005 and Lab21-006 submitted. • Batch size on COA 30 litres mentioned.
7.	3.2.P.2.3 and 3.2.P.3.3	In manufacturing method no step for sterilization of water for injection included than how the	Revised manufacturing method with step for terminal sterilization submitted.

		product is Sterile water for injection.	
8.	3.2.P.5,4	On certificate of analysis water for injection mentioned. Clarification is required..	Revise certificate of analysis with sterile water for injection are submitted.

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Highnoon Laboratories Limited, Lahore **(New Section)**

CLB in its 277th meeting held on 15th & 16th October 2020 has considered and approved the Three (03) Additional section/Revised Section to M/s Highnoon Laboratories Limited.

Sr.No	Name of Section
3.	Dry Powder Inhaler Capsule (Steroid) Section
4.	Capsule (General) Section (Revised)
5.	Tablet (General)Section (Revised) except Compression VI area

Accordingly, firm has applied for following products for consideration by Drug Registration Board**.**

Dry Powder Inhaler (Steroid)
02 Molecules/02 Products

354.	Name, address of Applicant / Marketing Authorization Holder	Highnoon Laboratories Limited, Lahore
	Name, address of Manufacturing site.	Highnoon Laboratories Limited of 17.5km, Multan Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17395 dated 14/06/2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 8653515941
	The proposed proprietary name / brand name	Seevair 50mcg Rotacaps
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Glycopyrronium Bromide 63mcg equivalent to Glycopyrronium …..50mcg Each delivered dose contains: Glycopyrronium bromide 55mcg equivalent to 44mcg Glycopyrronium
	Pharmaceutical form of applied drug	Capsule for DPI (White to off-white powder filled in capsule shell no 3 containing grey opaque cap and transparent body.)

	Pharmacotherapeutic Group of (API)	Cholinergic Antagonist. long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).
	Reference to Finished product specifications	Manufacturer's Specs/ Innovator
	Proposed Pack size	5's, 7's, 10's, 14's, 20's, 28's, 30's, 50's, 60's, 100's, 120's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Seebri Breezhaler® 44 micrograms inhalation powder, hard capsules, Ireland.
	For generic drugs (me-too status)	Seebri Breezhaler inhalational Powder hard capsules by M/s. Novartis Pharma, Pakistan., Reg. No. 078111
	GMP status of the Finished product manufacturer	Copy of GMP certificate based on the evaluation conducted on 11-11-2021 and valid till 11/11/2023.
	Name and address of API manufacturer.	M/s MELODY HEALTHCARE PVT. LTD. Plot No. J-73, MIDC, Tarapur, Boisar Dist. Palghar – 401 506, Maharashtra, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Glycopyrronium bromide is present in BP/ Ph. Eur. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (GLY/20003M1, GLY/20004M1, GLY/20005M1)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard,

		container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Seebri breezhaler inhalation powder hard capsule 50mcg by Novartis (Singapore) PTE LTD by performing tests (DUSA (Delivered dose uniformity by dosage sampling apparatus), ACI (Aerodynamic particle size distribution by Andersen cascade impactor (USP Apparatus 3)). CDP is not applicable in case of Dry powder inhalers.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
	Description of the delivery devices(Inhaler intended to be marketed along applied formulation	Complete description and specifications of Delivery device describe orange and white body with transparent cavity inhaler device properly sealed packed polythene and suitable to open shell size 3 with smooth opening and closing of device.

STABILITY STUDY DATA			
Manufacturer of API	M/s MELODY HEALTHCARE PVT. LTD. Plot No. J-73, MIDC, Tarapur, Boisar Dist. Palghar – 401 506, Maharashtra, India.		
API Lot No.	GLY/20001		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (3 x 10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-21116	RD-21172	RD-21173
Batch Size	24,000 capsules	24,000 capsules	24,000 capsules
Manufacturing Date	29-6-2021	25-8-2021	25-8-2021
Date of Initiation	16-09-2021	16-09-2021	16-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. NEW-WHO-GMP/ CERT/KD/91716/2020/11/31377 issued by WHO valid till 19/03/2023.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (invoice# MBR2021/GEB00070) Dated 28-8-2020 cleared by DRAP Lahore office dated 23-10-2020 specifying import 25gm Glycopyrronium bromide (Batch# GLY/20001).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.1	Clarify which specification were followed for drug substance testing by drug product manufacturer.	We are following Ph. Eur. Specifications for testing of drug substance. In case, of Assay drug product manufacturer adopted HPLC method of related substance because: 1. In titration method Acetic anhydride is used which is banned in Pakistan. 2. Also, HPLC method is more specific than titration method to assure the specificity and DRAP also prefer the HPLC method over titration.
2.	3.2.P.1	Justification of overages in the formulation(s) shall be submitted.	As, drug substance is in micrograms (63mcg), so 10% overage is taken to ensure content delivery dose of product. The same also mandated by assay limit (80% - 120%) of Product Monograph.
3.	3.2.P.8	• As per submitted record Batch No # RD-21116 was manufactured in 29-6-2021 while and samples were placed in stability chamber on 09-2021 Clarification is required. • Furthermore, Please justify where batch was stored before placement in stability chamber.	• Batch No # RD-21116 was manufactured in 29-6-2021, while samples were placed in stability chamber on 09-2021, because it was the initial trial batch which was used for development of testing method. During this period, this batch was stored in quarantine under control storage condition. • Moreover, other two Batches RD-21172 & RD-21173 were manufactured in Aug-2021 and placed in stability chamber on 09-2021 and each batch having batch size of 24,000 capsules. Both batches comply with the stability

			studies requirements of CTD guidelines which stated that: "3.2.P.8 Stability: b). At least 2 batches having the following minimum batch size considering the scientific reliability • OSDs: 5000 Units • Oral Liquid/Suspension: 2000 • Injectable: 2000 • Aerosol and any other specialized preparations: 500".

Decision: Approved with innovator's specification.

- **Firm shall submit master formulation without overage before issuance of registration letter along with fee of Rs. 30,000/- for change/correction in composition as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

355.	Name, address of Applicant / Marketing Authorization Holder	Highnoon Laboratories Limited, Lahore
	Name, address of Manufacturing site.	Highnoon Laboratories Limited of 17.5km, Multan Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17391 dated 16/06/2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 0435062737
	The proposed proprietary name / brand name	Ultivair 50mcg/ 110mcg rotacaps
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Glycopyrronium (as bromide) …….50mcg Indacaterol (as Maleate) …….110mcg Each delivered dose contains: Glycopyrronium (as bromide) …….43mcg Indacaterol (as Maleate) …….85mcg
	Pharmaceutical form of applied drug	DPI Capsule (White to off white powder filled in capsule shell no 3 containing grey opaque cap & transparent body.)
	Pharmacotherapeutic Group of (API)	Cholinergic Antagonist.

		long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).
	Reference to Finished product specifications	Manufacturer's Specs/ Innovator
	Proposed Pack size	5's, 7's, 10's, 14's, 20's, 28's, 30's, 50's, 60's, 100's, 120's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ultibro Breezhaler 85 micrograms/43 micrograms inhalation powder hard capsules (MHRA Approved).
	For generic drugs (me-too status)	Inbro DPI Capsule 110mcg + 50mcg by M/s. Martin Dow Limited, Karachi, Pakistan approved in 307th DRB meeting.
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 06/2022-DRAP (AD-334240006) issued by DRAP valid till 11/11/2023.
	Name and address of API manufacturer.	M/s MELODY HEALTHCARE PVT. LTD. Plot No. J-73, MIDC, Tarapur, Boisar Dist. Palghar – 401 506, Maharashtra, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Glycopyrronium bromide is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Whereas, Indacaterol maleate complies Manufacturer's specifications. So, firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance as per inhouse specifications.

	Stability studies	Stability study conditions: **1. Glycopyrronium bromide:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (GLY/20003M1, GLY/20004M1, GLY/20005M1) **2. Indacaterol maleate:** Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ICM/19004, ICM/19005, ICM/19006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Ultibro Breezhaler 85 micrograms/43 micrograms inhalation powder hard capsules by Novartis Pharma Stein AG by performing tests (DUSA (Delivered dose uniformity by dosage sampling apparatus), ACI (Aerodynamic particle size distribution by Andersen cascade impactor (USP Apparatus 3)). CDP is not applicable in case of Dry powder inhalers.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
	Description of the delivery devices(Inhaler intended to be marketed along applied formulation	Complete description and specifications of Delivery device describe orange and white body with transparent cavity inhaler device properly sealed packed polythene and suitable to open shell size 3 with smooth opening and closing of device.

STABILITY STUDY DATA	
Manufacturer of API	M/s MELODY HEALTHCARE PVT. LTD. Plot No. J-73, MIDC, Tarapur, Boisar Dist. Palghar – 401 506, Maharashtra, India.
API Lot No.	Glycopyrronium bromide: GLY/20001 Indacaterol maleate: ICM/20005
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (3 x 10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months

	Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-21115	RD-21170	RD-21171
Batch Size	24,000 capsules	24,000 capsules	24,000 capsules
Manufacturing Date	11-6-2021	25-8-2021	25-8-2021
Date of Initiation	16-09-2021	16-09-2021	16-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. NEW-WHO-GMP/ CERT/KD/91716/2020/11/31377 issued by WHO valid till 19/03/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Glycopyrronium bromide:** Firm has submitted copy of invoice (invoice# MBR2021/GEB00070) Dated 28-8-2020 cleared by DRAP Lahore office dated 23-10-2020 specifying import 25gm Glycopyrronium bromide (Batch# GLY/20001). **Indacaterol maleate:** Firm has submitted copy of invoice (invoice# MBR2021/GEB00070) Dated 28-8-2020 cleared by DRAP Lahore office dated 23-10-2020 specifying import 25gm Indacaterol maleate (Batch# ICM/20005).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.1	Clarify which specification were followed for drug substance (Glycopyrronium bromide**)** testing by drug product manufacturer.	We are following Ph. Eur. Specifications for testing of drug substance. In case, of Assay drug product manufacturer adopted HPLC method of related substance because: 3. In titration method Acetic anhydride is used which is banned in Pakistan.

			4. Also, HPLC method is more specific than titration method to assure the specificity and DRAP also prefer the HPLC method over titration.
2.	3.2.P.1	Justification of overages in the formulation(s) shall be submitted.	As, drug substance is in micrograms (63mcg), so 10% overage is taken to ensure content delivery dose of product. The same also mandated by assay limit (80% - 120%) of Product Monograph.
3.	3.2.P.8	• As per submitted record Batch No # RD-21115 was manufactured in 11-06-2021 while and samples were placed in stability chamber on 16-09-2021 Clarification is required. • Furthermore, Please justify where batch was stored before placement in stability chamber.	• Batch No # RD-21115 was manufactured in 11-6-2021, while samples were placed in stability chamber on 09-2021, because it was the initial trial batch which was used for development of testing method. During this period, this batch was stored in quarantine under control storage condition. • Moreover, other two Batches RD-21170 & RD-21171 were manufactured in Aug-2021 and placed in stability chamber on 09-2021 and each batch having batch size of 24,000 capsules. Both batches comply with the stability studies requirements of CTD guidelines which stated that: "3.2.P.8 Stability: b). At least 2 batches having the following minimum batch size considering the scientific reliability • **<u>OSDs: 5000 Units</u>** • Oral Liquid/Suspension: 2000 • Injectable: 2000 • Aerosol and any other specialized preparations: 500".

Decision: Approved with innovator's specification.

- **Firm shall submit master formulation without overage before issuance of registration letter along with fee of Rs. 30,000/- for change/correction in composition as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case no. 03 Registration applications for local manufacturing of (veterinary) drugs

a. Deferred Cases

356.	Name and address of manufacturer / Applicant	M/s Farm Aid Group. Plot # 3/2, Phase I & II, Hattar Industrial Estate, Haripur
	Brand Name +Dosage Form + Strength	CB DOX Powder
	Composition	Each 1000gm contains: Doxycycline HCL…200gm Tylosin Tartrate…100gm Colistin Sulphate…480MIU Bromhexine HCL…5gm
	Diary No. Date of R& I & fee	Dy.No. 44454 dated 31-12-2018 Rs.20,000/- Dated 27-12-2018
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer specification
	Pack size & Demanded Price	10gm, 20gm, 30gm, 50gm, 100gm, 250gm, 500g, 1kg, 5kg, 10kg,: Decontrolled
	Me-too status	Emeria Shell Powder Of M/S Inshal Pharmaceutical
	GMP status	Last GMP inspection conducted on 03-10-2018 report concludes that firm was considered to be maintaining satisfactory level of the cGMP
	Remarks of the Evaluator[IV]	
	Previous decision (M-295)	Deferred for conversion of Colistin Sulphate MIU to grams
	Evaluation by PEC	Firm submitted conversion as follows: Conversion of Colistin Sulphate (MIU to grams) 19000 IU of Colistin Sulphate = 0.001 grams of Colistin Sulphate 1 IU of Colistin Sulphate = 0.001/19000 grams of Colistin Sulphate 1 MIU of Colistin Sulphate = 0.001/19000 x 1,000,000 grams of Colistin Sulphate 480 MIU of Colistin Sulphate = 25.263 grams
	Decision: Registration Board deferred the case for justification of Colistin sulphate conversion in the light of as per the document No. EMEA/MRL/016/95-Final (Summary Report for colistin) issued by Committee for Veterinary Medical Products, Colistin Base has been assigned a potency of 1000ug base activity per mg (30,000 IU/mg) and theoretical potency of Colistin Sulphate is 800ug per mg (24,000IU/mg).	
357.	Name and address of manufacturer / Applicant	M/s Farm Aid Group. Plot # 3/2, Phase I & II, Hattar Industrial Estate, Haripur
	Brand Name +Dosage Form + Strength	U Mox Powder
	Composition	Each gm contains: Amoxicillin Trihydrate…200mg Colistin Sulphate…60,000,000 IU
	Diary No. Date of R& I & fee	Dy.No. 44453 dated 31-12-2018 Rs.20,000/- Dated 27-12-2018
	Pharmacological Group	Antibiotic

	Type of Form	Form-5
	Finished product Specification	Manufacturer specification
	Pack size & Demanded Price	10gm, 20gm, 30gm, 50gm, 100gm, 250gm, 500g, 1kg, 5kg, 10kg,: Decontrolled
	Me-too status	Almoxin-C Water Soluble Powder Of M/S Breeze Pharma
	GMP status	Last GMP inspection conducted on 03-10-2018 report concludes that firm was considered to be maintaining satisfactory level of the cGMP
	Remarks of the Evaluator[iv]	Colistine Sulphate 60,000,000 in applied formulation while in submitted generic reference contain Colistine Sulphate 60,00,000. Clarify.
	Previous decision (M-295)	Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Evaluation by PEC	Firm said that they applied formulation as follows: Each gm contains: Amoxicillin Trihydrate…200mg Colistin Sulphate…60,00,000 IU And submitted copy of covering letter as proof.(However in form 5 a different strength) Firm submitted conversion as follows: Conversion of Colistin Sulphate (MIU to grams) 19000 IU of Colistin Sulphate = 0.001 grams of Colistin Sulphate 1 IU of Colistin Sulphate = 0.001/19000 grams of Colistin Sulphate 60,00,000 IU of Colistin Sulphate = 0.3158 grams
	Decision: Deferred for following: • **Submission of Complete Dossier with revised form 5 for corrected formulation and fee.** • **For justification of Colistin sulphate conversion in the light of as per the document No. EMEA/MRL/016/95-Final (Summary Report for colistin) issued by Committee for Veterinary Medical Products, Colistin Base has been assigned a potency of 1000ug base activity per mg (30,000 IU/mg) and theoretical potency of Colistin Sulphate is 800ug per mg (24,000IU/mg).**	

Case no. 04 Registration applications of categories to be considered on priority

a. Import applications of priority categories defined by Registration Board in its 257th meeting

i. Human

Deferred case:

358.	Name, address of Applicant / Importer	M/s Titlis Pharmaceuticals., 528-A Industrial Estate, Raiwind Road, Lahore-Pakistan.
	Details of Drug Sale License of importer	**License No:** 05-352-0066-035681D **Address:** 528-A, Sunder Industrial Estate ,Raiwind Road, Lahore **Validity:** 02-Oct-2022

		Status: by way of distributor
	Name and address of marketing authorization holder (abroad)	The Mentholum Company Limited, 1 Redwood Avenue Peel Park campus East Killbride Scotland G74 5PE United Kingdom.
	Name, address of manufacturer(s)	The Mentholum Company Limited, 1 Redwood Avenue Peel Park campus East Killbride Scotland G74 5PE United Kingdom.
	Name of exporting country	UK
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)** • Original legalized COPP (Certificate# PP10165236) issued by Medicine and Healthcare Products Regulatory Agency (MHRA) Dated: **19-02-2020** • Free Sale status: The COPP endorses the free sale status of the applied product in UK. GMP status: Firm has submitted Legalized copy of GMP certificate (Certificate No. UK MIA 189 Insp GMP/GDP 189/11483-0019) issued by Medicine and Healthcare Products Regulatory Agency (MHRA) in the name of M/s **The Mentholatum Company Limited** issued on 22-01-2022
	Details of letter of authorization / sole agency agreement	Sole agency agreement has been submitted The Mentholum Company Limited, 1 Redwood Avenue Peel Park campus East Killbride Scotland G74 5PE United Kingdom with M/s Titlis Pharmaceuticals., 528-A Industrial Estate, Raiwind Road, Lahore-Pakistan Pakistan. Dated: 18-02-2020
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 24081 dated: 01-09-2021
	Details of fee submitted	PKR 100,000/- dated :05-10-2020
	The proposed proprietary name / brand name	**Deep Relief Gel/ Deep Relief Pain Relief Gel**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1g of gel Contains: Ibuprofen…….50mg (5%) Levomenthol…..30mg (3%)
	Pharmaceutical form of applied drug	Topical gel for external use only.
	Pharmacotherapeutic Group of (API)	Non-steroidal anti-inflammatory drug (NSAID)
	Reference to Finished product specifications	Manufacturer specifications (In house)
	Proposed Pack size	1's x50gm, 1's x100gm,
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	MHRA Approved
	For generic drugs (me-too status)	----
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	**Levomenthol:** M/s BASF SE Carl- Bosch-Straβe 38-67056 Ludwingshafen Feral Republic of Germany **Ibuprofen:** ➢ M/s BASF Corporation, Highway 77 South USA- 78343 bishop Texas & ➢ Hubei Granules-Biocause Pharmaceutical Co.Ltd/China 122 Yangwan- Biocause China city Hubei Province
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Levomenthol:** Firm has submitted long term stability study data of 3 batches of drug substance at 25°C ± 2°C / 60 ± 5% RH for 24 **Ibuprofen:** 25°C ± 2°C / 60 ± 5% months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months.

<table>
<tr><td></td><td>Module-III Drug Product:</td><td>Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.</td></tr>
<tr><td></td><td>Pharmaceutical Equivalence and Comparative Dissolution Profile</td><td>Firm submitted that Deep Relief Gel (approved by MHRA-UK is an originator's product manufactured by Mentholatum company Limited UK. Therefore pharmaceutical equivalence through comparative dissolution profile is not applicable on it.</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Firm has submitted analytical method verification studies of the drug product.</td></tr>
<tr><td></td><td>Container closure system of the drug product</td><td>Printed, collapsible aluminium tube with a membrane nozzle.</td></tr>
<tr><td></td><td>Stability study data of drug product, shelf life and storage conditions</td><td>Accelerated stability studies have been conducted at 40°C ±2°C / 75%±5% RH for 06 months.
Real time stability studies conducted at 25 °C±2°C / 60% ± 5% RH and at 30 °C±2°C / 65% ± 5% RH for 36months.
However stability studies data at & 30 °C±2°C / 65% ± 5% RH starts from 9th month and in protocols mentioned as Bracketing as per ICH Q1A (R2) employed at the three and six month time points means sample at & 30 °C±2°C / 65% ± 5% RH were only analysed in the event of unsatisfactory results from 40°C ±2°C / 75%±5% RH storage condition.
Batch submitted:
<table>
<tr><th>Batch No</th><th>Trail start date</th><th>Trial end date</th><th>Time points for Long Term stability studies</th></tr>
<tr><td>12401</td><td>24-Apr- 03</td><td>24-Apr-06</td><td>0,9,12,18,24 and 36 months</td></tr>
<tr><td>20181</td><td>16-Jul-09</td><td>16- Jul-09</td><td>0,9,12,18,24 and 36 months</td></tr>
<tr><td>21812</td><td>26-Aug-10</td><td>26-Aug- 13</td><td>0,9,12,18,24 and 36 months</td></tr>
<tr><td>14050</td><td>02-Dec- 04</td><td>02- Dec-07</td><td>0,9,12,18,24 and 36 months</td></tr>
</table></td></tr>
<tr><td colspan="3">Evaluation by PEC:</td></tr>
</table>

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Name and address of API manufacturer not mentioned in this section.	Submitted
2.	3.2.P.8	In Submitted stability studies batches it is not evident that Drug substance Ibuprofen from which source is used.	Firm submitted details that 8 batches stability data submitted out of which in 6 batches source of Ibuprofen was M/s BASF Corporation, Highway 77 South USA- 78343 bishop Texas And in 2 batches source of Ibuprofen was Hubei Granules-Biocause Pharmaceutical Co.Ltd/China 122 Yangwan- Biocause China city Hubei Province

Previous Decision (M-317): Deferred for Evaluation of stability studies in the light of ICH Q1 D guidelines.

Firm Reply: In response to valued decision of Drug Registration Board; we would like submit that the stability of Deep Relief Gel is as per **ICH Q1-D guidelines;** and following clauses are being presented for your kind review:

1- Clause 2.4.1 "Design factors that can be matrixed include batches made by using the same process and equipment, and container sizes and/or fills in the same container closure system."

2- Clause 2.4.2"In a design where time points are matrixed, all selected factor combinations should be tested at the initial and final time points."

3- Clause 2.4.2" data from at least three time points, including initial, should be available for each selected combination through the first 12 months of the study."

4- Clause 2.4.4"a matrixing design is applicable if the supporting data indicate predictable product stability. Matrixing is appropriate when the supporting data exhibit only small variability."

It is humbly stated that the stability of Deep Relief Gel complies all the above clauses and hence it is in accordance to ICH Q1-D Guidelines. The justification letter from the Manufacturer (Mentholatum Company Limited/UK) is attached

_In addition, we are also submitting the Complete Stability studies of three batches of Deep Relief Gel according to Zone-IVA conditions (30±2 ℃ & 65%±5 RH)

Evaluation by PEC: Firm submitted Stability data of 3 batches in which Accelerated stability studies have been conducted at 40^{o}C ±2^{o}C / 75%±5% RH for 06 months.
Real time stability studies conducted at 25 ^{o}C±2^{o}C / 60% ± 5% RH and at 30 ^{o}C±2^{o}C / 65% ± 5% RH for 36months.And stability studies data at 30 ^{o}C±2^{o}C / 65% ± 5% RH includes all the time points **i.e** 0, 3, 6,9,12,18,24 and 36 months.

Batches submitted.

Batch No	Trail start date	Trial end date	Time points for Long Term stability studies
34982	13- Feb- 19	13- Feb- 22	0,3,6, 9,12,18,24 and 36 months
33789	14- May- 18	14- May- 21	0,3,6, 9,12,18,24 and 36 months
34048	06- Aug- 18	06- Aug- 21	0,3,6, 9,12,18,24 and 36 months
34938	29- Mar- 19	29- Mar- 22	0,3,6, 9,12,18,24 and 36 months

Decision: Approved with Innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility. • **Firm shall submit the fee of Rs. 7,500 for revision of specifications per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		
359.	Name, address of Applicant / Importer	M/s Hakimsons Private Limited., Hakimsons House, A-58/B, S.I.T.E, Manghopir Road, Karachi-75700, Pakistan.
	Details of Drug Sale License of importer	**License No:** 001 No. DHOKW (Drugs)/-0431 **Address:** A-58/B, S.I.T.E, Karachi **Address of Godown:** NA **Validity:** 21-08-2022 **Status:** Drug license by the way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Eugia Pharma Specialities Limited. Survey No. 550, 551 & 552, Kolthur Village, Shamirpet Mandal, Medchal-Malkajgiri, District Medchal, Telangana, 500101, India.
	Name, address of manufacturer(s)	M/s Eugia Pharma Specialities Limited. Survey No. 550, 551 & 552, Kolthur Village, Shamirpet Mandal, Medchal-Malkajgiri, District Medchal, Telangana, 500101, India
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted Original Legalized CoPP (Certificate#2850/STORES/2020-38) issued by Drugs Control Administration, Government of Telangana, India for ENZASTIK Capsules 40mg (Enzalutamide). CoPP confirms facilities and operations conforming to GMP as recommended by the World Health Organization. The certificate is valid till 28.11.2021. **GMP certificate:** The firm has submitted copy of GMP certificate for M/s Eugia Pharma Specialities Ltd. India issued by Drugs control Administration, Government of Telangana, India. The certificate is valid till 28-11-2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted a copy of letter of authorization from M/s Aurobindo Pharma Limited, plot No.2, Maitri Vihar, Ameerpet, Hyderabad. According to the letter, the firm has appointed "M/s Hakimsons Pvt. Ltd," with principal place of business at A-58/B, S.I.T.E, Manghopir Road, Karachi as its Exclusive Distributor for the territory of Islamic Republic of Pakistan. The letter was issued on 10-12-2020 and it is valid for a period of five years. **The applicant has submitted notarized copy of letter clarifying the relationship between Eugia pharma specialities Limited and Aurobindo Pharma Ltd.**

		Eugia pharma specialities Limited is wholly owned subsidiary company of Aurobindo Pharma Limited with registered office address "Plot No.2, Maitrivihar, Ameerpet, Hyderabad, Telanagana State, India. Eugia pharma specialities Limited, with manufacturing site address "survey no. 550, 551 & 552, kolthur village, shamirpet Mandal, Medchal -Malkagiri District, Telangana, India, manufactures oncology & Hormonal products and is one of the manufacturing facilities associated with Aurobindo Pharma Limited.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 23873 dated: 31-08-2021
	Details of fee submitted	PKR 100,000/- dated :04-02-2021
	The proposed proprietary name / brand name	**ENZASTIK – 40 Capsules 40mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Enzalutamide…….40mg
	Pharmaceutical form of applied drug	Soft gelatin capsule (Anti-neoplastic Agent)
	Pharmacotherapeutic Group of (API)	L02BB ; Anti-androgens XTANDI is an androgen receptor inhibitor indicated for the treatment of patients with: • castration-resistant prostate cancer. • Metastatic castration-sensitive prostate cancer.
	Reference to Finished product specifications	In house
	Proposed Pack size	4 x 28's
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	XTANDI (enzalutamide) capsules 40mg **(USFDA** Approved).
	For generic drugs (me-too status)	----
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized

		information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Name, address of drug substance manufacturer	M/s Laurus Labs Limited, Plot No. 21, Jawaharlal Nehru Pharma City, Parawada, Visakhapatnam-531021 Andhra Pradesh, India Tel: +91-891-3061222 Fax: +91-891-3061270
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 03 batches of API at accelerated as well as real time conditions 40 ± 2° C / 75 ± 5% RH . The real time stability data is conducted at 25 ± 2° C/60 ± 5%RH. The stability study data is till 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has submitted physicochemical evaluation of **XTANDI 40 mg Capsules manufactured by Astellas Pharma, Europe B.V, Netherlands (Reference Drug Product)** and also submitted finished product evaluation of Enzalutamide Capsules 40 mg by **Eugia Pharma Specialties Limited (Proposed Generic Product) (B.No: EN4017003-B)**
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	PVC/PVDC/Aluminum foil blister pack
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 03 batches The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 06 months. The real time stability study data is conducted at 30^{o}C ±2^{o}C / 75% ± 5% RH. The real time stability study data of 03 batches is for 24months.

Evaluation by PEC:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer drug substance(s) shall be submitted.	Submitted
2.	3.2.P.3.5	process validation reports including the protocols and results for critical process steps mentioned in 2.3.P.3.4 / 3.2.P.3.4 shall be provided.	All critical quality attributes mentioned in 2.3.P.3.4/3.3.P.3.4 are covered in process validation reports except "Gelatin shell weight and Gelatin gross weight of capsule" are not covered in process validation report. However, these are regularly monitored as in process checks at initial and every 30 minutes and results are reported in batch manufacturing record.
3.	3.2.P.5.2	US FDA review document of the Innovator product, specifies the dissolution limit as "NLT Q in 15 minutes" 0.1N HCl/ 0.3% CTAB, whereas submitted specifications declare the dissolution limits as "NLT 75% in 30 minutes" . Justify the variation in time point of dissolution.	Our product is a dosage form of soft gelatin capsule formulation. Gelatin cross-linking is a common problem of gelatin capsule, which is typically triggered by catalytic amounts of aldehydes and /or from exposure to high temperature and humidity. This impact is commonly seen in stability testing and results in lower and/or incomplete dissolution invitro. Enzymes like pepsin and pancreatin act by cleavage of peptide bonds present in cross- linked gelatin and there by resulting in release of content from capsule Dissolution method for drug product (Enzalutamide capsule 40mg) includes both Tier-I media (with out enzymes) and Tier-II media [ith inclusion of enzymes i.e., Pepsin added in 0.3%

<table>
<tr><td></td><td></td><td></td><td>CTAB(cetyl trimethyl ammonium bromide) in 0.1N HCl]. In the instance of drug product failing to meet the acceptance criteria in Tier-I due to gelatin cross-linking , Tier-II method would be adopted.
Since the test product shows the cross linking tendency, we have adopted the dissolution method bot Tier-I and Tier-II in the analytical testing methodology.. The tier-II dissolution testing for cross-linked capsules involves two steps:
1) Pre-treatment
2) After Pre-treatment (main treatment)
In first step pre-treatment the cross-linked capsules were subjected to exposure (pre-soaking) to pepsin enriched media (450ml)for 10 minutes . After pre-treatment remaining pre-warmed plain 0.1N HCl/ 0.3% CTAB (without any pepsin) is added to makeup the final volume to 900ml. therefore the representation of dissolution time point [Q time point in Tier-I media is 30 minutes, which includes 10 minutes of pre-treatment step and remaining 20 minutes of main treatment in final volume.
Hence based on the above dissolution testing discussion and considering the higher disintegration time allowed for soft gelatin capsule, the following dissolution limits are proposed for release and stability shelf life testing of Enzalutamide capsule.

<table><tr><td rowspan="2">Test</td><td colspan="2">Adopted dissolution Limits</td></tr><tr><td>Release</td><td>Shelf life</td></tr><tr><td>Dissolution (%)</td><td>NLT 75% Q in 30 minutes</td><td>NLT 75% Q in 30 minutes</td></tr></table></td></tr>
<tr><td>4.</td><td>3.2.P.8</td><td>From submitted stability data for product it is not evident that dissolution testing conducted either on Tier-1, or Tier-2 or both.</td><td>All batches were tested with Tier-1 method up to 12 months and from 18 months station batches are tested with Tier-2 method. Stability data results with note “ Results pass at Tier-2 stage” are enclosed.</td></tr>
<tr><td colspan="4">Previous Decision: Deferred for following:
• Details of Reference Drug Product against which pharmaceutical equivalence and CDP studies were performed.
• Clarification that Gelatin shell weight and Gelatin gross weight of capsule” are not monitored in
process validation. (M- 317 RB)</td></tr>
<tr><td colspan="4">Response of firm:</td></tr>
<tr><td colspan="2">Details of Reference Drug Product against which pharmaceutical equivalence and CDP studies were performed.</td><td colspan="2">The details of reference used against pharmaceuticals equivalence and CDP studies are:
XTANDI 40 mg Capsules
Manufactured by Astellas Pharma, Europe B.V, Netherlands.
Batch No. 15 D11/15</td></tr>
<tr><td colspan="2">Clarification that Gelatin shell weight and Gelatin gross weight of capsule” are not monitored in process validation.</td><td colspan="2">Please be informed that all critical quality attributes mentioned in 2.3.P.3.4/3.3.P.3.4 are covered in process validation reports except</td></tr>
</table>

	"Gelatin shell weight and Gelatin gross weight of capsule" are not covered in process validation report. However, these are regularly monitored as in process checks at initial and every 30 minutes and results are reported in batch manufacturing record Please find enclosed herewith the pages of in process control parameters along with in process check record of the BMR for your ready reference. **[Firm submitted BMR pages of 03 Batches (Batch No# EN4017001, EN4017002 and EN4017003) in which In process Control parameters, where frequency(During start up and every 30 minutes alternate by production and QA) and limits for Gelatin shell weight and Gelatin gross weight of capsule checks is mentioned. Moreover they submitted sheets for Start up checks by production and by QA for Gelatin shell weight and gross weight of capsule and In process check record every 30 minutes alternate by production and QA for Gelatin shell weight and gross weight of capsule]**
Decision: Deferred for following points: • **Evidence of requisite manufacturing facility i.e. soft gelatin cytotoxic as provided document does not mention about dedicated facility.** • **Submission of fee of Rs. 7,500 for revision of specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

Case no. 05 Miscellaneous cases
Azithromycin Tablet 500mg:
Composition:
Each Film coated tablet contains:
Azithromycin as dihydrate…….500mg
Availability in RRAs:
MHRA Approved
ME too status:
" Azic 500mg Tablet by M/s Nabi Qasim Reg # 055584
Specifications:USP

360.	M/s Biorex Pharmaceuticals Plot No 251-A, Industrial Triangle, Kahuta Road, Islamabad, Pakistan	Zithrorex 500mg Tablet	Each tablet contains: Azithromycin as trihydrate…500mg	Form-5 Dy.No 13098 dated 06-03-2019 Rs.20,000/- Dated 06-03-2019	10's	Last inspection report is older than 3 years

	Previous Decision (295-DRB)	Deferred for updated status of GMP from QA & LT.
	Evaluation by PEC	The firm have submitted GMP certificate issued on 28-01-2022 based on inspection conducted on 09-12-2021
	Previous decision (M-295)	Approved as per following label claim with USP specifications.: Each film coated tablet contains: Azithromycin as trihydrate…500mg Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021**.**
	Response of firm	The firm has applied Azithromycin (as dihydrate), but in 316th meeting Decision Azithromycin as trihydrate is mentioned. Kindly correct it. Submitted fee of Rs: 7500/- Deposit slip # 52758099460 Dated: 24-05-2022
Decision: Approved with USP specifications. **Firm shall submit remaining fee for correction/pre-approval change in the salt form , as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		

Agenda of Evaluator PEC-V

Item No. I: Agenda of Evaluator PEC-V

Case No. 1: Priority Consideration of drugs for Covid-19

361.	Name, address of Applicant / Importer	M/s Pfizer Pakistan Limited, 12 Dockyard Road West Wharf, Karachi.
	Details of Drug Sale License of importer	DHOKW(Drugs)/148/License No. 029 Address: 12 Dockyard Road West Wharf, Karachi. Address of go-down 12 Dockyard Road West Wharf, Karachi. Validity: 25-02-2023 Status: License to sell drugs by way of Whole sale.
	Name and address of marketing authorization holder (abroad)	M/s Pfizer Limited Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom
	Name, address of manufacturer(s)	Ritonavir Tablets Bulk Tabs. Manufacturer, Testing and Release M/s. Hetero Labs Limited, Unit-III, 22-110, Industrial Development Area, Jeedimetla, Hyderabad-500055, Telangana, India Nirmatrelvir Tablets Manufacturer,Primary Packaging,Secondary Packaging,Testing, Stability,Release of co-packs Pfizer Manufacturing Deutschland GmbH Betriebsstätte Freiburg,Mooswaldallee 1,79090 Freiburg, Germany
	Name of exporting country	Germany

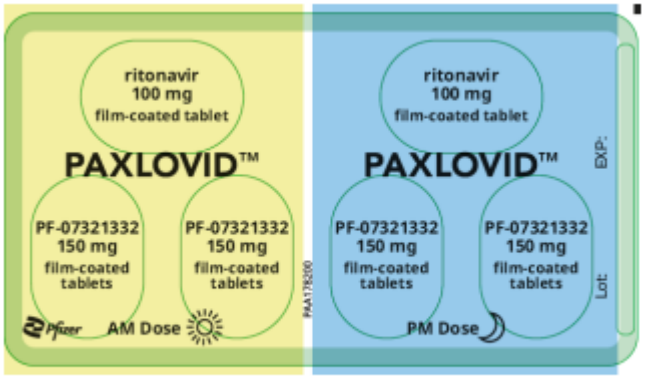
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted copy **GMP** Certificate (No. DE_BW-01_GMP_2021_0006 dated 21-02-2021 valid till 07-10-2023 issued by Germany. The GMP certificate specifies the GMP status of the manufacturer. • Firm has submitted Original and Legalized **CoPP** (PP10175835) dated 18-02-2022 valid for five years issued by Medicine and Healthcare Products Regulatory Agency United Kingdom. The CoPP specifies free sale status of the product in country of origin along with its availability.
	Details of letter of authorization / sole agency agreement	Original LOA has been submitted by firm dated 10-02-2022
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dairy No. 6640 Dated 10-03-2022
	Details of fee submitted	PKR 75,000/-: 20-01-2022
	The proposed proprietary name / brand name	**PAXLOVID 150 mg/100mg Film-Coated Tablets**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Pink Coloured Film coated tablet contains: Nirmatrelvir……150mg Each White Coloured Film coated tablet contains: Ritonavir……100mg
	Pharmaceutical form of applied drug	Film Coated Tablets
	Pharmacotherapeutic Group of (API)	Protease Inhibitor Antiviral PF-07321332 and ritonavir, in two different tablets. PF-07321332 works by reducing the ability of SARS-CoV-2 (the virus that causes COVID-19) to multiply in the body while ritonavir prolongs the action of PF-07321332 enabling it to remain longer in the body at levels that affect the multiplication of the virus.
	Reference to Finished product specifications	Pfizer Specs
	Proposed Pack size	30's
	Proposed unit price	Firm has stated it will be provided later.
	The status in reference regulatory authorities	MHRA approved (Conditional Grant) EMA:Conditional marketing authorisation

<table>
<tr><td></td><td>For generic drugs (me-too status)</td><td>NA</td></tr>
<tr><td></td><td>Module-II (Quality Overall Summary)</td><td>Firm has not provided QOS.
Firms response
An up-to-date Quality Overall Summary (QOS) that summarizes the complete module 3 content is not available currently. Due to accelerated development timelines in response to the pandemic, the dossier was submitted to MHRA and subsequently updated as part of a rolling submission process. The QOS included with this dossier is intended to provide a brief introduction to the product only.</td></tr>
<tr><td></td><td colspan="2">Nirmatrelvir (PF-07321332)</td></tr>
<tr><td></td><td>Name, address of drug substance manufacturer</td><td>The following commercial sites are involved in manufacturing of drug substance:<table><tr><td>Site 1</td><td>Pfizer Ireland Pharmaceuticals, Ringaskiddy Active Pharmaceutical Ingredient Plant Ringaskiddy County Cork, Ireland</td></tr><tr><td>Site 2</td><td>Jilin Asymchem Laboratories Co. Ltd, No. 99, Hongda Road, Economic Development Zone, Dunhua, Jilin 133700, China (CHN)</td></tr><tr><td>Site 3</td><td>Changzhou SynTheAll Pharmaceutical Co. Ltd No.589, North Yulong Road, Xinbei District, Changzhou, CH 213127, China (CHN)</td></tr></table></td></tr>
<tr><td></td><td>Module-III Drug Substance:</td><td>General Information
Nirmatrelvir was formally known as PF-07321332.
Polymorphism: Form 1 is the thermodynamically most stable form at relevant temperatures and humidity and is used for development and emergency application supplies.
Chirality: PF-07321332 has 6 asymmetric centers, giving 32 possible stereoisomers.
There are no cis-trans isomers for PF-07321332.
White to pale colored powder.
Manufacture, characterisation and process controls
A total of six synthetic routes have been used to manufacture supplies of PF-07321332. There are two processes used in the manufacture of PF-07321332, Synthetic Route F and Synthetic Route G.
There is no process validation as there is no aseptic processing or sterilization in the manufacture of PF-07321332.
Specification
Provisional Specifications have been provided for synthetic route F and G.
Provisional analytical procedures used to control the manufacture of PF-07321332. The final analytical methods for registration will be validated in accordance with ICH guidelines.</td></tr>
</table>

		Container Closure System PF-07321332 is packaged in two sealed, low density polyethylene (LDPE) anti-static liners.The bagged material is then inserted in a high density polyethylene (HDPE) drum or equivalent secondary container.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	The stability of PF-07321322 synthetic routes C and D are supportive of synthetic routes F and G as all synthetic routes have the same polymorph, similar synthetic chemistry, and same final solvents. **Condition (6months)** 40°C/75% RH 25°C/60% RH **Shelf life** A retest date has been assigned to be 12 months at 15 – 30°C. Emergency supply batches of PF-07321332 drug substance manufactured at the commercial site will be placed on stability at 30°C/75% RH and 40°C/75% RH in support of this storage condition. The stability data sheets of synthetic route F and G are not available.
	Ritonavir	
	Name, address of drug substance manufacturer	The following commercial sites are involved in manufacturing of ritonavir: M/s. Hetero Drugs Limited, Unit-IX, Plot No. 1, Hetero Infrastructure SEZ Ltd., N. Narasapuram (Village), Nakkapalli (Mandal), Visakhapatnam District-531081, Andhra Pradesh, INDIA.
	Module-III Drug Substance:	**General Information** • Polymorphism : Ritonavir exhibits polymorphism. Hetero produces crystalline Form-I. • Isomerism : Ritonavir (Form-I) exhibits isomerism. It contains four chiral centers. • White or almost white powder. **Manufacture, characterisation and process controls** The molecular structure of Ritonavir (Form-I) (B. No. RI0020410) was investigated and confirmed by IR, UV, NMR (Proton & Carbon), Mass spectroscopic techniques. **Specification** • The specification limits followed for drug substance is fixed based on process capability, Ph. Eur. monograph of Ritonavir (Form-I) and ICH recommendations. • The analytical methods used in the analysis of Ritonavir (Form-I) are Related compounds (By HPLC), Assay (By HPLC, on anhydrous basis), Residual solvents (By GC). These methods were qualified for regular analysis. **Container Closure System**

		The API is packed in transparent polythene bags placed in an HDPE drum.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Accelerated 40±2°C/75±5% RH 0, 1, 2, 3, 4, 5, 6 Intermediate 30±2°C/65±5% RH 0, 1, 3, 6, 9, 12 Long Term 25±2°C/60±5%RH 0, 1, 2, 3, 4, 5, 6, 9,12, 18, 24, 36, 48, 60 Shelf life/Retest Retest period of 60 months
	Paxlovid finished medicinal product The proposed medicinal product Paxlovid consists of PF-07321332 150 mg film-coated tablets and ritonavir 100 mg film-coated tablets, which are separately manufactured, but co-packaged on the same blister for ease of daily co-administration.	
	Nimatrelvir film-coated tablets	
	Module-III Drug Product: Nimatrelvir film-coated tablets	Description of the product and pharmaceutical development The proposed dosage form for PF-07321332 is an immediate release (IR) film-coated tablet in dosage strength of 150 mg. The dosage form is presented as an oval, pink, film-coated tablet with "PFE" debossed on one tablet face and "3CL" debossed on the opposite tablet face. Manufacture of the product and process controls Manufacturing Site Pfizer Manufacturing Deutschland GmbH Betriebsstätte Freiburg Mooswaldallee 1 79090 Freiburg,Germany Process validation: The manufacturing process for PF-07321332 150 mg film-coated tablets use conventional manufacturing techniques and equipment. The manufacturing & packaging process validation will be completed and provided as part of a forthcoming submission when final process and controls will have been identified and appropriate process understanding has been developed. Stability data Manufacture Site:Pfizer ,Freiburg, PPD Container:Foil blister 3 months data submitted
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Nirmatrelvir: Not applicable for innovator products.
	Analytical method validation/verification of product	Nirmatrelvir: Firm has submitted that analytical method validation studies for drug product has been performed. These analytical procedures were verified and confirmed suitable for their intended use. Non-compendial

		analytical procedures used for batch release and stability studies.
	Ritonavir Film coated Tablets	
	Module-III Drug Product: Ritonavir film-coated tablets	Description of the product and pharmaceutical development White to off white, capsule shaped, film-coated tablets, debossed with 'H' on one side and 'R9' on other side. Manufacture of the product and process controls Manufacturing Site Ritonavir: I. Bulk tablet manufacturing M/s. Hetero Labs Limited, Unit-III, 22-110, Industrial Development Area, Jeedimetla, Hyderabad-500055, Telangana, India II. Ritonavir Premix (Amorphous) manufacturing M/s. Hetero Drugs Limited, Unit-IX, Plot No. 1, Hetero Infrastructure Ltd.- SEZ, Narasapuram Village, Nakkapally Mandal, Visakhapatnam District-531081, Andhra Pradesh, India. Stability data of bulk Tablets is available.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Ritonavir tablets were developed in reference to NORVIR® Manufactured by Abbott Laboratories Ltd., (Manufactured by Abbott laboratories. North Chicago, IL 60064, U.S.A). The dissolution methods developed indicated good comparison with Norvir®.
	Analytical method validation/verification of product	The method validations were performed for Related compounds (By HPLC), Assay (By HPLC), Residual solvents (By GC).
	Paxlovid finished medicinal product The proposed medicinal product Paxlovid consists of PF-07321332 150 mg film-coated tablets and ritonavir 100 mg film-coated tablets, which are separately manufactured, but co-packaged on the same blister for ease of daily co-administration.	
	Container closure system of the co-pack	Paxlovid is packaged in cartons containing 5 daily-dose OPA/Al/PVC foil blister cards of 30 tablets. Each daily blister card contains 4 Nirmatrelvir tablets (Pink) and 2 ritonavir tablets (White). The container closure system for PF-07321332 150 mg film-coated tablets and externally sourced ritonavir 100 mg film-coated tablets consists of a foil/foil blister system made from a composite Oriented PolyAmide/Aluminium Foil/Polyvinylchloride (OPA/Al/PVC) foil blister with aluminium foil lidding where each tablet is placed into an individual blister cavity.

		 **Figure 1. Blister configuration of Paxlovid**
	Stability study data of Co-pack drug product, shelf life and storage conditions	Stability data for Ritonavir 100 mg Tablets in the Pfizer co-packaged foil/foil blister system is currently not available. Stability studies for the co-packaged drug product (containing both Nirmatrelvir and ritonavir tablets) in commercial packaging are currently scheduled to start between March and May 2022. Stability studies will be performed at long term storage conditions of 30 °C/75% RH and 25°C/60% RH and accelerated conditions of 40 °C/75% RH. Stability data for the individual tablets are provided. **Nirmatrelvir film coated tablets Shelf life** Due to the accelerated pharmaceutical development, limited primary stability data is currently available for the PF-07321332 150 mg film-coated tablet. Preliminary stability data for three primary batches of the 150 mg tablets were reported for three months at the long-term storage conditions of 30°C/ 75% RH and 25°C/60% RH and at the accelerated storage conditions of 40°C/ 75% RH. To support the proposed 12-month shelf life, six months of stability data for PF-07321332 tablets from the three primary stability batches will be available in March 2022. **Ritonavir Film coated shelf life** The commercially available Hetero Ritonavir 100 mg tablet in foil/foil blister container closure system has an approved shelf life of 24 months. **Copack Shelf Life** The final shelf life and storage condition for co-package product will be based on the more stringent shelf-life and storage condition Based on the 3 months stability data for 3 batches of Nirmatrelvir 150 mg film-coated tablets from the primary registration stability program and up to 6 months stability data for supportive stability batches, the proposed shelf-life is 12 months when “Stored at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F)” for product packaged in foil/foil blisters.

Remarks of the evaluator

	Shortcomings Query	Firms response

1.	QOS is not available.	It is not available currently. Due to accelerated development timelines in response to the pandemic, the dossier was submitted to MHRA and subsequently updated as part of a rolling submission process.
2.	Total 6 synthetic routes have been used in manufacture of Nirmatrelvir (A,B,C,D,.E.F.G) but the submitted stability data is of route C and D only. Clarification regarding synthetic route, manufacturing and stability site is required? • Pfizer Ireland Pharmaceuticals, Ringaskiddy Active Pharmaceutical Ingredient Plant Ringaskiddy County Cork, Ireland • Jilin Asymchem Laboratories Co. Ltd, No. 99, Hongda Road, Economic Development Zone, Dunhua, Jilin 133700, China (CHN) • Changzhou SynTheAll Pharmaceutical Co. Ltd No.589, North Yulong Road, Xinbei District, Changzhou, CH 213127, China (CHN).	A total 6 synthetic routes have been used in the manufacturing of Nirmatrelvir. The routes that will provide supplies to emergency supply are route F(Pfizer Ireland Current Source) and route G (China, future assessment).These routes have been used for initial manufacturing of Nirmatrelvir. Five previous routes A,B,C,D and E(China)were used to provide earlier development ,preclinical and clinical supplies. Stability studies at Pfizer Ireland Pharmaceuticals, Ringaskiddy are ongoing. The 3-month interval stability analysis is under progress. The data will be made available by April 2022. Given stability of 6 months of another site Wuxi Apptec China(route C and D) is available. **STA** Pharmaceutical (**WuXi STA**), a subsidiary of **WuXi** AppTec.
3.	3.2.P.3.5. Process validation has not been performed for Nirmatrelvir Tablets?	The manufacturing process for PF-07321332 150 mg film-coated tablets uses conventional manufacturing techniques and equipment. The manufacturing & packaging process validation will be completed and provided as part of a forthcoming submission when final process and controls will have been identified and appropriate process understanding has been developed. Manufacturing site is expected to complete the protocol development by July 2022.
4.	Stability Data of co-pack has not been submitted?	Stability studies for the co-packaged drug product (containing both nirmatrelvir and ritonavir tablets) in commercial packaging are currently scheduled to start between March and May 2022 at all three sites, depending on site packaging schedules. Stability studies will be performed at long term conditions 30°C/75% RH ,25°C/60% RH and accelerated conditions of 30°C/75%. To support 12 months shelf life ,six months stability for nirmatrelvir tablets from the three primary stability batches will be available in March 2022. We commit to monitor stability data according to ICH guidelines and will inform the authorities according to GMP processes in the case of OOS results.
5.	Clarification for Final release site for drug product with respect to COPP as it mentions Germany	Germany site is responsible for manufacturing and final release of drug product. MHRA can mention a site name once only.

	site as manufacturer and at release site Ireland and Italy.	

Decision of M-316: Registration Board deliberated the case in details and opined that as MHRA of UK and US FDA has approved EUA (Emergency Use Authorisation) with certain post-marketing conditions and Registration Board may also consider on same pattern / conditions. However, the Board referred the case to DRAP Authority for priority consideration of registration applications or otherwise considering the current situation of COVID-19 pandemic in Pakistan.

Decision of 136th meeting of the Authority held on 20-05-2022:
The Authority in light of its previous decisions regarding out of queue treatment of drugs/biologicals for COVID-19 treatment decided that registration applications of combo pack of Nirmatrelvir 150mg and Ritonavir 100mg shall be considered out of queue considering the potential of resurgence of COVID-19 in future. The same will also be communicated to M/o NHS,R&C.

Fresh Evaluation

	Shortcomings Query	**Firms response**	**Firms Response Dated 03-08-2022**	**Firms Response Dated 25-08-2022**
1.	QOS is not available.	It is not available currently. Due to accelerated development timelines in response to the pandemic, the dossier was submitted to MHRA and subsequently updated as part of a rolling submission process.	Fresh Evaluation Firm has not submitted QOS.	QOS is not available Due to application of Emergency Use Authorization, QOS document has not been prepared. We will provide the QOS upon conversion to full registration.
2.	Total 6 synthetic routes have been used in manufacture of Nirmatrelvir (A,B,C,D,.E.F.G) but the submitted stability data is of route C and D only. Clarification regarding synthetic route, manufacturing and stability site is required? • Pfizer Ireland Pharmaceuticals, Ringaskiddy Active Pharmaceutical Ingredient Plant Ringaskiddy County Cork, Ireland • Jilin Asymchem Laboratories Co. Ltd, No. 99,	A total 6 synthetic routes have been used in the manufacturing of Nirmatrelvir. The routes that will provide supplies to emergency supply are route F(Pfizer Ireland Current Source) and route G (China, future assessment).These routes have been used for initial manufacturing of Nirmatrelvir. Five previous routes A,B,C,D and E(China)were used to provide earlier development ,preclinical and clinical supplies. Stability studies at Pfizer Ireland Pharmaceuticals, Ringaskiddy are ongoing. The 3-month interval stability analysis is under progress. The data will be made available by April 2022.	Fresh Evaluation Firm has submitted Stability data of Route F Pfizer Ireland Pharmaceuticals, Ringaskiddy and Route G.	*Clarification regarding manufacturing and stability site of Nirmatrelvir* As informed through our initial application dossier (3.2.S.2.1 & Table 3.2.S.2.6-5), three sites will be involved in API manufacturing & supplies: (a) Pfizer Ireland Pharmaceuticals, Ringaskiddy, Ireland, (b) Jilin Asymchem Laboratories Co. China & (c) Changzhou SynTheAll Pharmaceutical Co. Ltd, China. As of now, Jilin Asymchem Laboratories Co. China is supplying

	Hongda Road, Economic Development Zone, Dunhua, Jilin 133700, China (CHN) • Changzhou SynTheAll Pharmaceutical Co. Ltd No.589, North Yulong Road, Xinbei District, Changzhou, CH 213127, China (CHN).	Given stability of 6 months of another site Wuxi Apptec China(route C and D) is available. **STA** Pharmaceutical (**WuXi STA**), a subsidiary of **WuXi** AppTec.		the API. We have already submitted 3-month Stability Data of all above mentioned sites through our letter dated August 1, 2022 (3.2.S.7.3 Stability Data).
3.	3.2.P.3.5. Process validation has not been performed for Nirmatrelvir Tablets?	The manufacturing process for PF-07321332 150 mg film-coated tablets uses conventional manufacturing techniques and equipment. The manufacturing & packaging process validation will be completed and provided as part of a forthcoming submission when final process and controls will have been identified and appropriate process understanding has been developed. Manufacturing site is expected to complete the protocol development by July 2022.	Fresh Evaluation Process validation of Nirmatrelvir Tablets has not been submitted.	*3.2.P.3.5. Process Validation document for Nirmatrelvir Tablets* 3.2.P.3.5. Process Validation document for Nirmatrelvir Tablets will be available shortly and provided to you as soon it is received.
4.	Stability Data of co-pack has not been submitted?	Stability studies for the co-packaged drug product (containing both nirmatrelvir and ritonavir tablets) in commercial packaging are currently scheduled to start between March and May 2022 at all three sites, depending on site packaging schedules. Stability studies will be performed at long term conditions 30°C/75% RH ,25°C/60% RH and accelerated conditions of 30°C/75%.	The stability data at all three sites, depending on site packaging schedules has not been submitted <u>Stability data of site Pfizer Ascoli, Italy</u> Stability data of 3 months has been submitted. Manufacturing site:Pfizer , Freiburg, Germany Packaging Site:Pfizer ,Ascoli, Italy API Site :Jilin, China	*Stability Data of co-packaged drug product* We have submitted 3-month stability data for co-packaged drug product, packaged at Ascoli, Italy site. Please note Ascoli, Italy is one of our qualified packaging sites. Data for Germany as packaging site will be

		To support 12 months shelf life ,six months stability for nirmatrelvir tablets from the three primary stability batches will be available in March 2022. We commit to monitor stability data according to ICH guidelines and will inform the authorities according to GMP processes in the case of OOS results.	Nirmatrelvir Mfg Date: 27 Jan 2022 Packaging date:7-Feb-2022 Stability Start Date:11-March 2022 Ritonavir Mfg Date: 01 Sep 2021 Packaging date:7-Feb-2022 Stability Start Date:11-March 2022 Fresh Evaluation The API manufacturing site as mentioned in co-pack stability data is Jilin, China but as per your previous submission it will be Pfizer Ireland. Clarification is required.	submitted as soon the activity takes place at site.
5.	Clarification for Final release site for drug product with respect to COPP as it mentions Germany site as manufacturer and at release site Ireland and Italy.	Germany site is responsible for manufacturing and final release of drug product. MHRA can mention a site name once only.	The packaging site mentioned in stability data of co-pack is Pfizer, Ascoli, Italy whereas, as per your previous submission Germany site will be responsible for manufacturing and final release of drug product. Clarification is required.	*Clarification for Final release site for drug product with respect to COPP* We submitted in our initial registration application & CPP, that there is one manufacturing & three packaging sites approved for Paxlovid, (a) Pfizer Manufacturing Freiburg, Germany, (b) Pfizer Pharmaceuticals Newbridge, Ireland, & (c) Pfizer Ascoli, Italy.
6.	The storage condition for Co-pack is Store Below 25.			*Storage condition / label of co-pack* The stringent long-term condition of

		30°C/75%RH is being used in stability data to support climatic zones IVa/b for labelling up to 30°C. Since we have applied for EUA and Paxlovid will be supplied as international standard export Pack, hence the label will mention 25°C.

Decision: Approved with Innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

- **Firm shall submit the fee of Rs. 7,500 for revision of specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Firm will provide Quality Overall summary (QOS) on the basis of which MHRA has accorded Emegency Use Authorization before issuance of Registration letter.**

Case no. 02 Registration applications for local manufacturing of (Human) drugs

a. New cases

362.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Sitafed Tablets 25mg
	Composition	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…25mg
	Diary No. Date of R& I & fee	Dy.No 11912 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Dipeptidyl peptidase 4 (DPP-4) inhibitor
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO,10's,14's,30's.
	Approval status of product in Reference Regulatory Authorities.	JANUVIA® (sitagliptin) Tablets. USFDA Approved.
	Me-too status	064195 Sitagen Tablets 25mg. Manufacturer Name Ferozsons Laboratories
	GMP status	Not submitted.
	Remarks of the Evaluator V	Each film-coated tablet of innovator contains 32.13mg of sitagliptin phosphate monohydrate, which is equivalent to 25mg whereas, master formulation mentions sitagliptin 32mg.Revision of master formulation with submission of requisite fee is required.
	Decision: Approved with USP specifications.	

	Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/-, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
363.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Sitafed Tablets 50mg
	Composition	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…50mg
	Diary No. Date of R& I & fee	Dy.No 11915 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Dipeptidyl peptidase 4 (DPP-4) inhibitor
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO,10's,14's,30's.
	Approval status of product in Reference Regulatory Authorities.	JANUVIA® (sitagliptin) Tablets. USFDA Approved.
	Me-too status	064196 Sitagen Tablets. Manufacturer Name Ferozsons Laboratories
	GMP status	Not submitted.
	Remarks of the Evaluator V	Each film-coated tablet of sitagliptin contains 64.25mg of sitagliptin phosphate monohydrate, which is equivalent to 50mg whereas, master formulation mentions sitagliptin 50mg. Revision of master formulation with submission of requisite fee is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/-, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
364.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Sitafed Tablets 100mg
	Composition	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…100mg
	Diary No. Date of R& I & fee	Dy.No 11916 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Dipeptidyl peptidase 4 (DPP-4) inhibitor
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO,10's,14's,30's.
	Approval status of product in Reference Regulatory Authorities.	JANUVIA® (sitagliptin) Tablets USFDA Approved.
	Me-too status	064197 Sitagen Tablets. Manufacturer Name Ferozsons Laboratories
	GMP status	Not submitted.

	Remarks of the Evaluator V	Each film-coated tablet of innovator product contains 128.5 mg of sitagliptin phosphate monohydrate, which is equivalent to 100mg whereas, master formulation mentions sitagliptin 100mg. Revision of master formulation with submission of requisite fee is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/-, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
365.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Sitamet Tablets 50/500mg "
	Composition	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…50mg Metformin hydrochloride…500mg
	Diary No. Date of R& I & fee	Dy.No 11913 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Drugs used in Diabetes A10BD07
	Type of Form	Form 5
	Finished product Specification	Not submitted.
	Pack size & Demanded Price	As per SRO,10's.
	Approval status of product in Reference Regulatory Authorities.	Janumet. Approved in USFDA with box warning.
	Me-too status	076399 Silmax-M 50mg/500mg Tablet M/s High-Q Pharmaceuticals, Karachi . .
	GMP status	Not submitted.
	Remarks of the Evaluator V	Each film-coated tablet of sitagliptin contains 64.25,mg of sitagliptin phosphate monohydrate, which is equivalent to 50mg whereas, master formulation mentions sitagliptin 50mg. Revision of master formulation with submission of requisite fee is required.
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/-, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
366.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Sitamet Tablets 50/1000mg
	Composition	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…50mg Metformin hydrochloride…1000mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 11914 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Drugs Used In Diabetes A10BD07
	Type of Form	Form 5
	Finished product Specification	Not submitted.

	Pack size & Demanded Price	10's,
	Approval status of product in Reference Regulatory Authorities.	Janumet Approved in USFDA with box warning.
	Me-too status	076400 Silmax-M 50mg/1000mg Tablet M/s High-Q Pharmaceuticals, Karachi . .
	GMP status	Not submitted.
	Remarks of the Evaluator V	Each film-coated tablet of sitagliptin contains 64.25,mg of sitagliptin phosphate monohydrate, which is equivalent to 50mg whereas, master formulation mentions sitagliptin 50mg. Revision of master formulation with submission of requisite fee is required.
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/-, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
367.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Terbifed Tablets 125mg
	Composition	Each film coated tablet contains: Terbinafine hydrochloride…125mg
	Diary No. Date of R& I & fee	Dy.No 11922 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antifungals for systemic use D01BA02
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10s ,As per SRO.
	Approval status of product in Reference Regulatory Authorities.	LAMISIL terbinafine 125mg (uncoated tablets) TGA Approved.
	Me-too status	070118 "Terbizine Tablet Candid Pharmaceuticals,Opposite Pasrur Sugar Mills,Sialkot Road, Pasrur"
	GMP status	Not submitted.
	Remarks of the Evaluator V	Evidence of approval of the applied formulation as film coated tablet in one of the reference regulatory authority specified by Registration Board or revision of label claim as per innovator with submission of requisite fee is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of formulation from film-coated tablet to uncoated tablet along with submission of Rs. 7,500/- , as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
368.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Tramafed Tablet 325/37.5mg

	Composition	Each film coated tablet contains: Paracetamol…325mg Tramadol hydrochloride…37.5mg
	Diary No. Date of R& I & fee	Dy.No 11924 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Opioids in combination with non-opioid analgesics. N02AJ13
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO, 10's
	Approval status of product in Reference Regulatory Authorities.	Tramacet Manufacturer/sponsor:Janssen Ortho Inc. Health Canada Approved
	Me-too status	081956 Radol-P Tablet 325/37.5 mg M/s Regal Pharmaceuticals, Plot # 2-A, Street # S-5, National industrial zone Rawat.Islamabad
	GMP status	Not submitted.
	Remarks of the Evaluator V	
	Decision: Approved with USP specifications. Registration letter will be issued after submission of updated GMP status of the firm.	
369.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Olanz F 6mg/25mg Capsules
	Composition	Each capsule contains: Olanzapine citrate equivalent to Olanzapine…6mg Fluoxetine hydrochloride equivalent Fluoxetine…25mg
	Diary No. Date of R& I & fee	Dy.No 11920 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antipsychotics
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO,14's.
	Approval status of product in Reference Regulatory Authorities.	Symbyax USFDA Approved with box warning.
	Me-too status	081974 Olanzo – F 6/25 Capsule M/s Regal Pharmaceuticals, Plot # 2-A, Street # S-5, National industrial zone Rawat.Islamabad
	GMP status	Not submitted.
	Remarks of the Evaluator V	The master formulation mentions olanzapine citrate 6 mg and fluoxetine Hydrochloride 25 mg. Revision of formulation as per innovator is required. Evidence of olanzapine as citrate is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of salt form of the drug substance along with submission of Rs.30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
370.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar

	Brand Name +Dosage Form + Strength	Olanz F 12mg/25mg Capsules
	Composition	Each capsule contains: Olanzapine citrate equivalent to Olanzapine…6mg Fluoxetine hydrochloride equivalent to Fluoxetine…25mg
	Diary No. Date of R& I & fee	Dy.No 11921 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antipsychotics
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Symbyax USFDA Approved with box warning.
	Me-too status	081975 Olanzo – F 12/25mg Capsule M/s Regal Pharmaceuticals, Plot # 2-A, Street # S-5, National industrial zone Rawat.Islamabad
	GMP status	Not submitted.
	Remarks of the Evaluator V	The master formulation mentions olanzapine citrate 12 mg and fluoxetine HCl 25 mg. Revision of formulation as per innovator is required. Evidence of olanzapine as citrate is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of salt form of the drug substance along with submission of Rs.30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
371.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Amloval Tablet 5mg/80mg
	Composition	Each film coated tablet contains: Almodipine besylate equivalent to amlodipine…5mg Valsartan…80mg
	Diary No. Date of R& I & fee	Dy.No 11917 dated 06-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	C09DB01 Angiotensin II receptor blockers (ARBs) and calcium channel blockers
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's,14's,As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Exforge USFDA Approved.
	Me-too status	081932 Amlodine Tablet 5/160 M/s Jupiter Pharma Plot # 25, St# S6 RCCI, Rawat Islamabad
	GMP status	Not submitted.
	Remarks of the Evaluator V	➢ The pack size has not been provided on Form 5. ➢ The master formulation mentions amlodipine besylate 5mg instead of amlodipine besylate

		equivalent to Amlodipine…5mg.Revision of formulation with submission of requisite fee is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
372.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Cordfed V Tablet 5mg/320mg
	Composition	Each film coated tablet contains: Amlodipine besylate equivalent to amlodipine…5mg Valsartan…320mg
	Diary No. Date of R& I & fee	Dy.No 11918 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	C09DB01 Angiotensin II receptor blockers (ARBs) and calcium channel blockers
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's,14's,As per SRO
	Approval status of product in Reference Regulatory Authorities.	Exforge USFDA Approved.
	Me-too status	081932 Amlodine Tablet 5/320 M/s Jupiter Pharma Plot # 25, St# S6 RCCI, Rawat Islamabad
	GMP status	Not submitted.
	Remarks of the Evaluator V	➢ The pack size has not been provided on Form 5. ➢ The master formulation mentions amlodipine besylate 5 mg instead of amlodipine besylate equivalent to Amlodipine…5mg.Revision of formulation with submission of requisite fee is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
373.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Cordfed V Tablet 10mg/320mg
	Composition	Each film coated tablet contains: Amlodipine besylate equivalent to amlodipine…10mg Valsartan…320mg
	Diary No. Date of R& I & fee	Dy.No 11919 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	C09DB01 Angiotensin II receptor blockers (ARBs) and calcium channel blockers
	Type of Form	Form 5
	Finished product Specification	USP

	Pack size & Demanded Price	10's,14's,As per SRO
	Approval status of product in Reference Regulatory Authorities.	Exforge USFDA Approved.
	Me-too status	126414 Lodopin-V Tablet 10mg/320mg Martin Dow Marker Limited
	GMP status	107700 Jemvartan by M/s Jaens Pharma, Lahore
	Remarks of the Evaluator V	➢ The pack size has not been provided on Form 5. ➢ The master formulation mentions amlodipine besylate 10 mg instead of amlodipine besylate equivalent to amlodipine…10 mg. Revision of formulation with submission of requisite fee is required.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of updated GMP status of the firm and correction of composition as per innovator product along with submission of Rs. 30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
374.	Name and address of manufacturer / Applicant	M/s Fedro Pharmaceuticals Laboratories Private Limited. 149-Industrial Estate, Hayatabad, Peshawar
	Brand Name +Dosage Form + Strength	Valfed Tablet 80mg
	Composition	Each film coated tablet contains: Valsartan…80mg
	Diary No. Date of R& I & fee	Dy.No 11923 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Angiotensin II receptor blockers (ARBs), plain
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO,14's
	Approval status of product in Reference Regulatory Authorities.	MHRA Approved
	Me-too status	024040 Brand Name Varlan Tablets Manufacturer Name Siza International (Pvt) Ltd, 18 KM, Main Ferozepur Road, Lahore-53001
	GMP status	Not submitted.
	Remarks of the Evaluator V	The signature of applicant is missing on Form 5.
	Decision: Approved with USP specifications. **Registration letter will be issued after submission of signed Form 5 by the applicant.**	
375.	Name and address of manufacturer / Applicant	"M/s Friends Pharma Pvt Ltd. 31-km, Ferozepur Road, Lahore, Pakistan"
	Brand Name +Dosage Form + Strength	Ketafend Injection 500mg
	Composition	"Each 10ml Contains: Ketamine Hcl Eq To Ketamine…500mg
	Diary No. Date of R& I & fee	Dy.No 13121 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	General anaesthetics

	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO, Glass ampoule 10ml.
	Approval status of product in Reference Regulatory Authorities.	USFDA approved in Vial .
	Me-too status	Ketarol of Global
	GMP status	GMP inspection 08-03-2019 General Liquid section (Vial and Ampoule)
	Remarks of the Evaluator V	• Revision of master formulation as per innovator is required i.e. "50 mg ketamine base (equivalent to 57.67 mg ketamine hydrochloride" along with submission of requisite fee. • Availability of applied product in ampoule. **Evaluation** • Initially, the firm has applied for ampoule now the firm has changed the container closure system to vial without submitting relevant documents as per Form 5. • Evidence of SVP couldn't be confirmed from section letter and panel inspection report. • Firm has corrected the master formulation with submission of Rs 7500/- dated 17-03-2022.
	Decision: Deferred for the following reasons: • **Submission of evidence of approval of SVP section by the Central Licensing Board or panel inspection report for renewal of DML verifying the section.** • **Firm shall submit the full fee of Rs. 30,000/- for correction/pre-approval change in composition (correction of salt form of the drug substance) and change of container closure system, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
376.	Name and address of manufacturer / Applicant	High Q Pharmaceuticals ,Plot No. 224, Sector 23,Korangi Industrial
	Diary No. Date of R& I & fee	Dy. No.280 dated 18..9.2014
	Brand Name +Dosage Form + Strength	Lefra 10mg Tablet
	Composition	Each film coated tablet contains: Leflunomide USP…10mg
	Pharmacological Group	L04AA13 Selective immunosuppressants
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per brand Leader
	Approval status of product in Reference Regulatory Authorities.	ARAVA (leflunomide), tablets USFDA Approved
	Me-too status	Registration Number:103249 Brand Name:Ck-lef Manufacturer Name:CKD Pharmaceuticals
	GMP status	GMP inspection report dated:30-06-2021
	Remarks of the Evaluator V.	
	Decision: Approved with USP specifications.	
377.	Name and address of manufacturer / Applicant	High Q Pharmaceuticals ,Plot No. 224, Sector 23,Korangi Industrial
	Diary No. Date of R& I & fee	Dy. No.285 dated 18..9.2014

	Brand Name +Dosage Form + Strength	Lefra 20mg Tablet
	Composition	Each film coated tablet contains: Leflunomide USP…20mg
	Pharmacological Group	L04AA13 Selective immunosuppressants
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per brand Leader, 30's
	Approval status of product in Reference Regulatory Authorities.	ARAVA (leflunomide), tablets USFDA Approved
	Me-too status	Registration Number:026652 Brand Name:Lefora 20mg Tablet Manufacturer Name:Hilton Pharma (Pvt) Ltd,
	GMP status	GMP inspection report dated:30-06-2021
	Remarks of the Evaluator V.	
	Decision: Approved with USP specifications.	
378.	Name and address of manufacturer / Applicant	High Q Pharmaceuticals ,Plot No. 224, Sector 23,Korangi Industrial
	Diary No. Date of R& I & fee	Dy. No.286 dated 18..9.2014
	Brand Name +Dosage Form + Strength	Topzol Capsule 100mg
	Composition	Each Capsule Contains: Itraconazole …. 100mg
	Pharmacological Group	J02AC02 Antimycotic
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per brand Leader, 4 capsule
	Approval status of product in Reference Regulatory Authorities.	SPORANOX® (itraconazole) Capsules USFDA Approved.
	Me-too status	Registration Number:024491 Brand Name:Rolac 100mg Capsules Each capsule Manufacturer Name:Sami Pharmaceuticals (Pvt) Ltd, F-95 Off Hub River Road , SITe, Karachi
	GMP status	GMP inspection report dated:30-06-2021
	Remarks of the Evaluator V.	Revision of formulation as per innovator is required i.e. SPORANOX® Capsules contain 100 mg of itraconazole coated on sugar spheres ,also submit fee for revision of formulation. **USFDA Storage Condition** Store at controlled room temperature 15°-25°C. Protect from light and moisture. **MHRA Storage Condition** **Special precautions for storage** Do not store above 25°C Store in the original package in order to protect from light. **Nature and contents of container** Aluminium/Aluminium Blister **<u>Firms Response</u>** <u>Firm has revised their formulation with submission of Rs 7500/- dated 11-05-22.</u>

		Source of pellets: M/s Vision Pharmaceuticals.
	Decision: Approved with USP specifications and storage condition "Do not store above 25°C". **Registration letter will be issued after submission of remaining fee of Rs. 22,500/-, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021, as Rs 7500/- has already been submitted.**	
379.	Name and address of manufacturer / Applicant	High Q Pharmaceuticals ,Plot No. 224, Sector 23,Korangi Industrial
	Diary No. Date of R& I & fee	Dy. No.282 dated 18..9.2014
	Brand Name +Dosage Form + Strength	Toprax 25mg tablet
	Composition	Each film coated tablet contains: Topiramate …25mg
	Pharmacological Group	N03AX11 Anti-epileptic
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per Brand Leader, 30's.
	Approval status of product in Reference Regulatory Authorities.	MHRA Approved
	Me-too status	Registration Number: 076387 Brand Name: Neutop 25mg Tablet Manufacturer Name :Nabiqasim Kar.
	GMP status	GMP inspection date:30-06-2021
	Remarks of the Evaluator V.	
	Decision: Approved with USP specifications.	
380.	Name and address of manufacturer / Applicant	High Q Pharmaceuticals ,Plot No. 224, Sector 23,Korangi Industrial
	Diary No. Date of R& I & fee	Dy. No.282 dated 18..9.2014
	Brand Name +Dosage Form + Strength	Toprax 50mg tablet
	Composition	Each film coated tablet contains: Topiramate …50mg
	Pharmacological Group	N03AX11 Anti-epileptic
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per Brand Leader, 60's.
	Approval status of product in Reference Regulatory Authorities.	Topamax Tablets USFDA Approved
	Me-too status	Registration Number: 076388 Brand Name: Neutop 25mg Tablet Manufacturer Name :Nabiqasim Kar.
	GMP status	GMP inspection date:30-06-2021
	Remarks of the Evaluator V.	
	Decision: Approved with USP specifications.	
381.	Name and address of manufacturer / Applicant	High Q Pharmaceuticals ,Plot No. 224, Sector 23,Korangi Industrial
	Diary No. Date of R& I & fee	Dy. No.284 dated 18..9.2014

	Brand Name +Dosage Form + Strength	Ezolin 400mg tablet
	Composition	Each film coated tablet contains: Linezolid …400mg
	Pharmacological Group	Antibacterial for systemic use. J01XX08
	Type of Form	Form-5
	Finished product Specification	Inhouse Spec.
	Pack size & Demanded Price	As per Brand leader,10's
	Approval status of product in Reference Regulatory Authorities.	ZYVOX Tablets 400MG **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons* Discontinued USFDA Approved.
	Me-too status	055434 Lyzon 400mg Tablet By M/s Getz Pharma Karachi
	GMP status	GMP inspection date:30-06-2021
	Remarks of the Evaluator V.	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500 for correction in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

b. Deferred Cases

382.	Name and address of manufacturer / Applicant	"M/s Universal Pharmaceuticals Pvt Ltd. 131-A, Hayatabad Industrial Estate, Peshawar"
	Brand Name +Dosage Form + Strength	Napsum Tablet
	Composition	Each film coated tablet contains: Sumatriptan succinate equivalent to sumatriptan…85mg Naproxen sodium…500mg
	Diary No. Date of R& I & fee	Dy.No 6982 dated 19-02-2019 Rs.20,000/- 19-02-2019
	Pharmacological Group	Migraine Management
	Type of Form	Form-5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	2's,As per SRO.
	Approval status of product in Reference Regulatory Authorities.	TREXIMET (sumatriptan and naproxen sodium) tablets USFDA Approved with box warning.
	Me-too status	075904 /Sumtan Plus Tablet M/s Medisure Karachi.
	GMP status	09-01-2019 The firm has rectified majority of observations noted in the previous inspection and the management is committed to improve their cGMP compliance. The firm may be considered operating in satisfactory level of cGMP compliance. Recommendations: They are advised to: • Purchase FTIR and column oven for HPLC • Provide a shelter on material entry gate. • Increase number of dehumidifier in general production area.

		• Provide a split AC in dispensing room. • Provide room for retention samples.
	Remarks of the Evaluator (V)	
	Decision of 295th Meeting: Deferred for updated GMP status from QA Division.	
	Evaluation by PEC-V: Firm has submitted GMP inspection report dated:14-09-2020,15-09-2020. Conclusion: Fair level of compliance. Recommendation: The firm should rectify all the observations mentioned in the report within 30 days as agreed by the management of the firm.	
	Decision of M-307: Deferred for updated status of the GMP from QA and LT division for rectification of shortcomings identified during the inspection.	
	Evaluation by PEC: Date of Inspection 31-12-2021. Satisfactory level of GMP compliance.	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500/- for correction in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
383.	Name and address of manufacturer / Applicant	"M/s Universal Pharmaceuticals Pvt Ltd. 131-A, Hayatabad Industrial Estate, Peshawar"
	Brand Name +Dosage Form + Strength	Delor 5mg tablets
	Composition	"Each film coated tablet Contains: Desloratadine…5mg"
	Diary No. Date of R& I & fee	Dy.No 6979 dated 19-02-2019 Rs.20,000/- 19-02-2019
	Pharmacological Group	Anti-histamine for systemic use.
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	CLARINEX® (desloratadine) Tablets, USFDA Approved.
	Me-too status	080821 /Desdine 5mg Tablet M/s Hygeia Pharma, Isbd.
	GMP status	09-01-2019 The firm has rectified majority of observations noted in the previous inspection and the management is committed to improve their cGMP compliance.The firm may be considered operating in satisfactory level of cGMP compliance. Recommendations:They are advised to: • Purchase FTIR and column oven for HPLC • Provide a shelter on material entry gate. • Increase number of dehumidifier in general production area. • Provide a split AC in dispensing room. • Provide room for retention samples.
	Remarks of the Evaluator (V)	
	Decision of 295th Meeting: Deferred for updated GMP status from QA Division.	
	Evaluation by PEC-V: Firm has submitted GMP inspection report dated:14-09-2020,15-09-2020. Conclusion : Fair level of compliance. Recommendation: The firm should rectify all the observations mentioned in the report within 30 days as agreed by the management of the firm.	

	Decision of M-307: Deferred for updated status of the GMP from QA and LT division for rectification of shortcomings identified during the inspection.	
	Evaluation by PEC: Date of Inspection 31-12-2021 Satisfactory level of GMP compliance.	
	Decision: Approved with USP specifications.	
384.	Name and address of manufacturer / Applicant	"M/s Universal Pharmaceuticals Pvt Ltd. 131-A, Hayatabad Industrial Estate, Peshawar"
	Brand Name +Dosage Form + Strength	Ternix forte 4mg Tablets
	Composition	"Each Tablet Contains: Tizanidine…4mg"
	Diary No. Date of R& I & fee	Dy.No 6981 dated 19-02-2019 Rs.20,000/- 19-02-2019
	Pharmacological Group	Muscle relaxants
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO
	Approval status of product in Reference Regulatory Authorities.	ZANAFLEX® (tizanidine hydrochloride) tablets, USFDA Approved.
	Me-too status	080865 /Zinzan 4mg Tablet " Wellborne Pharmachem and Biologicals, Hattar."
	GMP status	09-01-2019 The firm has rectified majority of observations noted in the previous inspection and the management is committed to improve their cGMP compliance.The firm may be considered operating in satisfactory level of cGMP compliance. Recommendations:They are advised to: • Purchase FTIR and column oven for HPLC • Provide a shelter on material entry gate. • Increase number of dehumidifier in general production area. • Provide a split AC in dispensing room. • Provide room for retention samples.
	Remarks of the Evaluator (V)	• The firm has applied for only Tizanidine however, the product is internationally approved as Tizanidine as HCl.
	Decision: Deferred for clarification regarding salt form of API along with submission of requisite fee and updated GMP status of firm.	
	Evaluation by PEC-V: Firm has submitted GMP inspection report dated:14-09-2020,15-09-2020. Conclusion : Fair level of compliance. Recommendation: The firm should rectify all the observations mentioned in the report within 30 days as agreed by the management of the firm.	
	Decision of M-307: Deferred for the following reasons: • **Updated status of the GMP from QA and LT division for rectification of shortcomings identified during the inspection.** • **Revision of formulation as per reference product along with submission of requisite fee.**	
	Evaluation by PEC: • Date of Inspection 31-12-2021 Satisfactory level of GMP compliance.	

	Firm has not revised the formulation.	
	Decision: Approved with USP specifications. **Registration letter will be issued after correction of salt form of the drug substance as per innovator product along with submission of Rs. 30,000/- as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
385.	Name and address of manufacturer / Applicant	"M/s Universal Pharmaceuticals Pvt Ltd. 131-A, Hayatabad Industrial Estate, Peshawar"
	Brand Name +Dosage Form + Strength	Doksal 100mg/5ml Syrup
	Composition	"Each 5ml contains: Doxofylline…100mg"
	Diary No. Date of R& I & fee	Dy.No 6983 dated 19-02-2019 Rs.20,000/- 19-02-2019
	Pharmacological Group	Systemic Drugs for Obstructive Airway Diseases
	Type of Form	Form 5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	60ml glass bottle, plastic bottle. As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Ansimar Company: Abc Farmaceutici Spa AIFA Approved.
	Me-too status	047180/Unifyline Syrup M/s Platinum Pharmaceuticals, Karachi
	GMP status	09-01-2019 The firm has rectified majority of observations noted in the previous inspection and the management is committed to improve their cGMP compliance.The firm may be considered operating in satisfactory level of cGMP compliance. Recommendations: They are advised to: • Purchase FTIR and column oven for HPLC • Provide a shelter on material entry gate. • Increase number of dehumidifier in general production area. • Provide a split AC in dispensing room. • Provide room for retention samples.
	Remarks of the Evaluator (V)	Liquid syrup section is present.
	Decision: Deferred for updated GMP status from QA Division.	
	Evaluation by PEC-V: Firm has submitted GMP inspection report dated:14-09-2020,15-09-2020. Conclusion : Fair level of compliance. Recommendation: The firm should rectify all the observations mentioned in the report within 30 days as agreed by the management of the firm.	
	Decision of M-307: Deferred for updated status of the GMP from QA and LT division for rectification of shortcomings identified during the inspection.	
	Evaluation by PEC: Date of Inspection 31-12-2021 Satisfactory level of GMP compliance.	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500/- for correction in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
386.	Name and address of manufacturer / Applicant	"M/s Universal Pharmaceuticals Pvt Ltd. 131-A, Hayatabad Industrial Estate, Peshawar"

	Brand Name +Dosage Form + Strength	Delor Syrup 2.5mg/ml
	Composition	"Each 5ml contains: Desloratadine…2.5mg"
	Diary No. Date of R& I & fee	Dy.No 6978 dated 19-02-2019 Rs.20,000/- 19-02-2019
	Pharmacological Group	Antihistamines For Systemic Use
	Type of Form	Form 5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	60ml amber glass,plastic bottle, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	Clarinex® (Desloratadine) and Oral Solution USFDA Approved.
	Me-too status	076743/Genelor 2.5mg Syrup M/s Zanctok Karachi.
	GMP status	09-01-2019 The firm has rectified majority of observations noted in the previous inspection and the management is committed to improve their cGMP compliance. The firm may be considered operating in satisfactory level of cGMP compliance. Recommendations:They are advised to: • Purchase FTIR and column oven for HPLC • Provide a shelter on material entry gate. • Increase number of dehumidifier in general production area. • Provide a split AC in dispensing room. • Provide room for retention samples.
	Remarks of the Evaluator (V)	Liquid syrup section is present.
	Decision: Deferred for updated GMP status from QA Division.	
	Evaluation by PEC-V: Firm has submitted GMP inspection report dated:14-09-2020,15-09-2020. Conclusion : Fair level of compliance. Recommendation: The firm should rectify all the observations mentioned in the report within 30 days as agreed by the management of the firm.	
	Decision of M-307: Deferred for updated status of the GMP from QA and LT division for rectification of shortcomings identified during the inspection.	
	Evaluation by PEC: Date of Inspection 31-12-2021 Satisfactory level of GMP compliance.	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500/- for correction in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
387.	Name and address of manufacturer / Applicant	"M/s Universal Pharmaceuticals Pvt Ltd. 131-A, Hayatabad Industrial Estate, Peshawar"
	Brand Name +Dosage Form + Strength	Lezene 2.5mg/5ml
	Composition	"Each 5ml contains: Levocetirizine Dihydrochloride…2.5mg"
	Diary No. Date of R& I & fee	Dy.No 6980 dated 19-02-2019 Rs.20,000/- 19-02-2019
	Pharmacological Group	Antihistamines for systemic use
	Type of Form	Form 5
	Finished product Specification	Not submitted.
	Pack size & Demanded Price	60ml plastic bottle,amber glass,As per SRO.

	Approval status of product in Reference Regulatory Authorities.	XYZAL oral solution USFDA approved.
	Me-too status	076688/Atiza Syrup 2.5mg/ 5ml M/s Asian Continental
	GMP status	09-01-2019 The firm has rectified majority of observations noted in the previous inspection and the management is committed to improve their cGMP compliance. The firm may be considered operating in satisfactory level of cGMP compliance. Recommendations: They are advised to: • Purchase FTIR and column oven for HPLC • Provide a shelter on material entry gate. • Increase number of dehumidifier in general production area. • Provide a split AC in dispensing room. • Provide room for retention samples.
	Remarks of the Evaluator (V)	Liquid syrup section is present.
	Decision: Deferred for updated GMP status from QA Division.	
	Evaluation by PEC-V: Firm has submitted GMP inspection report dated:14-09-2020,15-09-2020. Conclusion : Fair level of compliance. Recommendation: The firm should rectify all the observations mentioned in the report within 30 days as agreed by the management of the firm.	
	Decision of M-307: Deferred for updated status of the GMP from QA and LT division for rectification of shortcomings identified during the inspection.	
	Evaluation by PEC: Date of Inspection 31-12-2021 Satisfactory level of GMP compliance. Firm has not provided reference for specification.	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500/- for correction in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
388.	Name and address of manufacturer / Applicant	M/s Welborne Pharmachem and Biologicals, Plot no. 51/1, 52/2, Phase I and II Industrial Estate , Hattar, Pakistan
	Brand Name +Dosage Form + Strength	Nebron Tablet 2.5mg
	Composition	Each film coated tablet contains: Nebivolol as HCl……..2.5mg
	Diary No. Date of R& I & fee	Diary No:3056, 23/01/2018, Rs: 20,000/- Dated 22/01/2018
	Pharmacological Group	Beta blocking agents, selective (C07AB12)
	Type of Form	Form 5
	Finished product Specification	Not claimed
	Pack size & Demanded Price	2x7's , Alu Alu Blister, As per SRO
	Approval status of product in Reference Regulatory Authorities	Bystolic USFDA Approved
	Me-too status	061344 Nebil 2.5mg Tablet M/s Getz Karachi

	GMP status	Last GMP inspection was conducted on 27-06-2018 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator V	• The applied formulation is available as uncoated in MHRA and USFDA while the firm has applied as film-coated tablet. • No USP or BP monograph is available for the applied formulation.
	Decision of M-289th: Deferred for revision of formulation to uncoated tablet as per reference product along with submission of fee for revision of formulation.	
	Evaluation by PEC: Firm has revised its formulation from coated to uncoated tablet with submission of Rs 7500/- .	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500 for reference of product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
389.	Name and address of manufacturer / Applicant	M/s Welborne Pharmachem and Biologicals, Plot no. 51/1, 52/2, Phase I and II Industrial Estate , Hattar, Pakistan
	Brand Name +Dosage Form + Strength	Nebron Tablet 5mg
	Composition	Each film coated tablet contains: Nebivolol as HCl…….5mg
	Diary No. Date of R& I & fee	Diary No:3057, 23/01/2018, Rs: 20,000/- Dated 22/01/2018
	Pharmacological Group	Beta blocking agents, selective (C07AB12)
	Type of Form	Form 5
	Finished product Specification	Not claimed
	Pack size & Demanded Price	2x7's , AluAlu Blister, As per SRO
	Approval status of product in Reference Regulatory Authorities	Bystolic USFDA Approved
	Me-too status	061345 Nebil 5mg Tablet M/s Getz Karachi
	GMP status	Last GMP inspection was conducted on 27-06-2018 and thereport concludes good level of GMP compliance.
	Remarks of the Evaluator XIII	• The applied formulation is available as uncoated in MHRA and USFDA while the firm has applied as film-coated tablet. • No USP or BP monograph is available for the applied formulation.
	Decision of M-289th: Deferred for revision of formulation to uncoated tablet as per reference product along with submission of fee for revision of formulation.	
	Evaluation by PEC: Firm has revised its formulation from coated to uncoated tablet with submission of Rs 7500/-	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500 for reference of product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
390.	Name and address of manufacturer / Applicant	M/s Welborne Pharmachem and Biologicals, Plot no. 51/1, 52/2, Phase I and II Industrial Estate , Hattar, Pakistan

	Brand Name +Dosage Form + Strength	Nebron Tablet 10mg
	Composition	Each film coated tablet contains: Nebivolol as HCl……..10mg
	Diary No. Date of R& I & fee	Diary No:3058, 23/01/2018, Rs: 20,000/- Dated 22/01/2018
	Pharmacological Group	Beta blocking agents, selective (C07AB12)
	Type of Form	Form 5
	Finished product Specification	Not claimed
	Pack size & Demanded Price	2x7's , AluAlu Blister, As per SRO
	Approval status of product in Reference Regulatory Authorities	Bystolic USFDA Approved
	Me-too status	061345 Nebil 5mg Tablet M/s Getz Karachi
	GMP status	Last GMP inspection was conducted on 27-06-2018 and thereport concludes good level of GMP compliance.
	Remarks of the Evaluator [XIII]	• The applied formulation is available as uncoated in MHRA and USFDA while the firm has applied as film-coated tablet. • No USP or BP monograph is available for the applied formulation.
	Decision of M-289th: Deferred for revision of formulation to uncoated tablet as per reference product along with submission of fee for revision of formulation.	
	Evaluation by PEC: Firm has revised its formulation from coated to uncoated tablet with submission of Rs 7500/-	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500 for reference of product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
391.	Name and address of manufacturer / Applicant	M/s. Wellborne PharmaChem and Biologicals, Plot No. 51/1,52/2, Phase I-II, Industrial Estate Hattar
	Brand Name +Dosage Form + Strength	Zagrid Tablet 40mg
	Composition	Each tablet contains: Febuxostat….40mg
	Diary No. Date of R& I & fee	Dy. No. 152, 16-06-2015 , Rs.20,000/- (16-06-2015)
	Pharmacological Group	Xanthine oxidase inhibitor
	Type of Form	Form-5
	Finished product Specification	Manufacturer
	Pack size & Demanded Price	1x10's: Alu-Alu Blister: As per SRO
	Approval status of product in Reference Regulatory Authorities.	Film coated tablets (USFDA, MHRA Approved)
	Me-too status	Degouric by Atco
	GMP status	Last inspection conducted on 27-02-2017"Strictly following the GMP compliance."
	Remarks of the Evaluator.	The formulation is uncoated tablet while the product approved by reference regulatory authorities is film coated tablet.

	Previous Meeting (M-274)	Deferred for the clarification of dosage form as reference product is available as film coated tablet whereas firm has applied for uncoated tablet.
	Evaluation by PEC	Firm has revised their formulation as per innovator.
	Decision: Deferred for submission of fee as the firm has revised the formulation.	
	Evaluation by PEC: Firm has revised its formulation from uncoated to coated tablet with submission of Rs 7500/- .	
	Decision: Approved with innovator specifications. **Registration letter will be issued after submission of Rs. 7,500/- for correction in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

Agenda of Evaluator PEC-VI

Case no. 01 Registration applications for local manufacturing of (Human) drugs (Form 5)

New cases

392.	**Name and address of manufacturer / Applicant**	**M/s Jenner Pharmaceuticals (Pvt.) Ltd. Plot # 03, M-2 Pharmazone 26- km Lahore Sharaqpur Road Sheikhupura**
	Brand Name +Dosage Form + Strength	Fluzole Capsules 150mg
	Composition	Each Capsule Contains: Fluconazole: 150mg
	Diary No. Date of R& I & fee	Dy:35107, 23-10-2018 , Rs.20,000/- (22-10-2018)
	Pharmacological Group	Antifungal, Triazole derivatives
	Type of Form	Form-5
	Finished product Specification	BP
	Pack size & Demanded Price	1's As per SRO
	Approval status of product in Reference Regulatory Authorities.	MHRA Approved
	Me-too status	Conza Capsule, De-Mont Research Labs., Reg. No. 084049
	GMP status	Last GMP/Panel inspection conducted on 23-12-2020 for renewal of DML
	Remarks of the Evaluator.	M/s Jenner Pharmaceutical was established at address "Plot # 3, M-2, Pharmazone 26th km Lahore Sharqpur Road, Sheikhupura" but on Drug Manufacturing License it was mentioned as "Plot # 2, M-2, Pharmazone 28th km Lahore Sharqpur Road, Distt. Sheikhupura" The firm have applied for correction on DML through letter No. JEN/DRAP/034/2017 dated 30-11-2019 and got approval of correction of address through letter No. F.1.18/2009-Lic dated 12 November 2020.
	Decision: Approved.	

b. Deferred cases

393.	M/s Glitz Pharma, Plot No. 265, Industrial Triangle Kahota Road Islamabad	Imipra 75mg Tablets Each tablet contains: - Imipramine HCl ……. 75mg (USP Specs.)	Form 5 12-08-2014 Dy.No.3286 Rs.8000/= Rs. 12,000/= 11-10-2010 1x10's 2x10's 3x10's 5x10's 5x20's 10x10's 25x10's 20x20's 50x10's As Per SRO	International Availability not provided Local Availability: Tornal by M/s Novartis pharma Pakistan Last inspection report of 10-02-2016 submitted with compliance remarks		**Decision of 263rd:** Deferred for evidence of approval of applied formulation & strength in reference regulatory authorities
	Evaluation: The firm has revised the strength from 75mg to 10mg tablet as below: Each tablet contains Imipramine HCL…..10mg The firm has submitted fee of Rs.7500 only Deposit 9750728723 dated 8 March 2022. The firm did not submit revised form 5 . GMP certificate valid till 2023.					
	Decision: Approved. The firm shall submit fee of Rs. 30,000/- for correction/pre-approval change in product strength as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 along with submission of complete form 5 for revised composition.					
394.	M/s Glitz Pharma, Plot No. 265, Industrial Triangle Kahota Road Islamabad	Palidone XR 9mg Tablets Each extended release tablet contains:- Paliperidone …… 9mg (Psychotropic agent belonging to the chemical class of benzisoxazole derivatives. Recemic mixture of (+)- and (-)- paliperidone) (Manufacturer's Specs)	Form 5 13-02-2015 Dy.No.937 Rs.8000/= Rs.12,000/= 19-06-2012 1x10's 2x10's 3x10's 5x10's 10x10's 20x10's 50x10's 100x10's As Per SRO	Invega prolong release tablets- MHRA Local Availability: Invega 9mg Tablrts by M/s Johnson & Johnson Pharma, Pakistan Last inspection report of 10-02-2016 submitted with complianc e remarks		Deferred for evidence of me-too status
	Evaluation:					

	The firm has revised the strength from Paliperidone XR 9mg to Paliperidone XR 1.5mg as below: Palidone XR (Palinode XR) Each extended release tablet contains: Paliperidone…. 1.5mg The firm has submitted fee of Rs.7500 only Deposit 4805777154 dated 8 March 2022. The firm did not submit revised form5. GMP certificate valid till 2023.					
	Decision: Deferred for confirmation of manufacturing requirements as per reference product.					
395.	M/s Glitz Pharma, Plot No. 265, Industrial Triangle Kahota Road Islamabad	Mac-5 Tablets Each tablet contains:- Montelukast Sodium …….. 5mg (Antiasthmatic)	Form 5 12-08-2014 Dy.No.3285 Rs.8000/= Rs.12,000/= 24-11-2010 2x7's 20x7's As Per SRO	Singulair by Merck sharp and DOHMI corporation USA, Aerotel of M/s Highnoon Labs Last inspection report of 10-02-2016 submitted with compliance remarks		**Decision of 263rd Deferred for change of formulation as per innovator.**
	Evaluation: The firm has revised the formulation from plain tablet 5mg to chewable tablet 5mg as below Each chewable tablet contains: Montelukast as sodium…5mg Inhouse specification They have submitted revised form 5 but did not submit fee. GMP certificate valid till 2023.					
	Decision: Approved with USP specifications. The firm shall submit fee of Rs. 30,000/- for correction/pre-approval change in product dosage form as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 along with submission of complete form 5 for revised composition.					

396.	**Name and address of manufacturer / Applicant**	**Glitz Pharma, Plot No 265, Industrial Triangle, Kahuta Road Islamabad**
	Brand Name +Dosage Form + Strength	Mementa 10mg/5ml Syrup
	Diary No. Date of R& I & fee	Dy. No.1413 , R&I Dated 31-10-14 , Rs: 20,000/-
	Composition	Each 5ml contains:- Memantine HCl ……..10mg
	Pharmacological Group	(Anti-Parkinson)
	Type of Form	From 5
	Finished Product Specification	USP
	Pack size & Demanded Price	60ml,90ml,120ml,240ml,300ml, Amber glass bottle, As per policy of MOH

	Approval status of product in Reference Regulatory Authorities.	Memantine Sandoz 10mg/ml (MHRA)
	Me-too status	Zexa by English Pharm, Lahore (R. No. 071544)
	GMP status	GMP inspection Date: 29-11-2016, GMP status is not clear.
	Remarks of the Evaluator.	I. The evidence provided for liquid syrup section is of 2005. II. 251st meeting commitment not provided by the firm. III. Incorrect pharmacological group provided by firm. IV. Incorrect International availability provided by firm.
	Decision of 270th: Deferred for the following reasons: Confirmation of approval status by reference regulatory authorities. Clarification of pharmacological group. Submission of commitments as per decision of Registration board taken in its 251st meeting. Clarification of pharmacopoeial reference.	
	Evaluation: The firm has submitted pharmacological group: NDMA receptor antagonists or used to treat dementia. USP specification. International reference could not be confirmed. Commitments did not submit GMP certificate valid till 2023.	
	Decision: Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.	

397.	**Name and address of manufacturer / Applicant**	**M/s Glitz Pharma, Plot No. 265, Industrial Triangle Kahuta Road, Islamabad**
	Brand Name +Dosage Form + Strength	Gynezol 1.0% w/w Cream
	Composition	Each gram contains: Isoconazole Nitrate……1% w/w
	Diary No. Date of R& I & fee	Dy. No. 1433: 19-10-2015 PKR 20,000/-: 16-10-2015
	Pharmacological Group	(Antifungal for topical use)
	Type of Form	Form 5
	Finished product Specifications	Firm has claimed in house specifications
	Pack size & Demanded Price	10gm, 40gm: As per SRO
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed
	Me-too status	Ispgen by Shrooq
	GMP status	Last inspection report dated 29-11-2016 do not have any conclusion and remarks regarding GMP status
	Remarks of the Evaluator	• Evidence of approval of applied formulation in reference regulatory authorities could not be confirmed
	Decision of 273th : Deferred for following submissions • Comments of QA & LT Division regarding the GMP status of the firm • Evidence of approval in reference regulatory authorities	

	Evaluation: The firm has submitted GMP certificate valid till 2023.
	Decision: Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.

398.	**Name and address of manufacturer / Applicant**	**M/s Glitz Pharma, Plot No. 265, Industrial Triangle Kahuta Road, Islamabad**
	Brand Name +Dosage Form + Strength	Trimax cream
	Composition	Each gram contains Flucinolone acetonide……..0.01% w/w Hydroquinone……..4.0% w/w Tretinoin……..0.05% w/w
	Diary No. Date of R& I & fee	Dy No. 1807: 3-11-2015 PKR 20,000/-: 2-11-2015
	Pharmacological Group	Antiinflammatory and antipruritic drug
	Type of Form	Form 5
	Finished product Specifications	Firm has claimed in house specifications
	Pack size & Demanded Price	10g, 15g, 20g, 40g: As per SRO
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed
	Me-too status	Trimelasin cream by Valor
	GMP status	Last inspection report dated 29-11-2016 do not have any conclusion and remarks regarding GMP status
	Remarks of the Evaluator	Evidence of approval of applied formulation in reference regulatory authorities could not be confirmed
	Decision of 273th : Deferred for following submissions • Comments of QA & LT Division regarding the GMP status of the firm • Evidence of approval in reference regulatory authorities	
	Evaluation: The firm has submitted GMP certificate valid till 2023.	
	Decision: Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.	

399.	**Name and address of manufacturer / Applicant**	**M/s Zafa Pharmaceuticals Laboratories Private Limited. L-1/B, Block-22, Federal B industrial Area, Karachi**
	Brand Name +Dosage Form + Strength	Zodip-V Plus 5/160/12.5 mg Tablet
	Composition	Each tablet contains: Amlodipine as besylate…5mg Valsartan…160mg Hydrochlorothiazide…12.5mg
	Diary No. Date of R& I & fee	Dy No. 25680: 24.07.2018 PKR 20,000/-: 23.07.2018
	Pharmacological Group	Antihypertensive
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	EXFORGE HCT® Tablets. US-FDA approved
	Me-too status	Exforge HCT 5/160/12.5MG film coated tablets. Reg. No. 69548

	GMP status	GMP certificate was issued based on inspection conducted on 29 october 2020.
	Remarks of the Evaluator (VI)	□ The firm had mentioned amlodipine in label claim. In the revised Form 5, they corrected it to amlodipine as besylate in master formula. □ However, it was 'amlodipine as besylate' in Master formula. The firm did not revise it to amlodipine besilate. □ The firm has mentioned coating composition in Master formula. However, the label claim was "each tablet contains". The firm revised 'Each tablet contains' to 'Each film-coated tablet contains' in Form 5. □ Blistering/packaging process is missing in the manufacturing outlines
	Decision of 291th : Deferred for the following: □ Revision of 'amlodipine as besylate' to 'amlodipine besylate' in Master formula □ Submission of complete manufacturing outlines.	
	Evaluation by PEC (VI): The firm has revised their formulation as: Each film coated tablet contains: Amlodipine besylate eq. to Amlodipine…5mg Valsartan…160mg Hydrochlorothiazide…12.5mg Without submitting any correction fee.	
	Decision: Approved. Firm shall submit fee of Rs. 30,000/= for correction/pre-approval change/ in label claim and composition, as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	
400.	**Name and address of manufacturer / Applicant**	**M/s Zafa Pharmaceuticals Laboratories Private Limited.** **L-1/B, Block-22, Federal B industrial Area, Karachi**
	Brand Name +Dosage Form + Strength	Zodip-V Plus 10/160/12.5 mg Tablet
	Composition	Each tablet contains: Amlodipine as besylate…10mg Valsartan…160mg Hydrochlorothiazide…12.5mg
	Diary No. Date of R& I & fee	Dy No. 25682: 24.07.2018 PKR 20,000/-: 23.07.2018
	Pharmacological Group	Antihypertensive
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	EXFORGE HCT® Tablets. US-FDA approved
	Me-too status	Exforge HCT 10/160/12.5MG film coated tablets. Reg. No. 69550
	GMP status	GMP certificate issued on 23.05.2018
	Remarks of the Evaluator (VI)	□ The firm had mentioned amlodipine in label claim. In the revised Form 5, they corrected it to amlodipine as besylate in master formula.

		□ However, it was 'amlodipine as besylate' in Master formula. The firm did not revise it to amlodipine besilate. □ The firm has mentioned coating composition in Master formula. However, the label claim was "each tablet contains". The firm revised 'Each tablet contains' to 'Each film-coated tablet contains' in Form 5. □ Blistering/packaging process is missing in the manufacturing outlines
	Decision of 291th : Deferred for the following: □ Revision of 'amlodipine as besylate' to 'amlodipine besylate' in Master formula □ Submission of complete manufacturing outlines.	
	Evaluation by PEC (VI): The firm has revised their formulation as: Each film coated tablet contains: Amlodipine besylate eq to Amlodipine…10mg Valsartan…160mg Hydrochlorothiazide…12.5mg Without submitting any correction fee.	
	Decision: Approved. Firm shall submit fee of Rs. 30,000/= for correction/pre-approval change/ in label claim and composition, as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	
401.	**Name and address of manufacturer / Applicant**	**M/s Zafa Pharmaceuticals Laboratories Private Limited.** **L-1/B, Block-22, Federal B industrial Area, Karachi**
	Brand Name +Dosage Form + Strength	Zodip-V Plus 10/160/25 mg Tablet
	Composition	Each tablet contains: Amlodipine as besylate…10mg Valsartan…160mg Hydrochlorothiazide…25mg
	Diary No. Date of R& I & fee	Dy No. 25681: 24.07.2018 PKR 20,000/-: 23.07.2018
	Pharmacological Group	Antihypertensive
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities.	EXFORGE HCT® Tablets. US-FDA approved
	Me-too status	Exforge HCT 10/160/25MG film coated tablets. Reg. No. 69551
	GMP status	GMP certificate issued on 23.05.2018
	Remarks of the Evaluator (VI)	□ The firm had mentioned amlodipine in label claim. In the revised Form 5, they corrected it to amlodipine as besylate in master formula. □ However, it was 'amlodipine as besylate' in Master formula. The firm did not revise it to amlodipine besilate. □ The firm has mentioned coating composition in Master formula. However, the label claim was "each tablet contains". The firm revised 'Each tablet

		contains' to 'Each film-coated tablet contains' in Form 5. □ Blistering/packaging process is missing in the manufacturing outlines
	Decision of 291th : Deferred for the following: □ Revision of 'amlodipine as besylate' to 'amlodipine besylate' in Master formula □ Submission of complete manufacturing outlines.	
	Evaluation by PEC (VI): The firm has revised their formulation as: Each film coated tablet contains: Amlodipine besylate eq to amlodipine…10mg Valsartan…160mg Hydrochlorothiazide…25mg Without submitting any correction fee.	
	Decision: Approved. Firm shall submit fee of Rs. 30,000/ for correction/pre-approval change/ in label claim and composition, as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	
402.	**Name and address of manufacturer / Applicant**	**M/s Linta Pharmaceuticals Pvt Ltd. Plot No. 03, Street No S-5, National Industrial Zone, Rawat, Islamabad"**
	Brand Name +Dosage Form + Strength	Micolin Oral Gel 2.0% Dakrin, Micono.
	Composition	Each gram of Gel Contains: Miconazole Nitrate eq. to Miconazole…20mg
	Diary No. Date of R& I & fee	Dy.No 21762 dated 21-06-2018 Rs.20,000/- 21-06-2018 Rs. 5000/- for change of formulation
	Pharmacological Group	Antifungals For Topical Use D01AC02
	Type of Form	Form-5
	Finished product Specification	BP
	Pack size & Demanded Price	As per SRO, Alu tubes of 15g and 30g
	Approval status of product in Reference Regulatory Authorities.	Daktarin (Miconazole 2% w/w). MHRA Approved
	Me-too status	Mogel 20mg/g Oral Gel by M/s Sigma Pharma (Reg no. 079910)
	GMP status	12-06-2018, GMP Compliant.
	Remarks of the Evaluator (VI)	The reference formulation contains miconazole without nitrate salt
	Decision of 291th : Deferred for revision of formulation as per the reference product along with submission of fee for revision of formulation.	
	Evaluation by PEC VI: Firm has submitted as : Micolin Oral Gel 2% Each gram of gel contains: Miconazole Nitrate eq to Miconazole….20mg	
	Decision of 316th : Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.	
	Evaluation by PEC-VI: The firm has corrected formulation without submission of fee as: Each gram of Gel Contains: Miconazole…20mg	
	Decision: Approved. Firm shall submit the fee of Rs. 30,000 for correction/pre-approval change in composition (correction/change of salt form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. Registration letter will be issued upon confirmation of availability of required manufacturing facility for applied dosage form.	

Case no. 08 Registration applications of import (Human) drugs on Form 5F
b. Deferred cases

403.	**Name, address of Applicant / Importer**	**M/s Medical Equipment & System 60/61 FCC, Syed Maratib Ali Road, Gulberg IV District Lahore, Pakistan**
	Details of Drug Sale License of importer	License No: 05-352-0065-069537D Address: House No 59-C/III, Gulberg III District Lahore Address of Godown: NA Validity: 14-04-2-23 Status: License to sell drugs as distributor Renewal: Firm has submitted a receipt of renewal but it does not contain any date
	Name and address of marketing authorization holder (abroad)	M/s Guerbet BP 57400,F-95943 Roissy CdG Cedex
	Name, address of manufacturer(s)	M/s Guertbet BP 57400,F-95943 Roissy CdG Cedex (Responsible for manufacturing and Batch releasing)
	Name of exporting country	France
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized **copy** of CoPP certificate (No. 034191) dated 23-06-2020 issued CCI PARIS ILE-DE-FRANCE for Lipiodol Ultra Fluide(480mg I/ml) solution injectable . The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. **The name of importing country on CoPP is mentioned as France. Furthermore the CoPP was valid till 22-06-2022.**
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of distribution certificate from. The letter species that the manufacturer appoints M/s **Medical Equipment & System** register their products in Pakistan. The authorization letter is valid till 11-04-2023.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only

	Dy. No. and date of submission	Form-5F Dy. No. 22519: 1-07-2021
	Details of fee submitted	PKR 50,000/-: 09-05-2019
	The proposed proprietary name / brand name	LIPIODOL Injection 10ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 10ml of ampoule contains:4800mg of iodine Lipiodol in the form of ethyl ester of iodised fatty acids of poppy seed oil contains 48% w/v 480mg of iodine per ml)
	Pharmaceutical form of applied drug	White lyophilized mass packed in moulded amber type-I vials.
	Pharmacotherapeutic Group of (API)	Non-water-soluble x-ray contrast media
	Reference to Finished product specifications	In house
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Injection **(USFDA** Approved).
	For generic drugs (me-too status)	**Not applicable as it is an innovator product**
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Manufacture: M/s SIMAFEX Address: 16 avenue des Fours a Chauz MARANS, 17230 France
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at $5^{o}C \pm 3^{o}C$. The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of

		analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not submitted as The product is innovator.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	USP type-I glass
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30^{o}C ±2^{o}C / 75% ± 5% RH. The real time stability study data of 2 batches is for 12 months while the stability study data for 3rd batch is for 9 months only.

Evaluation by PEC VI:

Sr no	Short coming	Reply
1	• Different API and finish product manufacturers are written in your application. Please specify the one which is actually manufacturing API and finish product. Also submit valid GMP certificate of both manufacturers.	The firm has submitted valid GMP certificate of M/s Guerbet 16-24 rue Jean Chaptal, Aulnay Sous Bois, 93600, France issued by EudraGMP. Valid till 2024 The firm has submitted valid GMP certificate of M/s Simafex 16, Avenue des Fours a Chaux, Marans, 1720, France issued by EudraGMP. Valid till 2024
2	• Letter of authorization/agreement is required clearly showing the validity.	Similar product was considered in M-291st meeting in September 2019 from Applicant: M/s A & Z Health Services. Suit No. 2, Block 27, Industrial & Trade Center, G-9/4, Islamabad, Pakistan." MAH: M/s Guerbet BP 57400, F-95943, Roissy CdG CEDEX" Brand name: Lipiodol Ultra-Fluide (480mg I/ml) Solution for Injection
3	• 3.2.S.4 Control of Drug Substance /3.2.P.5 Control of Drug Product. You are following In-house specifications, although the product is present in pharmacopoeia. Justification is required.	

Appendix 1: Comparison between Lipiodol Ultra Fluid internal monograph, British Pharmac monograph "Iodised oil fluid injection" and US Pharmacopoeia monograph "Ethiodized oil in

	GUERBET specifications	BP monograph "iodised oil fluid injection"	USP monograph "ethiodized oil inject
CHARACTERS			
- Appearance	Clear, pale yellow to oil	Straw-coloured or yellow, oily liquid	-
- Solubility(*)			
. Water	-	Practically insoluble	-
. Chloroform	-	Soluble	-
. Ether	-	Soluble	-
. Petroleum Spirit	-	Soluble	-
IDENTIFICATION			
- Identification	IR	Iodine vapor	Iodine vapor
TESTS OF PURITY			
- Density at 20 °C	1.268 to 1.290 g/mL	1.28 to 1.30	1.280 to 1.293 at 1
- Viscosity at 20 °C	34 to 70 mPa.s	-	50 to 100 cP at 15
- Absorbance			
. at 420 nm	NMT 0.60	-	-
. at 460 nm	NMT 0.50	-	-
- Acid value	NMT 1.0	NMT 1.2	NMT 1.3
- Free iodine	NMT 100 ppm	NMT 500 ppm	No blue color
- Water content	NMT 0.06 % w/w	-	-
ASSAY			
Iodine content (potentiometry)	37.0 to 39.0 % w/w	37.0 to 39.0 % w/w	35.2 to 38.9 % v

NMT = Not More Than
(*) According to EP chapter 1 "General Notices", "the statements under the heading Characters are n interpreted in a strict sense and are not requirements".
Therefore, solubility is not routinely tested as it is under the heading Characters.

Decision of 316th : Deferred for clarification regarding sole agency agreement of applied product since same product was considered in 291st meeting of Registration Board from applicant M/s A & Z Health Services. Suit No. 2, Block 27, Industrial & Trade Center, G-9/4, Islamabad, Pakistan."

Evaluation by PEC VI: M/s Medical equipment and systems has submitted NOC from M/s A & Z . The NOC states "We M/s : A&Z health services, Suit #2, Block 27 I&T center, G-9/4 Islamabad do hereby state and undertake that we have no objection if the product LIPIDOL ULTRA FLUID register on the name M/s Medical Equipment & Systems 60/61, FCC Syed Maratib Ali Road, Gulberg IV Lahore."

Decision: Deferred for further deliberation upon marketing status of the applied product.

404.	**Name, address of Applicant / Importer**	**M/s Ahsan Pharma Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi**
	Details of Drug Sale License of importer	License No: 048 Address: Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi. Address of Godown: B-4, S.I.T.E. Karachi Validity: 15th Oct 2022 Status: Drug License by the way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/S Seacross Pharmaceutical Co., Ltd, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK **Product Licence/Marketing Authorization holder**

		SEACROSS PHARMACEUTICALS LIMITED BEDFORD BUSINESS CENTRE, 61 - 63 ST.PETER'S STREET, BEDFORD, BEDFORDSHIRE, MK40 2PR, UNITED KINGDOM
	Name, address of manufacturer(s)	**Manufacturer:** M/s Sichuan Huiyu Pharmaceutical Ltd. No. 5 Road Chengxi economic area, Neijiang, Sichuan-641000, China. (GMP is issued by CFDA and is valid until 27/5/2023) **Batch Release Site:** Seacross Pharmaceutical Co., Ltd Stanmore Place, Suite 205, Howard Road, Stanmore HA7 1BT, United Kingdom **Manufacturer Licence Holder:** Seacross Pharmaceutical Co., Ltd Stanmore Place, Suite 205, Howard Road, Stanmore HA7 1BT, United Kingdom
	Name of exporting country	UK
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** the firm has submitted CoPP from MHRA for Doxorubicin 2mg/ml Concentrate for Solution for Infusion, Certificate No: PP10165864 dated 03-Apr-2020. The firm has submitted copy of letter from MHRA regarding issuance of export certificates for medicines for humans which will not be available as hard copy with wet ink signature during the period pertaining to COVID-19 *"The export certificate will be processed by the MHRA named signatories and issued as electronic pdf copy. The certificate will refer to this covering letter which should be attached to any submissions."*
	Details of letter of authorization / sole agency agreement	Firm has submitted Copy of Exclusive Distribution Agreement is submitted M/S Seacross Pharmaceutical Co., Ltd Stanmore Business & Innovation Centre, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK authorizes M/s Ahsan Pharma Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi for marketing and selling the Seacross products including the applied product.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging

		☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 7319: 05-03-2021
	Details of fee submitted	PKR 100,000/- : 23-02-2021
	The proposed proprietary name / brand name	**Doxorubicin 2mg/ml Concentrate for Solution for Infusion,**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml vial contains: Doxorubicin hydrochloride…….10mg
	Pharmaceutical form of applied drug	Concentrate for Solution for infusion
	Pharmacotherapeutic Group of (API)	Anthracyclines and related substance (L01DB01)
	Reference to Finished product specifications	BP
	Proposed Pack size	5ml x 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved Each 5ml vial contains 10 mg of Doxorubicin hydrochloride. Concentrate for solution for infusion
	For generic drugs (me-too status)	
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	M/s Sterling Biotech Ltd Jambusar State Highway Taluka Padra, District Vadodara India-391 421 Masar Village, Gujarat
	Module-III Drug Substance:	Firm has submitted (EDQM has issued certificate of suitability which is deemed to replace the data.)
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	(EDQM has issued certificate of suitability which is deemed to replace the data.)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence has been compared with Adriblastina (Greece), Adriamycin (Denmark, Australia).
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type-I glass vial
	Stability study data of drug product, shelf life and storage conditions	2 months accelerated studies at 25C, 60% has been submitted. Long term stability studies at 5C for 18months has been submitted. Storage temperature is 2 to 8C.
Evaluation by PEC:		
Sr no	**Short Coming**	**Replies**
1	The address of manufacturer on GMP and COPP is different. Clarification is needed.	M/s Sichuan Huiyu changed the address as per requirements from local official administrative office. The CPP was applied before the address changed. However, the Eudra has updated the GMP to the current address, and the GMP certificate number is also updated to 0004 from 0003 version.
2	GMP certificates of M/s Seacross Pharmaceuticals and M/s Sterling Biotech Ltd Jambusar are required.	Did not provided.
3	3.2.P.8 You have provided Accelerated stability data for only 2 months. Remaining months data is not provided.	The product is thermal sensitive. The impurity content and assay were out of specification at 2nd month of accelerated stability study, so the storage condition of the product should be at 2~8℃. The product should be transferred on a controlled temperature during shipping. The shelf life is based on the long-term stability study. 2 months accelerated studies at 25C, 60% has been submitted. Long term stability studies at 5C for 18months has been submitted. Storage temperature is 2 to 8C.
4	3.2.P.5.3 Validation of analytical procedures: For in-house methods, analytical methods validation shall be performed. All the officially recognized compendial methods for assay, dissolution and impurities (as applicable) are required to be verified and verification shall include a demonstration of specificity, repeatability (method precision) and accuracy	The full validation reports, including specificity, repeatability and accuracy, for assay, degradation and related substance will be provided by you tomorrow.
Decision of 312th : Deferred for submission of complete stability study data of finished product as per Zone -IVA.		
Evaluation by PEC: The firm has submitted MHRA COPP and Smpc that states "Store at 2 to 8 'C". They also submitted declaration letter from the manufacturer "Doxorubicin is a thermal sensitive product, required to be stored in a refrigerator. The long-term stability study condition according to ICH Q1 is 2 to 8, which has been provided. It is not necessary to provide 30'C stability data for Doxorubicin, as significant change has occurred at 2nd month at 25 'C condition."		

Decision of 320th meeting: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.		
405.	Name, address of Applicant / Importer	M/s Ahsan Pharma Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi
	Details of Drug Sale License of importer	License No: 048 Address: Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi. Address of Godown: B-4, S.I.T.E. Karachi Validity: 15th Oct 2022 Status: Drug License by the way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/S Seacross Pharmaceutical Co., Ltd, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK **Product Licence/Marketing Authorization holder** SEACROSS PHARMACEUTICALS LIMITED BEDFORD BUSINESS CENTRE, 61 - 63 ST.PETER'S STREET, BEDFORD, BEDFORDSHIRE, MK40 2PR, UNITED KINGDOM
	Name, address of manufacturer(s)	**Manufacturer:** M/s Sichuan Huiyu Pharmaceutical Ltd. No. 5 Road Chengxi economic area, Neijiang, Sichuan-641000, China(GMP is issued by CFDA and is valid until 27/5/2023) **Batch Release Site:** Seacross Pharmaceutical Co., Ltd Stanmore Place, Suite 205, Howard Road, Stanmore HA7 1BT, United Kingdom **Manufacturer Licence Holder:** Seacross Pharmaceutical Co., Ltd Stanmore Place, Suite 205, Howard Road, Stanmore HA7 1BT, United Kingdom
	Name of exporting country	UK
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** the firm has submitted CoPP from MHRA for Doxorubicin 2mg/ml Concentrate for Solution for Infusion, Certificate No: PP10165864 dated 03-Apr-2020. The firm has submitted copy of letter from MHRA regarding issuance of export certificates for medicines for humans which will not be available as hard copy with wet ink signature during the period pertaining to COVID-19 *"The export certificate will be processed by the MHRA named signatories and issued as electronic pdf copy. The certificate will refer to this covering letter which should be attached to any submissions."*
	Details of letter of authorization / sole agency agreement	Firm has submitted Copy of Exclusive Distribution Agreement is submitted M/S Seacross Pharmaceutical Co., Ltd Stanmore Business & Innovation Centre, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK authorizes M/s Ahsan Pharma Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi for marketing and selling the Seacross products including the applied product.

	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 7320: 05-03-2021
	Details of fee submitted	PKR 100,000/- : 23-02-2021
	The proposed proprietary name / brand name	**Doxorubicin 2mg/ml Concentrate for Solution for Infusion,**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 25ml vial contains: Doxorubicin hydrochloride…….50mg
	Pharmaceutical form of applied drug	Concentrate for Solution for infusion
	Pharmacotherapeutic Group of (API)	Anthracyclines and related substance (L01DB01)
	Reference to Finished product specifications	B Pharmacopoeia
	Proposed Pack size	25ml x1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved
	For generic drugs (me-too status)	
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Sterling Biotech Ltd Jambusar State Highway Taluka Padra, District Vadodara India-391 421 Masar Village, Gujarat
	Module-III Drug Substance:	Firm has submitted (EDQM has issued certificate of suitability which is deemed to replace the data.)
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	(EDQM has issued certificate of suitability which is deemed to replace the data.)

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence has been compared with Adriblastina (Greece), Adriamycin (Denmark, Australia).
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type-I glass vial
	Stability study data of drug product, shelf life and storage conditions	2 months accelerated studies at 25C, 60% has been submitted. Long term stability studies at 5C for 18months has been submitted. Storage temperature is 2 to 8C.
Evaluation by PEC:		
Sr. no	**Short Coming**	**Replies**
1	The address of manufacturer on GMP and COPP is different. Clarification is needed.	M/s Sichuan Huiyu changed the address as per requirements from local official administrative office. The CPP was applied before the address changed. However, the Eudra has updated the GMP to the current address, and the GMP certificate number is also updated to 0004 from 0003 version.
2	GMP certificates of M/s Seacross Pharmaceuticals and M/s Sterling Biotech Ltd Jambusar are required.	Did not provided.
3	3.2.P.8 You have provided Accelerated stability data for only 2 months. Remaining months data is not provided.	The product is thermal sensitive. The impurity content and assay were out of specification at 2nd month of accelerated stability study, so the storage condition of the product should be at 2~8℃. The product should be transferred on a controlled temperature during shipping. The shelf life is based on the long-term stability study. 2 months accelerated studies at 25C, 60% has been submitted. Long term stability studies at 5C for 18months has been submitted. Storage temperature is 2 to 8C.
4	3.2.P.5.3 Validation of analytical procedures: For in-house methods, analytical methods validation shall be performed. All the officially recognized compendial methods for assay, dissolution and impurities (as applicable) are required to be verified and verification shall include a	The full validation reports, including specificity, repeatability and accuracy, for assay, degradation and related substance will be provided by you tomorrow.

	demonstration of specificity, repeatability (method precision) and accuracy	
Decision of 312th: Deferred for submission of complete stability study data of finished product as per Zone -IVA.		
Evaluation by PEC: The firm has submitted MHRA COPP and Smpc that states "Store at 2 to 8 'C". They also submitted declaration letter from the manufacturer "Doxorubicin is a thermal sensitive product, required to be stored in a refrigerator. The long-term stability study condition according to ICH Q1 is 2 to 8, which has been provided. It is not necessary to provide 30'C stability data for Doxorubicin, as significant change has occurred at 2nd month at 25 'C condition."		
Decision of 320th meeting: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.		

Case no. 03 Registration applications for local manufacturing of (veterinary) drugs

a. New Cases

b. Deferred Cases

406.	Name and address of manufacturer/ Applicant	M/s Bio-Oxime Pharmaceuticals Plot.no.31,32 Millat Garment City, Dry Port Road, Faisalabad
	Brand Name + Dosage Form + Strength	Biostin Oral Powder
	Composition	Each 100gm contains: Colistin Sulphate…500,000IU
	Diary No. Date of R & I & fee	Dy. No. 7971; 22.02.2019 PKR. 20,000/-; 22.02.2019
	Pharmacological Group	Antibiotics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	Decontrolled
	Me-too status	Could not be confirmed
	GMP status	The firm was inspected on 24.02.2021, wherein the renewal of DML was recommended.
	Remarks of the Evaluator	• Provide proof of approval of me-too product (name and registration number) approved by DRAP.
	Previous decision	The board in its 295th meeting deferred the case for: • Updated status of GMP since submitted inspection report is not within the period of three years. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Evaluation by PEC	Reply dated 03.06.2021: • GMP status updated. • The firm submitted me-too reference, which is not matching with the applied product.
	Decision of 312th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation: The firm has submitted me-too as: Polyrox Forte water soluble powder. Each 100gm contains: Colistin Sulphate….500MIU by M/s Vetrox Pharmaceutcals.	
	Decision: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.	

407.	Name and address of manufacturer/ Applicant	M/s Bio-Oxime Pharmaceuticals Plot.no.31,32 Millat Garment City, Dry Port Road, Faisalabad
	Brand Name + Dosage Form + Strength	Noflor Oral Powder
	Composition	Each gm contains: Neomycin sulphate…150mg Florfenicol…100mg Oxytetracycline…300mg
	Diary No. Date of R & I & fee	Dy. No. 7969; 22.02.2019 PKR. 20,000/-; 22.02.2019
	Pharmacological Group	Antibiotics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	500g, 1000g, 5000g; Decontrolled
	Me-too status	E-COL WATER SOLUBLE POWDER. Reg. No. 81733
	GMP status	The firm was inspected on 24.02.2021, wherein the renewal of DML was recommended.
	Remarks of the Evaluator	
	Previous decision	The board in its 295th meeting deferred the case for updated status of GMP since submitted inspection report is not within the period of three years.
	Evaluation by PEC	Reply dated 03.06.2021: • GMP status updated. • In the latest database, the me-too product contains Oxytetracycline HCl…300mg instead of Oxytetracycline…300mg.
	Decision of 312th : Deferred for revision of salt form along with submission of applicable fee.	
	Evaluation: The firm has submitted fee of Rs 7500 slip no 5132746736 and revised formulation with the addition of HCL as: Each gm contains: Neomycin sulphate…150mg Florfenicol…100mg Oxytetracycline HCl…300mg E-COL WATER SOLUBLE POWDER. Reg. No. 81733	
	Decision: Approved with Innovator specifications. Firm shall submit the differential fee of Rs. 22,500/- for correction/pre-approval change in composition (correction/change of salt form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
408.	Name and address of manufacturer/ Applicant	M/s Bio-Oxime Pharmaceuticals Plot.no.31,32 Millat Garment City, Dry Port Road, Faisalabad
	Brand Name + Dosage Form + Strength	Speclin 100 Oral Liquid
	Composition	Each 150gm contains: Lincomycin HCL…33.3 Spectinomycin HCL…66.7gm
	Diary No. Date of R & I & fee	Dy. No. 7968; 22.02.2019 PKR. 20,000/-; 22.02.2019
	Pharmacological Group	Antibiotics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	Decontrolled
	Me-too status	LINCO-S 100 W/S POWDER. Reg. No. 62169
	GMP status	The firm was inspected on 24.02.2021, wherein the renewal of DML was recommended.
	Remarks of the Evaluator	• Submit latest GMP inspection report.

		• You have applied for liquid pack size. Justify. • Revise Lincomycin HCl to Lincomycin as HCl and Spectinomycin HCl to Spectinomycin as HCl. Also, adjust their weight in master formula as per salt factor.
	Previous decision	The board in its 295th meeting deferred the case for: • Updated status of GMP since submitted inspection report is not within the period of three years. • Revision of formulation as per me-too reference • Confirmation of pack size
	Evaluation by PEC	Reply dated 03.06.2021: • GMP status updated. • The firm revised Lincomycin HCl to Lincomycin as HCl and Spectinomycin HCl to Spectinomycin as HCl, but did not adjust their weight in master formula as per salt factor. • The firm claimed 150g, 500g, and 1000g pack size.
	Decision of 312th: Deferred for adjustment of weights of APIs in master formula as per salt factor. Along with submission of applicable fee.	
	Evaluation: The firm has adjusted the weigh in master formulation and deposited fee Rs 7500 slip no 8755481265.	
	Decision: Approved with Innovator specifications. Firm shall submit the differential fee of Rs. 22,500/- for correction/pre-approval change in composition (correction/change of salt form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

409.	**Name and address of manufacturer / Applicant**	**M/s Eterna Pharma (Pvt.) Ltd. Plot# (99,100,101,198)C, Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir.**
	Brand Name+Dosage Form+Strength	DI-BP Benz Injection (10ml)
	Composition	Each ml contains:- Benzathine Penicillin G …100,000IU Procaine Penicillin …15,000IU Streptomycin sulphate …200mg
	Diary No. Date of R& I & fee	Dy No: 31176, Dated:12-11-2021, Rs. 30,000, Dated:11-11-2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack size & demanded price	10ml/ Decontrolled
	Me-too status	B.G Probenz Injection REG.# 072699 Biogen Pharma,Rawat.
	GMP status	The Central Licensing Board in its 283rd meeting held on 28th October,2021 has considered and approved the four (04) additional sections in the name of M//s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir by way of Formulation vide approval letter No. F. 5-1/2016- Lic dated 11th November, 2021.
	Remarks of the Evaluator	• Me-too status not confirms from available database. Composition of submitted me-too i.e B.G Probenz Injection by M/s. Biogen Pharma,Rawat (Reg#072699) is:

		Each ml contains:- Benzathine Penicillin G …100,000 IU Procaine Penicillin G …150,000 IU Dihydrostreptomycin Sulphate …200 mg
	Decision of 316th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation by PEC(VI):	
	Decision of 320th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
410.	**Name and address of manufacturer / Applicant**	**M/s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir.**
	Brand Name+DosageForm+Strength	DI-BP Benz Injection (30ml)
	Composition	Each ml contains:- Benzathine Penicillin G …100,000IU Procaine Penicillin …15,000IU Dihydrostreptomycin sulphate …200mg
	Diary No. Date of R& I & fee	Dy No: 31177, Dated:12-11-2021, Rs. 30,000, Dated:11-11-2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack size & demanded price	30ml/ Decontrolled
	Me-too status	B.G Probenz Injection REG.# 072699 Biogen Pharma,Rawat.
	GMP status	The Central Licensing Board in its 283rd meeting held on 28th October,2021 has considered and approved the four (04) additional sections in the name of M//s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir by way of Formulation vide approval letter No. F. 5-1/2016- Lic dated 11th November, 2021.
	Remarks of the Evaluator	• Me-too status not confirms from available database. Composition of submitted me-too i.e B.G Probenz Injection by M/s. Biogen Pharma,Rawat (Reg#072699) is: Each ml contains:- Benzathine Penicillin G …100,000 IU Procaine Penicillin G …150,000 IU Dihydrostreptomycin Sulphate …200 mg
	Decision of 316th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation by PEC(VI):	
	Decision of 320th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	

411.	**Name and address of manufacturer / Applicant**	**M/s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir.**
	Brand Name+DosageForm+Strength	DI-BP Benz Injection (50ml)
	Composition	Each ml contains:- Benzathine Penicillin G …100,000IU Procaine Penicillin …15,000IU Dihydrostreptomycin sulphate …200mg
	Diary No. Date of R& I & fee	Dy No: 31178, Dated:12-11-2021, Rs. 30,000, Dated:11-11-2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack size & demanded price	50ml/ Decontrolled
	Me-too status	B.G Probenz Injection REG.# 072699 Biogen Pharma,Rawat.
	GMP status	The Central Licensing Board in its 283rd meeting held on 28th October,2021 has considered and approved the four (04) additional sections in the name of M//s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir by way of Formulation vide approval letter No. F. 5-1/2016- Lic dated 11th November, 2021.
	Remarks of the Evaluator	• Me-too status not confirms from available database. Composition of submitted me-too i.e B.G Probenz Injection by M/s. Biogen Pharma,Rawat (Reg#072699) is: Each ml contains:- Benzathine Penicillin G …100,000 IU Procaine Penicillin G …150,000 IU Dihydrostreptomycin Sulphate …200 mg
	Decision of 316th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation by PEC(VI):	
	Decision of 320th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
412.	**Name and address of manufacturer / Applicant**	**M/s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir.**
	Brand Name+DosageForm+Strength	DI-BP Benz Injection (100ml)
	Composition	Each ml contains:- Benzathine Penicillin G …100,000IU Procaine Penicillin …15,000IU Dihydrostreptomycin sulphate …200mg
	Diary No. Date of R& I & fee	Dy No: 31179, Dated:12-11-2021, Rs. 30,000, Dated:11-11-2021

	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack size & demanded price	100ml/ Decontrolled
	Me-too status	B.G Probenz Injection REG.# 072699 Biogen Pharma,Rawat.
	GMP status	The Central Licensing Board in its 283rd meeting held on 28th October,2021 has considered and approved the four (04) additional sections in the name of M//s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir by way of Formulation vide approval letter No. F. 5-1/2016- Lic dated 11th November, 2021.
	Remarks of the Evaluator	• Me-too status not confirms from available database. Composition of submitted me-too i.e B.G Probenz Injection by M/s. Biogen Pharma,Rawat (Reg#072699) is: Each ml contains:- Benzathine Penicillin G …100,000 IU Procaine Penicillin G …150,000 IU Dihydrostreptomycin Sulphate …200 mg
	Decision of 316th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation by PEC(VI):	
	Decision of 320th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
413.	**Name and address of manufacturer / Applicant**	**M/s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir.**
	Brand Name+DosageForm+Strength	Brom-CTD Water Soluble Powder
	Composition	Each gm contains: - Doxycycline HCl ….100 mg Tylosin Tartrate …100 mg Colistin Sulphate …25, 00,000 IU Bromhexine HCl …5mg
	Diary No. Date of R& I & fee	Dy.No:31088 , dated:12-11-2021, Rs.30,000/-, dated: 11-11-2021
	Pharmacological Group	Antibiotic, Mucolytic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack size & demanded price	100gm,500gm,1 Kg,5Kg,10Kg, 25Kg./ Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	DOXIMAC-C WATER SOLUBLE POWDER REG.#049530 PRIX PHARMACEUTICA (PVT) LTD., LAHORE.
	GMP status	GMP inspection held on 14-10-2021 Panel Inspection

		Panel recommended the approval of 4 additional sections
	Remarks of the Evaluator	Firm has applied Doxycycline HCl ….100 mg, whereas, me-too contains Doxycycline Hyclate ….100 mg.
	Decision of 316th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation by PEC(VI):	
	Decision of 320th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
414.	**Name and address of manufacturer / Applicant**	**M/s Eterna Pharma (Pvt.)Ltd.Plot#(99,100,101,198)C,Sector D1,Old Industrial Estate, Mirpur,Azad Jammu & Kashmir.**
	Brand Name+DosageForm+Strength	Respityl-C Oral Powder
	Composition	Each 100gm contains: - Doxycycline HCL … 40 gm Tylosin Tartrate …20 gm Colistin Sulphate …10 MIU Bromhexine HCl …2 gm
	Diary No. Date of R& I & fee	Dy.No:31086 , dated:12-11-2021, Rs.30,000/-, dated: 11-11-2021
	Pharmacological Group	Antibiotic, Mucolytic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack size & demanded price	100gm,500gm,1 Kg,5Kg,10Kg, 25Kg./ Decontrolled
	Me-too status	MULTIDOX ORAL POWDER REG.# 078395 HAWK BIO PHARMA ISLAMABAD.
	GMP status	GMP inspection held on 14-10-2021 Panel Inspection Panel recommended the approval of 4 additional sections
	Remarks of the Evaluator	• Firm has applied Colistin Sulphate …10 MIU in Form-5, whereas, me-too contains Colistin Sulphate …10 gm.
	Decision of 316th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Evaluation by PEC(VI):	
	Decision of 320th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	

Case no. 04 Registration applications of newly granted DML or New section (human)

a. New DML /section

415.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Alfalah Pharma Private Limited 12-Km Sheikhupura Road, Lahore.**
	Name, address of Manufacturing site.	M/s Alfalah Pharma Private Limited

		12-Km Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26801 , dated 28/09/2021
	Details of fee submitted	PKR 30,000/-: dated 22/09/2021
	The proposed proprietary name / brand name	DU-LIFE 30 mg capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Duloxetine (as hydrochloride) …….30mg (As enteric coated pellets) from M/s vision Pharma
	Pharmaceutical form of applied drug	Red colour cap and body, oblong shaped capsules containing white to off white colour entric coated spherical pellets capsules.
	Pharmacotherapeutic Group of (API)	SSRI (Anti-depressant)
	Reference to Finished product specifications	USP
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cymbalta 30mg capsule by M/s Eli Lilly and Company, USFDA Approved.
	For generic drugs (me-too status)	Hapibar 30 mg Caspule by M/s Barrett Hodgson Pakistan (Pvt) Ltd., Reg. No. 061745
	GMP status of the Finished product manufacturer	New Section Approved on 13/02/2020 Capsule (General) section approved.
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot 22-23, Industrial Triangle, Kahuta Road, Islamabad, Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls,

		impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence /Comparative dissolution for their product against the reference product i.e. Dulan 30mg capsule manufactured by M/s Hilton Pharma (Pvt) Ltd. (Batch number 132101).
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method for the drug substance. Firm has submitted report of verification studies of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.		
API Lot No.	DXT275		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	DL301	DL302	DL303
Batch Size	500 Capsules	500 Capsules	500 Capsules
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	13-03-2020	13-03-2020	13-03-2020
No. of Batches	03		

Administrative Portion

a.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has submitted that their capsule section is a new facility and was inspected by panel of inspectors on 26-06-2019 and 16-09-2019 for grant of new section.
b.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate dated 31-07-2019 issued by Additional Director (QA&LT) DRAP Islamabad. The certificate is valid till 10-02-2022.
c.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 21-02-2020 specifying purchase of 1kg Duloxetine (as hydrochloride) 17.0% EC pellets.
d.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets, HPLC chromatograms COA and summary data sheets.
e.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
f.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence & CDP studies against the Innovator product i.e., Cymbalta.**

New license granted on 21/09/2021by CLB
Cephalosporin section approved.

2 molecules / 10products

416.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	Dy. No. and date of submission	Dy.No 5513 dated 28/02/2022
	Details of fee submitted	PKR 30,000/-: dated 23/10/2021
	The proposed proprietary name / brand name	Citi-Axone Injection IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 1g
	Pharmaceutical form of applied drug	Intra-Muscular Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 1gm by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 1gm by Sami Pharmaceuticals, Reg. No. 022422
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, t, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-013, TRI-014, TRI-015)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 1gm Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China		
API Lot No.	CC0121060125		
Description of Pack (Container closure system)	One clear glass vial 15ml with Glass ampule type-I of 1% Lidocaine HCl 3.5 ml along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-013	TRI-014	TRI-015
Batch Size (Scientifically rational batch size)	300 Vials	300 Vials	300 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	28-09-2021	28-09-2021	28-09-2021
No. of Batches	03		

Administrative Portion		
25.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
26.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
27.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021

28.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
29.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
30.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 1gm IM Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125 Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product i.e., Rocephin Injection.**		
417.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8241 dated 29/03/2022
	Details of fee submitted	PKR 30,000/-: dated 1/11/2021
	The proposed proprietary name / brand name	Citi-Axone Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 1g
	Pharmaceutical form of applied drug	Intra-venous Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 1gm by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 1gm by Sami Pharmaceuticals, Reg. No. 022422
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description

		of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-013, TRI-014, TRI-015)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Inocef 1gm Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
API Lot No.	CC0121060125
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI along with leaflet in unit carton.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-013	TRI-014	TRI-015
Batch Size (Scientifically rational batch size)	300 Vials	300 Vials	300 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	28-09-2021	28-09-2021	28-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.

c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 1gm IV Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125 Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product i.e., Rocephin Injection.**

418.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 9109 dated 11/04/2022

	Details of fee submitted	PKR 30,000/-: dated 31/3/2022
	The proposed proprietary name / brand name	Citi-Axone Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 2gm
	Pharmaceutical form of applied drug	Intra-venous Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 2gm by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 2gm by Sami Pharmaceuticals, Reg. No. 022424
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-CSI001, T-CSI002, T-CSI003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing

		process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 2gm Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China		
API Lot No.	CC0121060125		
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-CSI001	T-CSI002	T-CSI003
Batch Size (Scientifically rational batch size)	300 injections	300 injections	300 injections
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	28-09-2021	28-09-2021	28-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 2gm IV Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125 Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product i.e., Rocephin Injection.**		
419.	Name, address of Applicant / Marketing Authorization Holder	M/s Citi Pharma Private Limited Lahore
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 10559 dated 27/04/2022
	Details of fee submitted	PKR 30,000/-: dated 23-04-2022
	The proposed proprietary name / brand name	Citi-Axone Injection 250 IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 250mg
	Pharmaceutical form of applied drug	Intra-muscular Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 250mg by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 250mg by Sami Pharmaceuticals, Reg. No. 022421
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-001, TRI-002, TRI-003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Inocef 250mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
API Lot No.	CC0121060125
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI along with leaflet in unit carton.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months

	Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-001	TRI-002	TRI-003
atch Size (Scientifically rational batch size)	300 Vials	300 Vials	300 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	28-09-2021	28-09-2021	28-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being	Pharmaceutical Equivalence have been established against the brand leader that is

	compared with the innovator's product	Inocef 250mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125 Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

420.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 9109 dated 11/04/2022
	Details of fee submitted	PKR 30,000/-: dated 31-03-2022
	The proposed proprietary name / brand name	Citi-Axone Injection IV

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 250mg
	Pharmaceutical form of applied drug	Intra-venous Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 250mg by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 250mg by Sami Pharmaceuticals, Reg. No. 022421
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-001, TRI-002, TRI-003)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Inocef 250mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China		
API Lot No.	CC0121060125		
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-001	TRI-002	TRI-003
atch Size (Scientifically rational batch size)	300 Vials	300 Vials	300 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	28-09-2021	28-09-2021	28-09-2021
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021

10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 250mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125 Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity	Record of Digital data logger for temperature and humidity monitoring of stability

	monitoring of stability chambers (real time and accelerated).	chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

421.	Name, address of Applicant / Marketing Authorization Holder	M/s Citi Pharma Private Limited Lahore
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 10560 dated 27-04-2022
	Details of fee submitted	PKR 30,000/-: dated 23-04-2022
	The proposed proprietary name / brand name	Citi-Axone Injection IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 500mg
	Pharmaceutical form of applied drug	Intra-Muscular Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 500mg by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 500mg by Sami Pharmaceuticals, Reg. No. 022423
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-001, TRI-002, TRI-003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 500mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China	

API Lot No.	CC0121060125		
Description of Pack (Container closure system)	One clear glass vial 15ml with Glass ampule type-I of 1% Lidocaine HCl 2.0 ml along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-007	TRI-008	TRI-009
Batch Size (Scientifically rational batch size)	300 Vials	300 Vials	300 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	30-09-2021	30-09-2021	30-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 500mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125 Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product i.e., Rocephin Injection.**

422.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8240 dated 29/03/2022
	Details of fee submitted	PKR 30,000/-: dated 1/11/2021
	The proposed proprietary name / brand name	Citi-Axone Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile powder of Ceftriaxone sodium USP eq. to Ceftriaxone 500mg
	Pharmaceutical form of applied drug	Intra-venous Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin Injection 500mg by M/s Rouche Laboratories Inc. UK, USFDA Approved.
	For generic drugs (me-too status)	Oxidil Injection 500mg by Sami Pharmaceuticals, Reg. No. 022423
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium eq. to Ceftriaxone is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, ,

		specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-001, TRI-002, TRI-003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Inocef 500mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Qilu Antibiotics Pharmaceutical Co., Ltd. China		
API Lot No.	CC0121060125		
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-007	TRI-008	TRI-009
Batch Size (Scientifically rational batch size)	300 Vials	300 Vials	300 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	30-09-2021	30-09-2021	30-09-2021
No. of Batches	03		
Administrative Portion			

7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170635 issued by CFDA valid till 13/12/2022.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 10676/2021 DRAP dated 15-07-2021 B/L No. YML4S236121840 dated: 01-07-2021
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Inocef 500mg Injection by Barrett Hodgson Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	M/S Qilu Antibiotic Pharmaceutical Co. Ltd, China API Lot Number: CC0121060125

		Letter No. 10676/2021DRAP Dated: 15-07-2021. B/L No. YML4S236121840 Dated: 01-07-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product i.e., Rocephin Injection.**

423.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8241 dated 29/03/2022
	Details of fee submitted	PKR 30,000/-: dated 01/11/2021
	The proposed proprietary name / brand name	Citi-Taxime Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile Powder of Cefotaxime sodium USP eq. to Cefotaxime 1gm
	Pharmaceutical form of applied drug	Intra-venous
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic

	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefotaxime powder for solution Injection 1gm by M/s Wockhardt Ltd. UK, USFDA Approved.
	For generic drugs (me-too status)	Sporonil Injection 1gm by Global Pharmaceuticals, Reg. No. 025927
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Sinopharm Weiqida Pharmaceutical Co.,Ltd China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefotaxime Sodium eq. to Cefotaxime is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-004, TRI-005, TRI-006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its

		verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sporonil Injection 1g by Global Pharmaceuticals Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Sinopharm Weiqida Pharmaceutical Co.,Ltd China		
API Lot No.	FB-2021/03/13		
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI or 1% Lidocaine along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-004	TRI-005	TRI-006
Batch Size (Scientifically rational batch size)	1000 Vials	1000 Vials	1000 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	26-09-2021	26-09-2021	26-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SX20180255 issued by CFDA valid till 23/12/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 8084/2021 DRAP dated: 04-08-2021 B/L No. 229111000081 dated: 23-06-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
a.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
b.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
c.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Sporonil 1gm IV Injection by Global Pharmaceutical, Islamabad performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
d.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
e.	Documents for the procurement of API with approval from DRAP (in case of import).	• M/S Sinipharm Weiqida Pharmaceutical Co. Ltd. China API Lot Number: FB-2021/03/13 Letter No. 8084/2021 DRAP Dated: 04-08-2021. B/L No. 229111000081 Dated: 23-06-2021 API import documents has been submitted with ADC clearance
f.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
g.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product.**

424.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Citi Pharma Private Limited Lahore**
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8239 dated 29/03/2022
	Details of fee submitted	PKR 30,000/-: dated 01/11/2021
	The proposed proprietary name / brand name	Citi-Taxime Injection IV/IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile Powder of Cefotaxime sodium USP eq. to Cefotaxime 250mg
	Pharmaceutical form of applied drug	Intra-venous / Intra-muscular Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Claforan Injection 250mg by M/s Sanofi aventis Ltd. USA, USFDA Approved.
	For generic drugs (me-too status)	Sporonil Injection 250mg by Global Pharmaceuticals, Reg. No. 025928
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Sinopharm Weiqida Pharmaceutical Co.,Ltd China

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefotaxime Sodium eq. to Cefotaxime is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-004, TRI-005, TRI-006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sporonil Injection 250mg by Global Pharmaceuticals Pakistan performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		

Manufacturer of API	M/s Sinopharm Weiqida Pharmaceutical Co.,Ltd China		
API Lot No.	FB-2021/03/13		
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI or 1% Lidocaine along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-004	TRI-005	TRI-006
Batch Size (Scientifically rational batch size)	1000 Vials	1000 Vials	1000 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	26-09-2021	26-09-2021	26-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SX20180255 issued by CFDA valid till 23/12/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 8084/2021 DRAP dated: 04-08-2021 B/L No. 229111000081 dated: 23-06-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
h.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions:

		Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
i.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
j.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Sporonil Injection by Global Pharmaceutical, Islamabad performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).
k.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
l.	Documents for the procurement of API with approval from DRAP (in case of import).	• M/S Sinopharm Weiqida Pharmaceutical Co. Ltd. China API Lot Number: FB-2021/03/13 Letter No. 8084/2021 DRAP Dated: 04-08-2021. B/L No. 229111000081 Dated: 23-06-2021 API import documents has been submitted with ADC clearance
m.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
n.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product.**

425.	Name, address of Applicant / Marketing Authorization Holder	M/s Citi Pharma Private Limited Lahore
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Lahore Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8240 dated 29/03/2022
	Details of fee submitted	PKR 30,000/-: dated 01/11/2021
	The proposed proprietary name / brand name	Citi-Taxime Injection IV/IM
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Sterile Powder of Cefotaxime sodium USP eq. to Cefotaxime 500mg
	Pharmaceutical form of applied drug	Intra-venous / Intra-muscular Injection
	Pharmacotherapeutic Group of (API)	Broad-spectrum cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Claforan Injection 500mg by M/s Sanofi aventis Ltd. USA, USFDA Approved.
	For generic drugs (me-too status)	Sporonil Injection 500mg by Global Pharmaceuticals, Reg. No. 025926
	GMP status of the Finished product manufacturer	New license granted on 21/09/2021 Cephalosporin section approved.
	Name and address of API manufacturer.	M/s Sinopharm Weiqida Pharmaceutical Co.,Ltd China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefotaxime Sodium eq. to Cefotaxime is present in USP. The firm as submitted detail of nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TRI-004, TRI-005, TRI-006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sporonil Injection 500mg by Global Pharmaceuticals Pakistan performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Sinopharm Weiqida Pharmaceutical Co.,Ltd China		
API Lot No.	FB-2021/03/13		
Description of Pack (Container closure system)	One clear glass vial 15ml with LDPE ampoule of WFI or 1% Lidocaine along with leaflet in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-004	TRI-005	TRI-006
Batch Size (Scientifically rational batch size)	1000 Vials	1000 Vials	1000 Vials
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	26-09-2021	26-09-2021	26-09-2021

No. of Batches	03	
Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SX20180255 issued by CFDA valid till 23/12/2023.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter No. 8084/2021 DRAP dated: 04-08-2021 B/L No. 229111000081 dated: 23-06-2021
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Sr. no	Short comings	Response
o.	3.2.S.7 Stability studies are not as per zone IVA	Stability data has been submitted as per Zone IV Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
p.	Some parts of applications states Intra muscular (IM) injection whereas at some it states Intra venous (IV).	Its typographic error and rectified, correct data have been submitted.
q.	3.2.P.2 why not the pharmaceutical equivalence of the applied drug being compared with the innovator's product	Pharmaceutical Equivalence have been established against the brand leader that is Sporonil Injection by Global Pharmaceutical, Islamabad performing quality tests (Identification, Assay, Constituted Solution, Uniformity of dosage form).

r.	3.2.P.5 Justification is required for the use of 5% overage in master formulation.	Its typographic error, we didn't avail the overage
s.	Documents for the procurement of API with approval from DRAP (in case of import).	• M/S Sinipharm Weiqida Pharmaceutical Co. Ltd. China API Lot Number: FB-2021/03/13 Letter No. 8084/2021 DRAP Dated: 04-08-2021. B/L No. 229111000081 Dated: 23-06-2021 API import documents has been submitted with ADC clearance
t.	Compliance Record of HPLC software 21CFR &audit trail reports on product testing.	Record of HPLC software 21 CFR and audit trail reports has been submitted in detailed.
u.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical Equivalence studies against the Innovator product.**

Case no. 08 Registration applications for local manufacturing of (Human) drugs (Form 5F)

a. New cases

426.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi**
	Name, address of Manufacturing site.	M/s Indus Pharma (Pvt) Ltd. Plot No. 26-27, 64-67, Sector-27, Korangi Industrial Area, Karachi, Pakistan
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24853 dated 08-09-2021
	Details of fee submitted	PKR 75,000/-: dated 09-07-2021

	The proposed proprietary name / brand name	Fuvelox Infusion 500mg/100ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial of 100ml contains: Levofloxacin hemihydrate eq to Levofloxacin …… 500mg
	Pharmaceutical form of applied drug	Infusion
	Pharmacotherapeutic Group of (API)	Fluroquinolone antibiotic
	Reference to Finished product specifications	Firm has applied USP, however not available in USP pharmacopoeia.
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	"LEVAQUIN" USFDA Approved
	For generic drugs (me-too status)	Starlev Infusion 500mg by M/s Indus Pharma (Registration No. 044460)
	GMP status of the Finished product manufacturer	GMP certificate issued on 18-12-2020
	Name and address of API manufacturer.	M/s Shangyu Jingxin Pharmaceutical Co., Ltd. **Address:** No. 31 Weisan Road, Hangzhou Bay Shangyu Economic and Technological Development Area.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DK211508311, DK211508312 & DK211508313)
	Module-III (Drug Product):	The firm has submitted detail of manufacturer, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence of Fuvelox Infusion has been compared with the

		comparator product Leflox Infusion **500mg/100ml by M/s Getz Pharma** by performing quality tests.		
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Shangyu Jingxin Pharmaceutical Co., Ltd. **Address:** No. 31 Weisan Road, Hangzhou Bay Shangyu Economic and Technological Development Area.		
API Lot No.		DK211807031-II		
Description of Pack (Container closure system)		A round clear glass vial having 100ml filling capacity.		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		SL-384	SL-385	SL-386
Batch Size		3000 Vials	3000 Vials	3000 Vials
Manufacturing Date		11-2019	11-2019	11-2019
Date of Initiation		26-11-2019	26-11-2019	26-11-2019
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to their product Canazin Tablets 300mg which was approved in 289th Meeting of Registration Board. 1) Yes HPLC software is 21 CFR Part 11 compliant where all user levels are properly defined 2) Audit trail on the testing reports is available.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Certificate for M/s Shangyu Jingxin Pharmaceutical Co., Ltd issued by National Medical Products Administration China & valid up to 29-11-2024 is submitted		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted (invoice# JXHQ1807203) dated 20-07-2018 specifying import LEVOFLOXACIN cleared by DRAP Karachi office dated 15-08-2018.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets		

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Observations / Deficiency / Shortcomings	**Firm Response**
3.2.S.4.4 Compare the COA's of API from finish product manufacturer with COA of API supplier and justification is required for non-performance of test, if any.	Firm has provided comparison of COAs Residual solvents and microbial limit tests were not performed by M/s Indus Pharma as this does not exist in USP monograph.
3.2.P.5 Justification is required for the use of overage in master formulation.	**Batch Calculation for Levofloxacin:** In **Levofloxacin infusion**, there is no overage used instead potency adjustment is carried out to adjust the water content of API. As per USP, **Levofloxacin hemihydrate** contains **2.0 to 3.0%** water. This water content is adjusted using below mentioned calculation: Standard quantity of API for batch = ---------- Potency (as is basis) = ---------- Required quantity for batch = (Standard quantity of API x 100)/ Potency (as is basis) Required quantity for batch = ----------
Valid GMP certificate of API manufacturer is required.	Copy of GMP Certificate for M/s Shangyu Jingxin Pharmaceutical Co., Ltd issued by National Medical Products Administration China & valid up to 29-11-2024 is submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500 for revision of specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration letter will be issued after review of pharmacopoeia of reference regulatory authorities for availability of the product monograph.**

427.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi**
	Name, address of Manufacturing site.	M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25931 dated 17-09-2021
	Details of fee submitted	PKR 30,000/-: dated 10-09-2021
	The proposed proprietary name / brand name	**Solidow Tablets 5mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Solifenacin Succinate ……5mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-muscarinic
	Reference to Finished product specifications	As per innovator's specifications
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved **"VESICARE TABLET"** by Astellas Pharma US, Inc.
	For generic drugs (me-too status)	Solifen Tablets 5mg by Getz Pharma (Registration No. 061202)
	GMP status of the Finished product manufacturer	GMP certificate issued 11-6-2020
	Name and address of API manufacturer.	M/s Zhejiang Guobang Pharmaceuticals Co., Ltd. **Address:** No. 6, Weiwu Road, Hangzhou Gulf Shangyu Economic and Technological Development Zone, Zhejiang, PR China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (170501, 170502 & 170503)
	Module-III (Drug Product):	The firm has submitted detail of manufacturer, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Innovator product that is VESICARE TABLETS 5mg by Astellas Pharma Istanbul by performing quality tests (Identification, Disintegration, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is VESICARE TABLETS 5mg by Astellas Pharma Istanbul, in Acid media (pH 1.2), Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Zhejiang Guobang Pharmaceuticals Co., Ltd. **Address:** No. 6, Weiwu Road, Hangzhou Gulf Shangyu Economic and Technological Development Zone, Zhejiang, PR China.		
API Lot No.	2011000080 (Manufacturer's batch no. 200501)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2x5's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.	NPD-T-1488-S	NPD-T-1503-S	NPD-T-1504-S
Batch Size	1500 tablets	5000 tablets	5000 tablets
Manufacturing Date	21-05-2021	28-05-2021	28-05-2021
Date of Initiation	04-06-2021	04-06-2021	04-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to their product Empator Tablets 10mg which was approved in 291st Meeting of Registration Board held on 2nd - 4th September 2019. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML Certificate for Zhejiang Guobang Pharmaceuticals Co., Ltd. issued by Zhejiang Food and Drug Administration & valid up to 08-12-2024 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (invoice# GBPH2020-2023) Dated: 02-11-2020 from Zhejiang Guobang Pharmaceuticals Co., Ltd. cleared by DRAP Karachi office dated 03-11-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Shortcomings communicated	Response by firm
3.2.P.8 Stability: You have provided stability data of 3 months only.	Firm has submitted stability Data till 6 months on 22-12-2021.
Adjust the potency of Solifenacin succinate in BMR according to the assay report.	The potency is adjusted as per 100% since the results of assay are higher than 100 i.e., 100.4% due to analytical variation. Batch proceeded accordingly because adjusting the potency for higher than 100% will result in decreasing the amount of API per tablet. The statement is supported by satisfactory QC results of stability batches.

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

428.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Marker Limited,7-Jail Road, Quetta**
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited,7-Jail Road, Quetta
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 34000 dated 29/09/2021
	Details of fee submitted	PKR 30,000/-: dated 10/01/2021
	The proposed proprietary name / brand name	Angiolo-D Tablet 50mg+12.5mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Losartan Potassium, ……50mg Hydrochlorothiazide…..12.5mg
	Pharmaceutical form of applied drug	Dark yellow color, flat round shaped film coated tablets.
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor antagonist & Diuretics (Anti-hypertensive)
	Reference to Finished product specifications	USP
	Proposed Pack size	As Per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	HYZAAR® 50mg+12.5mg Tablets by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	Co-Eziday Tablet 50mg+12.5mg by Werrick Pharmaceutical Pakistan (Pvt.) Ltd., Reg. No. 027042
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Losartan Potassium:** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China.

		Hydrochlorothiazide: M/s Changzhou Pharmaceutical China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Losartan Potassium is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: T-01, T-02 & T-03 **Accelerated Time:** T-01, T-02 & T-03
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Hyzaar Tablets** by **Merck Sharp & Dohme Limited** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.

	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		**Losartan Potassium:** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China. **Hydrochlorothiazide:** M/s Changzhou Pharmaceutical China		
API Lot No.		**Losartan Potassium:** HH20201310 **Hydrochlorothiazide:** CY119019		
Description of Pack (Container closure system)		Blister in Alu-Alu Foil		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		T-01	T-02	T-03
Batch Size		3000 Tablets	3000 Tablets	3000 Tablets
Manufacturing Date		02-2021	02-2021	02-2021
Date of Initiation		02-2021	02-2021	02-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Acidex 60mg Capsule Dexlansoprazole was approved in 312th Registration Board meeting. 1) Compliance Record of HPLC software 21CFR & audit trail reports on product testing were present		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023. Copy of GMP certificate No. JS20180848 issued by CFDA valid till 09/07/2023.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Losartan Potassium:** ADC Invoice No: HH20201310, 29-June-2020 is submitted wherein the permission to import APIs (Losartan Potassium) for the purpose of test/analysis and stability studies is granted. **Hydrochlorothiazide:** ADC Invoice No: CY119019, 04-Feb-2019 is submitted wherein the permission to import APIs (Hydrochlorothiazide) for the purpose of test/analysis and stability studies is granted.		

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator IV:

Observations / Deficiency / Shortcomings	**Firm Response**
3.2.S.4.4 Compare the COA's of API from finish product manufacturer with COA of API supplier and justification is required for non-performance of test, if any. Furthermore, COA reflects that pharmacopeial method was not adopted in testing drug substance, please justify.	Firm has provided comparison of COAs and justified that the manufacturer has performed all the tests mentioned in Pharmacopeia.
3.2.P.5.3 Control of Drug Substance: Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted	Firm has provided Analytical Method Verification studies including specificity, accuracy and repeatability (method precision).
3.2.P.4.5 Excipients of human & animal origin shall be addressed for the use of "**Magnesium Stearate"** in the applied formulation.	Firm has submitted that there is no human or animal source used for Magnesium Stearate.
Valid GMP certificate of API manufacturer is required.	**Losartan Potassium:** Firm has provided GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023. **Hydrochlorothiazide:** Firm has provided GMP certificate No. JS20180848 issued by CFDA valid till 09/07/2023.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

429.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Marker Limited,7-Jail Road, Quetta**
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited,7-Jail Road, Quetta
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 34230 dated 29/09/2021
	Details of fee submitted	PKR 30,000/-: dated 10/01/2021
	The proposed proprietary name / brand name	Angiolo-D Tablet 100mg+12.5mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Losartan Potassium, ……100mg Hydrochlorothiazide…..12.5mg
	Pharmaceutical form of applied drug	White to off white, biconvex, oblong film coated, plain on one side engraved with 1.25 on other side.
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor antagonist & Diuretics (Anti-hypertensive)
	Reference to Finished product specifications	USP
	Proposed Pack size	As Per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	HYZAAR® 100mg+12.5mg Tablets by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	Acozar-H Tablet 100mg+12.5mg by AGP Ltd., Reg. No. 085660
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Losartan Potassium:** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China. **Hydrochlorothiazide:** M/s Changzhou Pharmaceutical China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Losartan Potassium is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: T-01, T-02 & T-03 **Accelerated Time:** T-01, T-02 & T-03
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Hyzaar Tablets** by **Merck Sharp & Dohme Limited** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API		**Losartan Potassium:** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China. **Hydrochlorothiazide:** M/s Changzhou Pharmaceutical China

API Lot No.	**Losartan Potassium:** HH20201310 **Hydrochlorothiazide:** CY119019		
Description of Pack (Container closure system)	Blister in Alu-Alu Foil		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	3000 Tablets	3000 Tablets	3000 Tablets
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	02-2021	02-2021	02-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Acidex 60mg Capsule Dexlansoprazole was approved in 312th Registration Board meeting. 1) Compliance Record of HPLC software 21CFR & audit trail reports on product testing were present
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023. Copy of GMP certificate No. JS20180848 issued by CFDA valid till 09/07/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Losartan Potassium:** ADC Invoice No: HH20201310, 29-June-2020 is submitted wherein the permission to import APIs (Losartan Potassium) for the purpose of test/analysis and stability studies is granted. **Hydrochlorothiazide:** ADC Invoice No: CY119019, 04-Feb-2019 is submitted wherein the permission to import APIs (Hydrochlorothiazide) for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator VI:

Observations / Deficiency / Shortcomings	**Firm Response**
3.2.S.4.4 Compare the COA's of API from finish product manufacturer with COA of API supplier and justification is required for non-performance of test, if any. Furthermore, COA reflects that pharmacopeial method was not adopted in testing drug substance, please justify.	Firm has provided comparison of COAs and justified that the manufacturer has performed all the tests mentioned in Pharmacopeia.
3.2.P.5.3 Control of Drug Substance: Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted	Firm has provided Analytical Method Verification studies including specificity, accuracy and repeatability (method precision).
3.2.P.4.5 Excipients of human & animal origin shall be addressed for the use of "**Magnesium Stearate"** in the applied formulation.	Firm has confirmed that there is no human or animal source used for Magnesium Stearate.
Valid GMP certificate of API manufacturer is required.	**Losartan Potassium:** Firm has provided GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023. **Hydrochlorothiazide:** Firm has provided GMP certificate No. JS20180848 issued by CFDA valid till 09/07/2023.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

430.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Marker Limited,7-Jail Road, Quetta**
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited,7-Jail Road, Quetta
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 34001 dated 29/09/2021
	Details of fee submitted	PKR 30,000/-: dated 10/01/2021
	The proposed proprietary name / brand name	Angiolo-D Tablet 100mg+25mg

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Losartan Potassium……100mg Hydrochlorothiazide…..25mg
	Pharmaceutical form of applied drug	Light yellow color, oblong biconvex shaped film coated tablets.
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor antagonist & Diuretics (Anti-hypertensive)
	Reference to Finished product specifications	USP
	Proposed Pack size	As Per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	HYZAAR® 100mg+25mg Tablets by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	Co-Eziday Tablet 100mg+25mg by Werrick Pharmaceutical Pakistan (Pvt.) Ltd., Reg. No. 056104
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Losartan Potassium:** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China. **Hydrochlorothiazide:** M/s Changzhou Pharmaceutical China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Losartan Potassium is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: T-01, T-02 & T-03 **Accelerated Time:** T-01, T-02 & T-03
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Hyzaar Tablets** by **Merck Sharp & Dohme Limited** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Losartan Potassium:** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China. **Hydrochlorothiazide:** M/s Changzhou Pharmaceutical China		
API Lot No.	**Losartan Potassium:** HH20201310 **Hydrochlorothiazide:** CY119019		
Description of Pack (Container closure system)	Blister in Alu-Alu Foil		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03

Batch Size	3000 Tablets	3000 Tablets	3000 Tablets
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	07-2021	07-2021	07-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Acidex 60mg Capsule Dexlansoprazole was approved in 312th Registration Board meeting. Compliance Record of HPLC software 21CFR & audit trail reports on product testing were present
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023. Copy of GMP certificate No. JS20180848 issued by CFDA valid till 09/07/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Losartan Potassium:** ADC Invoice No: HH20201310, 29-June-2020 is submitted wherein the permission to import APIs (Losartan Potassium) for the purpose of test/analysis and stability studies is granted. **Hydrochlorothiazide:** ADC Invoice No: CY119019, 04-Feb-2019 is submitted wherein the permission to import APIs (Hydrochlorothiazide) for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:	
Observations / Deficiency / Shortcomings	**Firm Response**
3.2.S.4.4 Compare the COA's of API from finish product manufacturer with COA of API supplier and justification is required for non-performance of test, if any. Furthermore, COA reflects that pharmacopeial method was not adopted in testing drug substance, please justify.	Firm has provided comparison of COAs and justified that the manufacturer has performed all the tests mentioned in Pharmacopeia.

3.2.P.5.3 Control of Drug Substance: Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted	Firm has provided Analytical Method Verification studies including specificity, accuracy and repeatability (method precision).
3.2.P.4.5 Excipients of human & animal origin shall be addressed for the use of "**Magnesium Stearate"** in the applied formulation.	Firm has confirmed that there is no human or animal source used for Magnesium Stearate.
Valid GMP certificate of API manufacturer is required.	**Losartan Potassium:** Firm has provided GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023. **Hydrochlorothiazide:** Firm has provided GMP certificate No. JS20180848 issued by CFDA valid till 09/07/2023.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

431.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Marker Limited, 7-Jail Road, Quetta**
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26935 dated 29/09/2021
	Details of fee submitted	PKR 30,000/-: dated 13/09/2021
	The proposed proprietary name / brand name	Angiolo Tablet 50mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Losartan Potassium……50mg
	Pharmaceutical form of applied drug	Peach, round shaped film coated Tablets
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor antagonist (Anti-hypertensive)
	Reference to Finished product specifications	USP
	Proposed Pack size	2×10's (20's)
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	AURO-LOSARTAN Tablet 50mg by M/s Auro Pharma Inc. HEALTH CANADA Approved.
	For generic drugs (me-too status)	Bespar Tablet 50mg by Nabiqasim Industries (Pvt.) Ltd. , Reg. No. 027206
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Losartan Potassium is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C5082-14-136, C5082-14-137, C5082-14-138 **Accelerated Time:** C5455-13-135, C5455-13-136, C5455-13-137
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities,

		specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Cozaar Tablets** by **Merck Sharp & Dohme Limited** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Cozaar Tablets** by **Merck Sharp & Dohme Limited** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Zhejiang Huahai Pharmaceutical Co., Ltd., Chuannan, Duqiao, Linhai, Zhejiang 317016, China		
API Lot No.	C5455-20-045		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	10000 Tablets	10000 Tablets	10000 Tablets
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	10-2020	10-2020	10-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Acidex 60mg Capsule Dexlansoprazole was approved in 312th Registration Board meeting. Compliance Record of HPLC software 21CFR & audit trail reports on product testing were present

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC Invoice No: HH20201310, 11-June-2020 is submitted wherein the permission to import APIs (Losartan Potassium) for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Observations / Deficiency / Shortcomings	**Firm Response**
3.2.S.4.4 Compare the COA's of API from finish product manufacturer with COA of API supplier and justification is required for non-performance of test, if any. Furthermore, COA reflects that pharmacopeial method was not adopted in testing drug substance, please justify.	Firm has provided comparison of COAs and justified that the manufacturer has performed all the tests mentioned in Pharmacopeia.
3.2.P.5.3 Control of Drug Substance: Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted	Firm has provided Analytical Method Verification studies including specificity, accuracy and repeatability (method precision).
Valid GMP certificate of API manufacturer is required.	Firm has provided GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

432.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Marker Ltd. ,7-Jail Road, Quetta**
	Name, address of Manufacturing site.	M/s Martin Dow Marker Ltd. ,7-Jail Road, Quetta
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26934 dated 29/09/2021
	Details of fee submitted	PKR 30,000/-: dated 13/09/2021
	The proposed proprietary name / brand name	Angiolo Tablet 25mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Losartan Potassium……25mg
	Pharmaceutical form of applied drug	Round, white to off-white tablets.
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor antagonist (Anti-hypertensive)
	Reference to Finished product specifications	USP
	Proposed Pack size	2×10's (20's)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cozaar 25mg tablet by M/s Organon Canada Inc, HEALTH CANADA Approved.
	For generic drugs (me-too status)	Sozaar 25mg Tablet by Alliance Pharmaceuticals (Pvt.) Ltd. , Reg. No. 044580
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies

		of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Losartan Potassium is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C5082-14-136, C5082-14-137, C5082-14-138 **Accelerated Time:** C5455-13-135, C5455-13-136, C5455-13-137
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Cozaar Tablets** by **Merck Sharp & Dohme Limited** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Cozaar Tablets** by **Merck Sharp & Dohme Limited** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API		M/s Zhejiang Huahai Pharmaceutical Co., Ltd., Chuannan, Duqiao, Linhai, Zhejiang 317016, China

API Lot No.	C5455-20-045		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	10000 Tablets	10000 Tablets	10000 Tablets
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	10-2020	10-2020	10-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Acidex 60mg Capsule Dexlansoprazole was approved in 312th Registration Board meeting. Compliance Record of HPLC software 21CFR & audit trail reports on product testing were present
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC Invoice No: HH20201310, 11-June-2020 is submitted wherein the permission to import API (Losartan Potassium) for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:	
Observations / Deficiency / Shortcomings	**Firm Response**

3.2.S.4.4 Compare the COA's of API from finish product manufacturer with COA of API supplier and justification is required for non-performance of test, if any. Furthermore, COA reflects that pharmacopeial method was not adopted in testing drug substance, please justify.	Firm has provided comparison of COAs and justified that the manufacturer has performed all the tests mentioned in Pharmacopeia.
3.2.P.5.3 Control of Drug Substance: Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted	Firm has provided Analytical Method Verification studies including specificity, accuracy and repeatability (method precision).
Valid GMP certificate of API manufacturer is required.	Firm has provided GMP certificate No. 201907047 issued by CFDA valid till 15/01/2023.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

433.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s ATCO Laboratories Limited Address: B-18,S.I.T.E., Karachi - 75700,Karachi.Sindh**
	Name, address of Manufacturing site.	ATCO Laboratories Limited Address: B-18,S.I.T.E., Karachi - 75700,Karachi.Sindh
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25929 Dated 17/ 09/ 2021
	Details of fee submitted	PKR 30,000/-: dated 28/07/2021
	The proposed proprietary name / brand name	Tapentadol Tablets 75mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tapentadol Hydrochloride eq to Tapentadol ……..75mg
	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	Opioid analgesic of the benzenoid class.
	Reference to Finished product specifications	As per Innovator's specifications
	Proposed Pack size	7s, 10s, 14s, 20s, 28s, 30s, 60s & 100s.
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	NUCYNTA **Manufactured by:** Janssen Ortho, LLC Gurabo, PR 00778 **Manufactured for:** PriCara® Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc. Raritan, NJ 08869
	For generic drugs (me-too status)	Tapento 75mg tablet SAMI Pharmaceuticals (Pvt) Ltd.
	GMP status of the Finished product manufacturer	Renewal for DML dated 27-03-2021submitted along with previous copy DML.
	Name and address of API manufacturer.	M/s Ami Lifesciences Private Limited, 2 Floor, Prestige Plaza, 40, Urmi Society, Nr. Urmi Cross Road, BPC Road, Akota, Vadodara-390 020.Gujarat, INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Stability studies	Stability study conditions: Real time:30°C±2°C/65% ± 5%RH for 12 months Accelerated:40°C±2°C/75%±5%RH for 6 months Batches: (TPT/50121119, TPT/50131119, TPT/5011119)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and

		justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **NUCYNTA 75mg Tablet** by M/s **Janssen Ortho, LLC Gurabo, PR 00778** performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is **NUCYNTA 75mg Tablet** by Janssen Ortho, LLC Gurabo, PR 00778 in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA

Manufacturer of API	Ami Lifesciences Private Limited INDIA		
API Lot No.	TPR/RD/60250618		
Description of Pack (Container closure system)	The material packed in double polyethylene bags inner white transparent and outer black		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 12 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0,3,6, 9,12 (Months)		
Batch No.	50111119	50121119	50131219
Batch Size	310kg	313kg	313kg
Manufacturing Date	11/2019	12/2019	12/2019
Date of Initiation	30/12/2019	30/12/2019	30/12/2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Rofl 500mg tablet Approved in DRB 277 held on 27-29 December 2017.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP issued by (Drug Control Administration, Government of Gujarat State India Validity: 25/04/2019 till 24/04/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Observations / Deficiency / Shortcomings	**Firm Response**
• 3.2.S.4 Control of Drug Substance: - You have submitted finished product specifications, COA, analytical method etc. instead of providing drug substance information.	We already have submitted Raw Material specification and testing method of Tapentadol Hydrochloride with Certificate of Analysis (CoA) by both, drug substance manufacturer and drug product manufacturer, now as per your requirement we are hereby re submitting the drug substance information
• 3.2.S.7 Stability study data is not as per zone IV A. •	Stability data of Tapentadol Hydrochloride drug substance by Ami Life Sciences, India as per zone IV-A has been provided already we are hereby resubmitting the stability study data as zone IV-A.
• 3.2.S.4 Control of Drug Substance:- A discussion and justification should be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification •	The Drug Substance/API "Tapentadol Hydrochloride" has been analyzed by Drug Product manufacturer according to the proposed specification and testing method submitted in Section 3.2.S.4.
• 3.2.P.5 Control of Drug Product, 3.2.P.8 Stability: - The submitted dissolution condition is different from the innovators'. **Dissolution conditions of innovator as per Biopharmaceutics Review:** Apparatus: Type I (Basket apparatus) Spindle rotation: 75 RPM Medium: 0.1 M HCl Medium volume: 900ml Time: 45 min Acceptance criteria: NLT 80% (Q) of the labelled amount of Tapentadol (as HCl) dissolved in 45 min	According to FDA Dissolution methods database, updated on 07/02/2020 for Tapentadol Hydrochloride Immediate release Tablets, Refer to FDA's Dissolution Guidance, 2018. Also, Tapentadol Hydrochloride belongs to Class I of Biopharmaceutics Classification System, so the Standard Dissolution Testing Condition has been employed for dissolution testing of drug product Tapentadol Hydrochloride and validated through Comparative dissolution profile studies as per "GUIDANCE DOCUMENT FOR SUBMISSION OF APPLICATION ON FORM 5-F (CTD) FOR REGISTRATION OF PHARMACEUTICAL DRUG PRODUCTS FOR HUMAN USE" Drug Regulatory Authority of Pakistan. Dissolution Method

	from FDA website with FDA's Dissolution Guidance "Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances – Guidance for Industry" is being attached for your reference. (Section 3.2.P.5)

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Manufacturer will revise dissolution specifications as per USFDA along with submission of fee 7500/- for revision of specifications.**
- **Manufacturer shall perform dissolution testing as per USFDA on commercial batches.**

434.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Hiranis Pharmaceuticals (Pvt) Ltd**
	Name, address of Manufacturing site.	M/s Hiranis Pharmaceuticals (Pvt) Ltd Plot E-145-149, North western industrial zone, Port Qasim, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25005 dated 09/09/2021
	Details of fee submitted	PKR 75,000/-: dated 16/07/2021
	The proposed proprietary name / brand name	Tapento Tablet 50mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tapentadol HCl equivalent to Tapentadol ……50mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Opioid Analgesics
	Reference to Finished product specifications	Manufacturer's Spec.
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	US-FDA Approved.
	For generic drugs (me-too status)	NA

	GMP status of the Finished product manufacturer	DML by way of formulation No. 000785 dated 03-02-2019
	Name and address of API manufacturer.	**Tapentadol HCL** M/s. AMI Lifesciences Private Limited. Address: Block no. 82/B, ECP Road, AT & Post: Karakhadi-391450. Taluka: Padra, District Vadodara Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls,), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Tapentadol HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Tapentadol HCl:** TPT/50040513, TPT/50050513, TPT/50060513.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Nucynta 50mg Tablet** by **Endo Ventures Tablet** by performing quality tests (Identification, Assay, Dissolution, and Uniformity of dosage form).

		CDP has been performed against the same brand that is **Nucynta 50mg Tablet** by Endo **Ventures Tablet** in Acid media (0.1 N HCL) & Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). F_2value calculation is not required as reference and test products released more than 85% within 15 minutes.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Tapentadol HCL** M/s. AMI Lifesciences Private Limited. Address: Block no. 82/B, ECP Road, AT & Post: Karakhadi-391450. Taluka: Padra, District Vadodara Gujarat, India.		
API Lot No.	**Tapentadol HCl:** TPT/50141018		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**TF-021219**	**TF-031219**	**TF-041219**
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	13-01-2020	13-01-2020	13-01-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Etoxib 90mg Tablet Etoxib 120mg Tablet Approved in 294th minutes of meeting of DRB
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Tapentadol HCl:** Copy of GMP certificate No. 19041306 issued by Food and Drugs Control Administration Gujarat valid till 24/04/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Attested invoice from ADC attached for Tapentadol HCl Invoice No. EXP/A/064/2018-19
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of

		drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator VI:

Observations / Deficiency / Shortcomings	**Firm Response**
• - The submitted dissolution condition is different from the innovators'. **Dissolution conditions of innovator as per Biopharmaceutics Review:** Apparatus: Type I (Basket apparatus) Spindle rotation: 75 RPM Medium: 0.1 M HCl Medium volume: 900ml Time: 45 min Acceptance criteria: NLT 80% (Q) of the labelled amount of Tapentadol (as HCl) dissolved in 45 min	• Dissolution medium proposed by innovator is 0.1M HCI, while our is 0.1N HCI, both are same and there is no difference. • Dissolution medium volume proposed by innovator is 900ml, while our is also 900ml, both are same & there is no difference. • Dissolution time proposed by innovator is 45 minutes, while our is 15 minutes which is shorter than innovator, it is acceptable in accordance to USP Chapter <711> Dissolution under procedure Apparatus 1 and Apparatus 2; IMMEDIATE-RELEASE DOSAGE FORMS, refer to: Time: Where a single time specification is given, the test may be concluded in a shorter period if the requirement for the minimum amount dissolved is met. Therefore, proposed dissolution time in our specification is justified & acceptable. • Acceptance criteria is NLT 80% (Q) in both scenario and acceptable % drug release is same, no difference. • Apparatus type and rpm is different in both cases, please note that while reviewing "Clinical pharmacology & Biopharmaceutics review" by "Center of drug evaluation and research", Application number 22-304 (submission date 16-09-2008); it was found that manufacturer performed dissolution test at various condition, including our condition 50 rpm with paddle.
• 3.2.S.4 Control of Drug Substance: - You have submitted finished product specifications, COA, analytical method etc. instead of providing drug substance information.	We already have submitted Raw Material specification and testing method of Tapentadol Hydrochloride with Certificate of Analysis (CoA) by both, drug substance manufacturer and drug product manufacturer, now as per your requirement we are hereby re submitting the drug substance information

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

• **Manufacturer will revise dissolution specifications as per USFDA along with submission of fee 7500/- for revision of specifications.** • **Manufacturer shall perform dissolution testing as per USFDA for commercial batches.**		
435.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.**
	Name, address of Manufacturing site.	M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.
	Status of the applicant	☒ Manufacturer √ ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 24058, Dated 01.09.2021
	Details of fee submitted	Rs.75,000/- dated 29.06.2021 Deposit Slip # 3849293923
	The proposed proprietary name / brand name	Rupasaf 1mg/mL Oral Solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each mL contains Rupatadine Fumarate equivalent to Rupatadine…… 1.0 mg
	Pharmaceutical form of applied drug	Oral Solution
	Pharmacotherapeutic Group of (API)	Antihistamine
	Reference to Finished product specifications	Manufacturer's Specifications
	Proposed Pack size	60mL & 120mL
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved **MHRA**
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	GMP certificate issued on 03.01.2022 Good Compliance
	Name and address of API manufacturer.	**Name:** M/s Vasudha Pharma Chem Limited, **Address:** 78/A, Vengalrao Nagar, Hyderabad-500 038, Telangana State, INDIA **Telephone:** +91 40 44763666 / 23711717 Fax: +91 40 23811576 **E-mail:** vasudha@vasudhapharma.com
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications,

		analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	**Rupatadine Fumarate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 60 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence Studies s against the reference product of "Rupall 1mg/mL Oral Solution".
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA	
Manufacturer of API	**Name:** M/s Vasudha Pharma Chem Limited, **Address:** 78/A, Vengalrao Nagar, Hyderabad- 500 038, Telangana State, INDIA **Telephone:** +91 40 44763666 / 23711717 Fax: +91 40 23811576 **E-mail:** vasudha@vasudhapharma.com
API Lot No.	BRPFA/1911009
Description of Pack (Container closure system)	**API Container:** Double polythene bags (as primary packaging material) and kept in HDPE container. **Product Container:** Amber glass bottles sealed with P.P caps and packed in card board carton
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH

		Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		T-001	T-002	T-003
Batch Size		2.40 L	2.40 L	2.40 L
Manufacturing Date		07.2020	08.2020	08.2020
Date of Initiation		18.08.2020	31.08.2020	31.08.2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to their last inspection report for Elixa (Apixaban) 2.5mg & 5mg conducted on 08.10.2019, approved in 293rd meeting of Registration Board. Following are details of few points; • The HPLC software is 21CFR Compliant. • Audit trail reports were available and physically checked by the inspection team. • Firm has adequate monitoring and controls for stability chambers. • Software is installed for continuous monitoring of chambers.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate (Certificate# 46/VP/AP/2007/B/R) issued by Govt. of Andhrapradesh, INDIA, valid upto 30.12.2022		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Lahore has been submitted. **Rupatadine Fumarate:** **Batch No.** / **Quantity Imported** / **Date of approval by DRAP** BRPFA/1911009 / 100gm / 14.10.2019		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail reports on product testing.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)		

SUBMITTED DATA REGARDING THE DEFICIENCIES		
7.	Valid GMP Certificate of finish product and API manufacturer.	Copy of GMP certificate (Certificate# 46/VP/AP/2007/B/R) issued by Govt. of Andhrapradesh, INDIA, valid upto 30.12.2022
8.	3.2.S.4 you are using in house specifications for some tests whereas the drug substance is present in British Pharmacopoeia. Justification is required for not following the pharmacopoeia and compares the limits and both specifications.	Specification for testing of Rupatadine Fumarate manufactured at Vasudh Pharma is adopted from Ph. Eur monograph. Assay by HPLC method of In-House developed is adopted to estimate the assay of Rupatadine. Analytical method validation report for the assay by HPLC method is performed and verification report is provided. An In-house GC method was developed for estimation of residual solvents in Rupatadine Fumarate. Analytical method validation for the residual solvents by GC method was performed and validation report is provided.
9.	3.2.P.2 Invoice are required for the procurement of innovator's product.	Firm has submitted Unit pack innovator product Rupall Oral Solution
Remarks of Evaluator:		
Decision: Approved with Innovator's specifications. • **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration letter will be issued upon submission of revised drug substance analytical method, analytical method verification studies & drug substance analysis report as per European Pharmacopoeia Monograph for "Rupatadine Fumarate".**		

436.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.**
	Name, address of Manufacturing site.	M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.
	Status of the applicant	☒ Manufacturer √ ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 24059, Dated 01.09.2021
	Details of fee submitted	Rs.75,000/- dated 10.06.2021 Deposit Slip # 10200204449

	The proposed proprietary name / brand name	Rupasaf 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains Rupatadine Fumarate equivalent to Rupatadine…….10 mg
	Pharmaceutical form of applied drug	Oral Tablet
	Pharmacotherapeutic Group of (API)	Antihistamine
	Reference to Finished product specifications	Manufacturer's Specifications
	Proposed Pack size	2x7's, 2x14's & 3x10's
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved by **UK MHRA**
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	GMP certificate issued on 03.01.2022 Good Compliance
	Name and address of API manufacturer.	**Name:** Vasudha Pharma Chem Limited, **Address:** 78/A, Vengalrao Nagar, Hyderabad-500 038, Telangana State, INDIA **Telephone:** +91 40 44763666 / 23711717 Fax: +91 40 23811576 **E-mail:** vasudha@vasudhapharma.com
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	**Rupatadine Fumarate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6

		months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 60 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence Studies s against the reference product of "Rupall 10mg Tablet".
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA			
Manufacturer of API	**Name:** M/s Vasudha Pharma Chem Limited, **Address:** 78/A, Vengalrao Nagar, Hyderabad- 500 038, Telangana State, INDIA **Telephone:** +91 40 44763666 / 23711717 Fax: +91 40 23811576 **E-mail:** vasudha@vasudhapharma.com		
API Lot No.	BRPFA/1911009		
Description of Pack (Container closure system)	**API Container:** Double polythene bags (as primary packaging material) and kept in HDPE container. **Product Container:** Alu-PVC blister packed in unit carton (2x7's, 2x14's & 3x10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	07.2020	07.2020	07.2020
Date of Initiation	17.07.2020	04.08.2020	04.08.2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to their last inspection report for Elixa (Apixaban) 2.5mg & 5mg conducted on 08.10.2019, approved in 293rd meeting of Registration Board. Following are details of few points;

<table>
<tr><td></td><td></td><td>• The HPLC software is 21CFR Compliant.
• Audit trail reports were available and physically checked by the inspection team.
• Firm has adequate monitoring and controls for stability chambers.
• Software is installed for continuous monitoring of chambers.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Copy of GMP certificate (Certificate# 46/VP/AP/2007/B/R) issued by Govt. of Andhrapradesh, INDIA, valid upto 30.12.2022</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore has been submitted.
Rupatadine Fumarate:<table><tr><th>Batch No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>BRPFA/1911009</td><td>100gm</td><td>14.10.2019</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms,
Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Firm has submitted audit trail reports on product testing.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
<tr><td colspan="3">SUBMITTED DATA REGARDING THE DEFICIENCIES</td></tr>
<tr><td>7.</td><td>Valid GMP Certificate of finish product and API manufacturer.</td><td>Copy of GMP certificate (Certificate# 46/VP/AP/2007/B/R) issued by Govt. of Andhrapradesh, INDIA, valid upto 30.12.2022</td></tr>
<tr><td>8.</td><td>3.2.S.4 you are using in house specifications for some tests whereas the drug substance is present in British Pharmacopoeia. Justification is required for not following the pharmacopoeia and compares the limits and both specifications.</td><td>Specification for testing of Rupatadine Fumarate manufactured at Vasudh Pharma is adopted from Ph. Eur monograph.
Assay by HPLC method of In-House developed is adopted to estimate the assay of Rupatadine.
Analytical method validation report for the assay by HPLC method is performed and verification report is provided.
An In-house GC method was developed for estimation of residual solvents in Rupatadine Fumarate. Analytical method validation for the residual solvents by GC method was performed and validation report is provided.</td></tr>
<tr><td>9.</td><td>3.2.P.2 Invoice are required for the procurement of innovator’s product.</td><td></td></tr>
</table>

		Firm has submitted Unit pack/Invoice of innovator product Rupall Tablet

Remarks of Evaluator:

Decision: Approved with Innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of revised drug substance analytical method, analytical method verification studies & drug substance analysis report as per European Pharmacopoeia Monograph for "Rupatadine Fumarate".**

437.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.**
	Name, address of Manufacturing site.	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 23859 dated 31-08-2021
	Details of fee submitted	PKR 50,000/-: dated 08/04/2021
	The proposed proprietary name / brand name	Cardrone 400mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains Dronedarone HCL eq to Dronedarone….400mg
	Pharmaceutical form of applied drug	Cream white color oval shaped film tablet coated tablet
	Pharmacotherapeutic Group of (API)	Class III antiarrhythmic agent
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	10's, 20's, 30's (as per SRO)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Multaq 400mg tablet by Sanofi,Ambares (France)
	For generic drugs (me-too status)	-------

	GMP status of the Finished product manufacturer	New license granted on 16/09/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Piramal enterprises limited, Digwal village(Sy.Nos.7-70,70/1 and 70/2), kohir Mandal, Medak dist.,502 321 Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Dronedarone is present in USP 40 vol.4. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 18 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(DD04/00216,DD04/00316,DD04/00416)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Multaq 400mg tablet by Sanofi performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Multaq 400mg Tablet by Sanofi in Acid media (pH 0.1N HCl) & Phosphate Buffer (pH 6.8, 4.5). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision, specificity,LOD)

STABILITY STUDY DATA			
Manufacturer of API	Piramal enterprises limited, Digwal village (Sy.Nos.7-70,70/1 and 70/2), kohir Mandal, Medak dist.,502 321 Telangana, India		
API Lot No.	N/A		
Description of Pack (Container closure system)	PVDC/ aluminum blister pack (10's, 20's, 30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 18 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18(Months)		
Batch No.	TF-02	TF-03	TF-04
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	18-01-2019	30-01-2019	30-01-2019
Date of Initiation	15-02-2019	15-02-2019	15-02-2019
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to their last onsite inspection conducted for product Rofair (Roflumilast) 500mcg Tablets on 25th June, 2019. The said inspection report was discussed in 290th meeting of Registration Board held on 3rd–4th July, 2019 and the case was approved. The inspection report confirms following points: • The firm has Shimadzu 's LC 20A, with software ―Lab solution DB‖ which is 21 CFR part 11 compliant with audit trail and date time stamped and with complete multi-level user authorization • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	L.Dis.No.3686/E(S)/TS/2017 issued to primal enterprises limited province FDA valid till 07-06-2019
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Form 6 license no. 0469 dated 11-02-2019

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Short coming	**Replies**
• **3.2.P** Which API polymorphic form was used by you in formulation development and how do you know the API polymorphic form was used by the innovator? Submit testing reports if you have performed any specific test • **3.2.P.2.1.2** Discussion of the choice of excipients, their concentration and characteristics that can influence the Drug Product performance shall be provided. • **3.2.P.2** Invoice is required for the procurement of innovator's product.	• Only one polymorphic form has been found. Solubility of Dronedarone HCl is greater in water than in buffers but in all cases it is practically insoluble. Only one polymorphic form was available as described in the TGA document. Attached for your reference. • We have added : hypromellose, starch, crospovidone, poloxamer 407, lactose monohydrate, colloidal silicon dioxide, magnesium stearate polyethylene glycol 6000, titanium dioxide, carnauba wax • We procured Innovator's product from a personal resource.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

438.	Name, address of Applicant / Marketing Authorization Holder	M/s Scotmann Pharmaceuticals, 5-D, I-10/3, Industrial Area, Islamabad, Pakistan
	Name, address of Manufacturing site.	M/s Scotmann Pharmaceuticals, 5-D, I-10/3, Industrial Area, Islamabad, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale

		☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 23860 dated 31-08-2021
	Details of fee submitted	PKR 75,000/- dated 28/05/2021
	The proposed proprietary name / brand name	Esonap DR Tablets 500/20mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Each Delayed Release Tablet contains**: Naproxen……...500mg Esomeprazole as magnesium…….20mg
	Pharmaceutical form of applied drug	Delayed Release Tablet
	Pharmacotherapeutic Group of (API)	**Naproxen:** Non-steroidal anti-inflammatory drug **Esomeprazole:** Proton pump inhibitor
	Reference to Finished product specifications	Innovator specification
	Proposed Pack size	7's, 10's, 14's, 20's, 28's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vimovo DR Tablet 500/20mg Manufacturer Horizon Pharma USA, Inc.,
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	New license granted on 17/12/2020 Tablet section approved.
	Name and address of API manufacturer.	**Name:** M/s EVEREST ORGANIC LIMITED. **Address:** AROOR VILLAGE, SADASIVAPET MANDAL, SANGAREDDY DIST, AROOR(V) SADASIVPET(M), SANGAREDDY(DIST.),502291 **Contact Person:** DR BOLLAM VENKATESWARLU
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Naproxen and Esomeprazole present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity related substances, specifications, analytical

		procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Long term: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-01, T-02, T-03)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Vimovo DR Tablets 500/20mg by Horizon Pharma USA, Inc. performing quality tests (Identification, Dissolution, Assay). CDP has been performed against the same brand that is Vimovo Tablets 500/20mg by Horizon Pharma USA, Inc, Dissolution profiles of both products (Vimovo Tablets 500/20mg and Esonap DR Tablets 500/20mg) were compared at three pH (1.2, 4.5, and 6.8) graphically and statistically.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, Robustness, accuracy, linearity, precision (Repeatability), specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Name:** M/s EVEREST ORGANIC LIMITED. **Address:** AROOR VILLAGE, SADASIVAPET MANDAL, SANGAREDDY DIST, AROOR(V) SADASIVPET(M), SANGAREDDY(DIST),502291 **Contact Person:** DR BOLLAM VENKATESWARLU		
API Lot No.	Naproxen: ANMA000240 Esomeprazole: ESM/E-108/19		
Description of Pack (Container closure system)	Alu-Alu blister with cold aluminum foil (7's, 10's, 14's, 20's, 28's & 30's)		
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Long term: 6 months Accelerated: 6 months		
Frequency	Accelerated: Initial,1,2 3,4, 6 (Months) Long term: Initial, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03

Batch Size		1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date		02-2020	02-2020	02-2020
Date of Initiation		15-02-2020	17-02-2020	19-02-2020
No. of Batches		03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Mekolade Tablets containing Metolazone 5mg DRAP Registration no. 108059	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 42005/TS/2020 issued by Drugs control Administration (Telangana State) Issue & Valid Upto Dt: 30/07/2020 - 30/07/2021	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Letter to Assistant Director (I&E) (R&I dated; Naproxen: 20/11/2019 and Esomeprazole: 29-01-2019) is submitted wherein the permission to import different APIs including Naproxen and Esomeprazole for the purpose of test/analysis and stability studies is granted.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.	

Remarks Of Evaluator:

Dissolution was according to USFDA. Details are as under

Dissolution 1 (naproxen at core), Dissolution 2 (naproxen at coating stage),Dissolution 3 (esomeprazole at coating stage)

Decision:

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

439.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Martin Dow Marker Limited, 7-Jail Road, Quetta**	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, F-126, S. I. T. E., Karachi, Pakistan	
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy.No 25930 dated 17/09/2021	
	Details of fee submitted	PKR 50,000/-: PKR 25,000/-:	dated 04/05/2020 dated 30/06/2021
	The proposed proprietary name / brand name	ADVITA 200,000 IU CAPSULES	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Soft gel Capsule contains: Cholecalciferol…..200,000 IU	
	Pharmaceutical form of applied drug	Clear light-yellow oily liquid	
	Pharmacotherapeutic Group of (API)	Vitamin D analogs	
	Reference to Finished product specifications	USP	
	Proposed Pack size	As per SRO	
	Proposed unit price	As per SRO	
	The status in reference regulatory authorities	Fultium 20,0000 IU Capsule by M/s Internis Pharmaceuticals Limited, MHRA Approved.	
	For generic drugs (me-too status)		
	GMP status of the Finished product manufacturer	Certificate No: F.14-1/DRAP/GMP/MDM-2022 issued on 03rd Feb 2022 Soft Gelatin Capsule (General) Dispensing, Mixing, Drying, Granulation, Compression, Coating, Blistering & Packaging.	
	Name and address of API manufacturer.	M/s DSM Nutritional Product, France	
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch	

		analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 25°C ± 2°C / 60% RH ± 5% RH for 24 months Accelerated: 30°C ± 2°C / 65% RH ± 5% RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that **Fultium 20,0000 IU Capsule by M/s Internis Pharmaceuticals Limited**. Since Vitamin D3 capsules are Fat soluble in nature so the dissolution in not recommended by any Pharmacopoeia & FDA dissolution guideline.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s DSM Nutritional Product, France
API Lot No.	11F01901004
Description of Pack (Container closure system)	Aluminum foil with PVC/PVDC blister (2×7's)
Stability Storage Condition	Real time: 25°C ± 2°C / 60% ± 5%RH Accelerated: 30°C ± 2°C / 65% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	TR-007/20	TR-008/20	TR-009/20
Batch Size	10000 capsule	10000 capsule	10000 capsule
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	02-2022	02-2022	02-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Acidex 60mg Capsule Dexlansoprazole was approved in 312th Registration Board meeting. 2) Compliance Record of HPLC software 21CFR & audit trail reports on product testing were present
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP Certificate No 18MPP077HFR02 issued by EUDRA . Period of validity is extended to 26.09.2023 in case of cholecalciferol .
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s DSM Nutritional Product, France** ADC Invoice No: 2831239200, 29-08-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Decision: Deferred for following points:

- **Clarification of conditions of stability studies of drug substance and drug product.**
- **Justification why comparative dissolution profile studies are not performed against the innovator drug product.**

440.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Rogen Pharmaceuticals Plot No. 30, S-4, National Industrial Zone, Rawat Islamabad "**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 7862 dated 10-03-2021
	Details of fee submitted	PKR 50,000/-: 03-03-2020 (#2005272)
	The proposed proprietary name / brand name	P-Becten Injection IV 4.5gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacillin ……. 4 gm Tazobactam Sodium eq. to Tazobactam …… …… 0.5 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Zoycin Injection 4.5gm By M/S Global Pharmaceuticals (Pvt) Ltd Reg No: 066599
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by M/s Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API		M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.
API Lot No.		TSP13000616N

Description of Pack (Container closure system)		Type II Glass VIAL (1s)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.		21H011	21H012	21H013
Batch Size		4120 Vial	4120 Vial	4120 Vial
Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		31-08-2021	31-08-2021	04-09-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 4.5g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. Pb.2019/5422) issued by Food and Drugs Administration Punjab dated 04-12-2019. The certificate is valid till 2 years from the date of issue.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		

Evaluation by PEC:		
Shortcomings communicated		**Response by the firm**
Valid GMP certificate of finish product and API manufacturer		Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue.
3.2.P.2 Invoice are required for the procurement of innovator product		Invoice for procurement of API Provided
Remarks OF Evaluator:		
Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.		
441.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Rogen Pharmaceuticals Plot No. 30, S-4, National Industrial Zone, Rawat Islamabad "**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 7863 dated 10-03-2021
	Details of fee submitted	PKR 50,000/-: 25-02-2021 (#2005274)
	The proposed proprietary name / brand name	P-Becten Injection IV 2.25 gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacillin…….2 gm Tazobactam Sodium eq. to Tazobactam……0.25 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Tazop Injection of Global Pharmaceuticals
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.		
API Lot No.		2105R0069, 2105R0070		
Description of Pack (Container closure system)		Type II Glass VIAL (1s)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.		21H008	21H009	21H128
Batch Size		4120 Vial	4120 Vial	4120 Vial
Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		01-09-2021	31-08-2021	30-08-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 2.25g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. Pb.2019/5422) issued by Food and Drugs Administration Punjab dated 04-12-2019. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Valid GMP certificate of finish product and API manufacturer	Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue.
3.2.P.2 Invoice are required for the procurement of innovator product	Invoice for procurement of API Provided

Remarks OF Evaluator:

Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.

442.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Carer Pharmaceuticals Industries Plot # 27, Main Road Rawat-Islamabad"**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy.No 11386 dated 14-04-2021
	Details of fee submitted	PKR 50,000/-: dated 08/03/2021 (#2077511)
	The proposed proprietary name / brand name	Salutem Injection IV 4.5gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacilli…….4 gm Tazobactam Sodium eq. to Tazobactam……0.5 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Zoycin Injection 4.5gm By M/S Global Pharmaceuticals (Pvt) Ltd Reg No: 066599
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical procedures and its

		verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance		
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months		
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.		
API Lot No.		TSP13000616N		
Description of Pack (Container closure system)		Type II Glass VIAL (1s)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.		21H011	21H012	21H013
Batch Size		4120 Vial	4120 Vial	4120 Vial
Manufacturing Date		08-2021	08-2021	08-2021

Date of Initiation		31-08-2021	31-08-2021	04-09-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 4.5g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue..		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		
Evaluation by PEC:				
Shortcomings communicated			**Response by the firm**	
Valid GMP certificate of finish product and API manufacturer			Valid GMP Certificate till 31-12-2022 Provided.	
3.2.P.2 Invoice are required for the procurement of innovator product			Invoice for procurement of API Provided	
Remarks OF Evaluator:				
Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.				
443.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Carer Pharmaceuticals Industries Plot # 27, Main Road Rawat-Islamabad"**		

	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 10092 dated 31-03-2021
	Dy. No. and date of submission	PKR 50,000/-: dated 08/03/2021 (2077512)
	Details of fee submitted	Salutem Injection IV 2.5gm
	The proposed proprietary name / brand name	P-Becten Injection IV 2.25 gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacillin…….2 gm Tazobactam Sodium eq. to Tazobactam……0.25 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Tazop Injection of Global Pharmaceuticals
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API		M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.
API Lot No.		2105R0069, 2105R0070
Description of Pack (Container closure system)		Type II Glass VIAL (1s)

Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.		21H008	21H009	21H128
Batch Size		4120 Vial	4120 Vial	4120 Vial
Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		01-09-2021	31-08-2021	30-08-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 2.25g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		
Evaluation by PEC:				
Shortcomings communicated			**Response by the firm**	

Valid GMP certificate of finish product and API manufacturer	Firm has submitted copy of GMP certificate (No. Pb.2019/5422) issued by Food and Drugs Administration Punjab dated 04-12-2019. The certificate is valid till 2 years from the date of issue.
3.2.P.2 Invoice are required for the procurement of innovator product	Invoice for procurement of API Provided
Remarks OF Evaluator:	
Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.	

444.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Nagarsons Pharmaceuticals (Pvt) Ltd Plot # 34, Street No. NS-2, National Industrial Zone, Rawat-Islamabad"**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8505 dated 16-03-2021
	Details of fee submitted	PKR 50,000/-: dated 04/0/2021 (#0822532)
	The proposed proprietary name / brand name	Darrel Injection IV 4.5gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacilli…….4 gm Tazobactam Sodium eq. to Tazobactam……0.5 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion

		MHRA Approved
	For generic drugs (me-too status)	Zoycin Injection 4.5gm By M/S Global Pharmaceuticals (Pvt) Ltd Reg No: 066599
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.		
API Lot No.		TSP13000616N		
Description of Pack (Container closure system)		Type II Glass VIAL (1s)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.		21H011	21H012	21H013
Batch Size		4120 Vial	4120 Vial	4120 Vial
Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		31-08-2021	31-08-2021	04-09-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 4.5g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Valid GMP certificate of finish product and API manufacturer	Firm has submitted copy of GMP certificate (No. Pb.2019/5422) issued by Food and Drugs Administration Punjab dated 04-12-2019. The certificate is valid till 2 years from the date of issue.
3.2.P.2 Invoice are required for the procurement of innovator product	Invoice for procurement of API Provided

Remarks OF Evaluator:

Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.

445.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Swiss Pharmaceuticals (Pvt) Ltd A/159, S.I.T.E-II, Super Highway, Karachi-Pakistan "**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 8678 dated 17-03-2021
	Details of fee submitted	PKR 50,000/-: dated 03/02/2021 (#2641137)
	The proposed proprietary name / brand name	Pectaz Injection IV 4.5gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacillin…….4 gm Tazobactam Sodium eq. to Tazobactam……0.5 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Zoycin Injection 4.5gm By M/S Global Pharmaceuticals (Pvt) Ltd Reg No: 066599
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of

		manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.		
API Lot No.	TSP13000616N		
Description of Pack (Container closure system)	Type II Glass VIAL (1s)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	21H011	21H012	21H013
Batch Size	4120 Vial	4120 Vial	4120 Vial

Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		31-08-2021	31-08-2021	04-09-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 4.5g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. Pb.2019/5422) issued by Food and Drugs Administration Punjab dated 04-12-2019. The certificate is valid till 2 years from the date of issue.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		
Evaluation by PEC:				
Shortcomings communicated			**Response by the firm**	
Valid GMP certificate of finish product and API manufacturer			Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue.	
3.2.P.2 Invoice are required for the procurement of innovator product			Invoice for procurement of API Provided	
Remarks OF Evaluator:				

Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.

446.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Swiss Pharmaceuticals (Pvt) Ltd A/159, S.I.T.E-II, Super Highway, Karachi-Pakistan "**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt) Ltd Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 7863 dated 10-03-2021
	Details of fee submitted	PKR 50,000/-: dated 03/02/2021 (#2041136)
	The proposed proprietary name / brand name	Pectaz Injection IV 2.25 gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacillin…….2 gm Tazobactam Sodium eq. to Tazobactam……0.25 gm
	Pharmaceutical form of applied drug	Lyophilized powder for injection/infusion
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	Glass vial USP type II partially sealed by rubber stopper and fully sealed by flip off seal. 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Tazop Injection of Global Pharmaceuticals
	GMP status of the Finished product manufacturer	**Global pharmaceuticals:** Firm has submitted copy of GMP certificate dated 04-01-2022. The certificate was issued based on the inspection dated 03-01-2022. The certificate specifies dry powder injection penicillin section.
	Name and address of API manufacturer.	M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh

		Nagar Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Zosyn Injection 4.5gm by Pfizer Pharmaceuticals, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API		M/s Nectar Lifesciences Ltd., (Unit No. 1) village saidpura Tehsil Derabassi District Sahibzada Ajit Singh Nagar Punjab India.
API Lot No.		2105R0069, 2105R0070

Description of Pack (Container closure system)		Type II Glass VIAL (1s)		
Stability Storage Condition		Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.		21H008	21H009	21H128
Batch Size		4120 Vial	4120 Vial	4120 Vial
Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		01-09-2021	31-08-2021	30-08-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	**PIPRABEN Injection 4.5g Injection (Piperacillin + Tazobactum)Approved in 316th Registration Board meeting.** **Applicant is :** M/s Benson Pharmaceuticals Plot No. 3, Main Road, National Industrial Zone, RCCI, Rawat. **Manufacturer:** **M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. Pb.2019/5422) issued by Food and Drugs Administration Punjab dated 04-12-2019. The certificate is valid till 2 years from the date of issue.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy ADC, duly endorsed by AD (1&E) Dated: 20-05-2021, Diary No: 1643		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		
Evaluation by PEC:				
Shortcomings communicated			**Response by the firm**	

Valid GMP certificate of finish product and API manufacturer	Firm has submitted copy of GMP certificate (No.Drugs (3) Pb.2021/6335) issued by Food and Drugs Administration Punjab dated 01-19-2021. The certificate is valid till 2 years from the date of issue.
3.2.P.2 Invoice are required for the procurement of innovator product	Invoice for procurement of API Provided
Remarks OF Evaluator:	
Decision: Approved. Registration Board Authorized its Chairman for issuance of registration letter upon capacity assessment of manufacturing and testing facility of M/s Global Pharmaceuticals (Pvt) Ltd. Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.	

447.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
	Dy. No. and date of submission	Dy.No 16908 dated 24-12-2021
	Details of fee submitted	Rs.30,000/- dated 24-12-2021
	The proposed proprietary name / brand name	Sinzon-S tablet 6.0/0.4mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Solifenacin Succinate(Immediate Release…….6.0mg Tamsulosin HCl (modified Release)…….0.4mg
	Pharmaceutical form of applied drug	Dark red colored round biconvex film coated tablet.
	Pharmacotherapeutic Group of (API)	**Solifenacin Succinate**: Urologicals, Drugs for urinary frequency and incontinence **Tamsulosin HCl**: Adrenergic α_1-receptor antagonist
	Reference to Finished product specifications	As per innovator Specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vesomni Tablet 6.0/0.4mg approved by **EMA**

<table>
<tr><td></td><td>For generic drugs (me-too status)</td><td>Tamsolin-S Tablet 6.0/0.4mg by Getz Pharma (Pvt) Ltd.</td></tr>
<tr><td></td><td>GMP status of the Finished product manufacturer</td><td>Last inspection report dated 18.06.2020 concluded good level of cGMP compliance.</td></tr>
<tr><td></td><td>Name and address of API manufacturer.</td><td>Solifenacin Succinate:
M/s Optimus Drugs (Pvt.) Limited.</td></tr>
<tr><td></td><td></td><td>Survey No. 239 & 240, Dothigudan (V), Pochampally (M), Yadadri, BhuvanagriIndia Tamsulosin HCl:
M/s Symed Labs (Pvt) Ltd.
Survey No, 353, Domadugu (Village), Jinnaram
(Mandal),Medak (Dist) ,Telangana, INDIA.</td></tr>
<tr><td></td><td>Module-II (Quality Overall Summary)</td><td>Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.</td></tr>
<tr><td></td><td>Module III (Drug Substance)</td><td>The firm as submitted detail of General information, General properties, Manufacturers, description of manufacturing process and process controls,
Characterization, Impurities, Control of drug substance, Reference standard or materials container closure system and stability studies of drug substance.</td></tr>
<tr><td></td><td>Stability studies</td><td>Solifenacin Succinate
Stability study conditions:
Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months

<table><tr><th>Batch No</th><th>Accelerated</th><th>Long Term</th></tr><tr><td>OP-SSC-S7-001-17</td><td>6 Months</td><td>48 Months</td></tr><tr><td>OP-SSC-S7-002-17</td><td>6 Months</td><td>48 Months</td></tr><tr><td>OP-SSC-S7-003-17</td><td>6 Months</td><td>48 Months</td></tr></table>
Tamsulosin HCl
Stability study conditions:
Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months
Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
<table><tr><th>Batch No</th><th>Accelerated</th><th>Long Term</th></tr><tr><td>XYZ 0010114</td><td>6 Months</td><td>60 Months</td></tr><tr><td>XYZ 0020114</td><td>6 Months</td><td>60 Months</td></tr><tr><td>XYZ 0030114</td><td>6 Months</td><td>60 Months</td></tr></table></td></tr>
</table>

	Module-III (Drug Product):	The firm has submitted detail of Drug Products including Description and composition of drug product, Pharmaceutical Development, Manufacturing process development, Microbiological attribution, Manufacturer, Master formulations, Description of Manufacturing Process and Process Controls, Control of Critical Steps and Intermediates, Process Validation and/ or Evaluation, Control of Excipients with specification and Analytical methods, Control of Drug Products including Finished

		product specifications and test methods, validation of Analytical methods, Batch analysis , Characterization of impurities, reference standard or impurities, Container closure and stabilities studies.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Tamsolin-S 6.0/0.4mg Tablet by Getz Pharma by performing quality tests (Identification, Assay, Dissolution) CDP has been performed against the same brand that is Tamsolin-S 6.0/0.4mg Tablet by Getz Pharma in Acid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)		
	Analytical method validation/verification of product	Method verification studies have submitted including Introduction, Verification of assay method, Specificity, Accuracy, Precision, Linearity concentration and peak range.		
STABILITY STUDY DATA				
Manufacturer of API		**Solifenacin Succinate:** M/s Optimus Drugs (Pvt.) Limited. Survey No. 239 & 240, Dothigudan (V), Pochampally (M), Yadadri, BhuvanagriIndia **Tamsulosin HCl:** M/s Symed Labs (Pvt) Ltd. Survey No, 353, Domadugu (Village), Jinnaram (Mandal),Medak (Dist) ,Telangana, INDIA.		
API Lot No.		**Solifenacin Succinate** OP-SCC/10/19/003 **Tamsulosin HCl** 6TSN0010519		
Description of Pack (Container closure system)		Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 8, 12, 16, 20, 24(Months)		
Batch No.		ST/001	ST/002	ST/003
Batch Size		2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date		09-2020	09-2020	09-2020

Date of Initiation		10-2020	10-2020	10-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product: EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) which was conducted on 1st June, 2021 and was presented in 307th meeting of Registration Board held on 08-10th June , 2021. Registration Board decided to approve registration of EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) by M/s. Horizon Healthcare (Pvt) Ltd. Lahore. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: i. The HPLC software is 21 CFR compliant. ii.Audit trail on the testing reports of EMPAZON 10mg and 25mg Tablets, Dayzol 30mg and 60mg Capsules is available. iii. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Solifenacin Succinate:** Firm had provided valid GMP and DML Certificate of M/s Optimus Drugs (Pvt.) Limited. Issued by Drugs Control Administration Government of Telangana, GMP Valid upto 24-05-2022 DML Valid upto: 09-09-2023 **Tamsulosin HCl:** Firm had provided valid GMP and DML Certificate of M/s Symed Labs (Pvt.) Limited. Issued by Drugs Control Administration Government of Telangana, GMP Valid upto 03-03-2022 DML Valid upto: 27-05-2023		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted. **Solifenacin Succinate:**		

		Batch No. / **Invoice No.** / **Quantity Imported** / **Date of approval by DRAP** OP-SSC/10/19/003 / 1920OD267/EXP / 07kgs / 13-01-2020 Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted. **Tamsulosin HCl:** **Batch No.** / **Invoice No.** / **Quantity Imported** / **Date of approval by DRAP** 6TSN0010519 / Symed-201921-20 / 0.020kgs / 23-04-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

Section#	Observation	Firm's response
3.2.S.4.4	Details of site address of the drug substance manufacturer mentioned on COA of drug substance are different form that mentioned in section 3.2.S.2.1	Firm has corrected site address in section 3.2.S.2.1 according to COA
3.2.P.3.2	Composition of each layer of Solifenacin succinate and Tamsulocin HCl shall be described separately in batch formula.	Firm has submitted batch formula where in composition for Solifenacin immediate release layer and Tamsulocin HCl extended release layer have been mentioned separately.
3.2.P.5.2	Justification shall be submitted for applying 100rpm with USP paddle apparatus , in the test of Dissolution of Tamsulocin HCl in the light of USP general chapter <1092>	Justification shall be submitted for applying 100rpm with USP Paddle apparatus in the test of dissolution of Tamsulosin HCL in the light of USP general chapter<1092> As per The united states

			pharmacopeia, The general Information chapters <1092> The dissolution Procedures: Development and Validation, Under the Sub section 2.3 Agitation of section 2.0 Method Development "If justified, 100 rpm may be used with Apparatus2, especially for Modified-release products". The tamsulosin is Modified release in our product, hence we used the 100 rpm with comparing the Tamsulosin Modified release capsule official Monograph in USP.	
	3.2.P.5.6	Justification shall be submitted for selection of dissolution parameters and limits for the test of Dissolution of both drug substances.	The Dissolution Parameters and Limits of Solifenacin (Immediate Release) was taken from FDA Dissolution method guidelines While the Tamsolusin Parameters and Limits was taken from Tamsulosin Modified release capsule official Monograph in USP. Also the time points Parameters was chosen from concerning the USP <1092> The dissolution Procedures: Development and Validation For testing an Modified-release dosage form, at least three time points are chosen, to guard against dose dumping, to define the in vitro release profile, and to show that essentially complete release (>80%) of the drug is achieved. Additional sampling times may be useful. Selection of the final time points is reflective of the data from the drug release profile that are generated during development. For products containing more than a single active ingredient, determine the drug release for each active ingredient. The Comparative dissolution profile for the both drug substances in Combination product also clarify our parameters and Limits.	
	3.2.P.8.3	• Valid GMP certificate or Drug Manufacturing License shall be submitted of the relevant unit of Symed labs, from which	• Firm has submitted copy of GMP certificate issued by DCA Goverrnment of Telangana, in the name of M/s Symed Labs, Unit VI valid upto 14-09-2022.	

		Tamsulocin HCl has been imported. • Evidence of availability of bi-layer compression machine shall be submitted.	• Firm has submitted copy of commercial invoice dated 18-05-2020 for the procurement of Tablet press machine ZP-31 along with bill of lading.

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

448.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Wimits Pharmaceuticals (Pvt) Ltd. Lahore**
	Name, address of Manufacturing site.	M/s Wimits Pharmaceuticals (Pvt) Ltd. Plot #129 Sundar Industrial Estate,Raiwind road,Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32415 dated 29/11/2021
	Details of fee submitted	PKR 30,000/-: dated 03/11/2021
	The proposed proprietary name / brand name	Ebatrix 5mg/5ml syrup
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Ebastine ---------- 5mg
	Pharmaceutical form of applied drug	Almost colourless, clear solution with characteristics odour of anise.
	Pharmacotherapeutic Group of (API)	Histamine H_1-receptor antagonist, Anti allergic agent
	Reference to Finished product specifications	In - house
	Proposed Pack size	1×30ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved.
	For generic drugs (me-too status)	Kestine 5mg/5ml oral liquid by M/s Highnoon Labortories Ltd, Reg. No. 028369

	GMP status of the Finished product manufacturer	New license granted on 03/02/2019 Tablet,oral liquid (General) section approved.
	Name and address of API manufacturer.	M/s Vasudha Pharma Chem Limited, Unit-I, Plot No**.** 37/A, 38, 39, A & B,Phase-I, IDA, Jeedimetla,Hyderabad – 500 055, Telangana, INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ebastine is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (TEK-001/2021, TEK-002/2021, TEK-003/2021)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand name is Kestine 5mg/5ml oral liquid by M/s Highnoon Labortories Ltd. by performing quality tests (Identification, Assay)
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	M/s Vasudha Pharma Chem Limited, Unit-I, Plot No**.** 37/A, 38, 39, A & B,Phase-I, IDA, Jeedimetla,Hyderabad – 500 055,Telangana, INDIA.		
API Lot No.	B# EB/2006004		
Description of Pack (Container closure system)	Solution is filled in amber glass bottle(1×30ml) that is packed in unit carton alongwuth leaflet insert.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TEK001	TEK002	TEK003
Batch Size	166 packs	166 packs	166 packs
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	03-03-2021	06-03-2021	08-03-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 22/03/19 issued by FDCA valid till 21/03/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of commercial invoice no. 0370/U1/E/20-21 attested by AD DRAP I&E Lahore dated 22-01-2021 for the import of 5Kg of Ebastine.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers.

Remarks OF Evaluator:

Section#	Observation	Firm's response
1.6.5	Valid GMP certificate of the drug substance manufacturer shall be submitted.	Firm has submitted copy of GMP certificate no. 73252/TS/2022 issued by Drug Control Administration Telangana, valid upto 03-2025.

3.2.P.2.2.1	Justification shall be submitted for not performing Pharmaceutical equivalence studies against the innovator product	Innovator product was not registered in Pakistan so we performed the pharmaceutical equivalence with local brand & attached
3.2.P.2.5	Preservative efficacy studies shall be submitted.	Firm has submitted microbial testing report for preservative effectiveness testing.
3.2.P.5.1	Justification/Reference shall be submitted for the limits of pH test.	Firm has referred to the results of pH test of Innovator product.
3.2.P.5.2	Details of the test of Uniformity of Dosage unit shall be submitted.	Firm has submitted analytical record for the performance of Uniformity of dosage unit by way of Assay.
3.2.P.8.3	Justification shall be submitted for not performing preservative efficacy studies during stability studies. Documents confirming import of drug substance shall be submitted. Analytical record i.e., Raw data sheets, Chromatograms shall be submitted for each time point of both accelerated and long term stability studies of three batches.	Firm has submitted microbial testing report for preservative effectiveness testing. Firm has submitted copy of letter No.1279/2021-DRAP-AD-CD(I&E) dated 22/01/2021 is submitted wherein the permission to import different APIs including EBASTINE for the purpose of test/analysis and stability studies is granted. Firm has submitted analytical record for complete stability studies for both accelerated and long term conditions.

Decision: Approved with Innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

b. Deferred cases

449.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novamed Pharmaceuticals(Pvt.)Ltd Lahore 28-KM Ferozepur Road, Lahore- Pakistan**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.)Ltd Lahore 28-KM Ferozepur Road, Lahore- Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 11786 dated 00/04/2021
	Details of fee submitted	PKR 50,000/-: dated 23/03/2021
	The proposed proprietary name / brand name	**Kefie Injection 1gm/5ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Levocarnitine ……1gm
	Pharmaceutical form of applied drug	Clear colorless liquid free from foreign particles Intravenous injection
	Pharmacotherapeutic Group of (API)	Amino Acid Derivative, belongs to the class of organic compounds known as carnitines.
	Reference to Finished product specifications	USP
	Proposed Pack size	1's (5ml)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Carnitor Injection 1gm/5ml, approved in FDA USA
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	Certificate of cGMP Dated:11-01-2019 on the basis of inspection conducted on 08-01-2019
	Name and address of API manufacturer.	Northeast Pharmaceutical Group Co., Ltd No.29 Shenxiliu Dong Road, Economic Technology Development District, Shenyang, P.R.China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Levocarnitine is present in USP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (01714080001, 01714080002, 01714080003)		
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Carnitor 1gm/5ml Injection** Novamed Pharmaceuticals by performing quality tests (Identification, Assay, , pH). CDP has not been Applicable.		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		Northeast Pharmaceutical Group Co., Ltd No.29 Shenxiliu Dong Road, Economic Technology Development District, Shenyang, P.R.China		
API Lot No.		DY0171900142		
Description of Pack (Container closure system)		Individual vial is placed in a PVC Tray which is blistered from its open end with printed aluminum foil. Each Blistered tray containing one clear vial of 5ml is packed in Specific Unit carton along with a patient information leaflet		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		**TP-160-T2**	**TP-160-T3**	**TP-160-T4**
Batch Size		500 vials	500 vials	500 vials
Manufacturing Date		03-2020	03-2020	03-2020
Date of Initiation		20-05-2020	20-05-2020	20-05-2020
No. of Batches		03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of Drug manufacturing license (License no. Liao 20150001) for M/s Northeast Pharmaceutical Group Co., Ltd No.29 Shenxiliu Dong Road, Economic Technology Development District, Shenyang, P.R.China. issued by Liaoning Food and Drug Administration of the People's Republic of China is submitted, valid upto 10-12-2025
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.8830/2019/DRAP-AD-CD(I&E) dated 25/06/2019 is submitted wherein the permission to import different APIs including Levocarnitine for the purpose of test/analysis and stability studies is granted. • Commercial invoice No # HR 19079 dated:24-05-2019, DRAP Lahore Attested dated: 28-06-2019 is also submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted compliance record of HPLC software 21 CFR and copies of audit trail on testing of drug product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5 (B)	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin	DML of API submitted.
2.	3.2.S.4	Differences from the officially recognized compendial standard(s) shall be justified, as claimed specifications are USP but certain testes are not included i.e Enantiomeric Purity, chloride and sulfate, limit of potassium, limit of sodium	All the required test has been performed and revised COA is attached. **Drug substance manufacturer and Drug product manufacturer claimed USP, API specification but both did not performed Enantiomeric Purity. According to USP NMT 0.2% of D-carnitine is mentioned.**

3.	3.2.S.5	COA of primary / secondary reference standard including source and lot number shall be provided.	Certificate of analysis of primary reference standard attached.
4.	3.2.P.2.1.1	As per relevant guidelines & structure of Form 5F, Pharmaceutical equivalence shall be established with the innovator / reference / comparator product at the time of formulation development, while according to your submitted data, Pharmaceutical equivalence have been performed 27-02-2021 which is after commencing stability studies.i.e 20-05-2020 Justification shall be submitted.	Owing to the prevailed condition of covid throughout the world We had performed PE after formulation development due to unavailability of the Innovator pack. So, as per the need of hour or to overcome this challenge we deviated from the flow. However, we confirm that this deviation will not be repeated.
5.	3.2.P.5.3	• As per relevant guidelines & structure of Form 5F Analytical test method verification has to be performed at the time of formulation development, while according to your submitted data, Analytical test method verification have been performed on 16-03-2021 while stability studies started on 20-05-2020. Justification shall be submitted in this regard. • Accuracy is not performed. • Range is not calculated • Justify the analytical method of repeatability and intermediate precision in accordance with performance.	USP Method was adopted for the testing of the finished product. During testing at each point the recovery or accuracy was as per predefined specification. Further system suitability was performed, for which the RSD is in limit, in other words we can say this method is repeatable. However, we confirm that this deviation will not be repeated. • Performed and Revised copy Attached. • Revised copy is attached.
6.	3.2.P.8	Documents for the procurement of API with approval from DRAP	Copy of DRAP attested invoice and import permission letter is attached.

Decision of 313th: Registration board deferred the case for following:
• Performance of Enantiomeric Purity test for Drug substance by drug product manufacturer.
• For confirmation of required manufacturing facility i.e filling of 5ml Vial.

Evaluation by PEC: The firm has submitted COA having Enantiomeric purity by fluorescence detector test.
The firm has submitted a letter from CLB having Liquid injectable Ampoule/Vial general-Revised. section

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

• **Registration letter will be issued upon submission of evidence of performance of Enantiomeric purity test of drug substance by drug product manufacturer as recommended by USP monograph.**		
450.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited** **B-23-C, S.I.T.E., Karachi**
	Name, address of Manufacturing site.	M/s AGP Limited B-23-C, S.I.T.E., Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 20777 dated: 30th July 2021
	Details of fee submitted	PKR 30,000/-: dated: 24th May 2021
	The proposed proprietary name / brand name	Rigix Oral Solution (Strawberry flavor)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Cetirizine HCl…….5mg
	Pharmaceutical form of applied drug	Clear colorless liquid with characteristic strawberry flavor and odor.
	Pharmacotherapeutic Group of (API)	Antihistamine for systemic use
	Reference to Finished product specifications	BP Specification Shelf life claimed is 24months.
	Proposed Pack size	60ml and 120ml
	Proposed unit price	Rs. 78.09/- for 60ml Rs. 124.17/- for 120ml
	The status in reference regulatory authorities	Cetirizine Hydrochloride 5mg/5ml by Chain Drug Consortium LLC (Premier Value), USA, USFDA Approved.
	For generic drugs (me-too status)	Zyrtec 5mg/5ml Oral Solution by M/s GlaxoSmithKline. Reg. No. 016937
	GMP status of the Finished product manufacturer	Renewal of DML on 30th June2020. Firm has oral liquid (general) section.
	Name and address of API manufacturer.	**Cetirizine Hydrochloride:** M/s PRAVEEN LABORATORIES PVT. LTD, India, Block No. 206, Village: Jolwa, Taluka: Palsana Dist.: Surat, Gujarat, INDIA.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Module III (Drug Substance)	Official monograph of Cetirizine Hydrochloride is present in BP. The firm as submitted detail of nomenclature, structure, general properties, Solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	API Stability study conditions: : 25°C ± 2°C / 60% ± 5%RH for 60 months 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is carried on with **Zyrtec Oral Solution manufactured by GSK pakistan**
	Analytical method validation/verification of product	Method verification studies have submitted including System suitability, accuracy, precision, specificity, Limit of detection, Limit of quantification.
STABILITY STUDY DATA		

Manufacturer of API		**Cetirizine Hydrochloride:** M/s PRAVEEN LABORATORIES PVT. LTD, India, Block No. 206, Village: Jolwa, Taluka: Palsana Dist.: Surat, Gujarat, INDIA.	
API Lot No.		Cetirizine Hydrochloride: MK40119136, MK40119137, MK40119138 & MK40119139	
Description of Pack (Container closure system)		Amber glass bottle with ALU fitted with wad. Each bottle is packed in printed carton.	
Stability Storage Condition		Real time: 25°C ± 2°C / 60% ± 5%RH Intermediate: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH	
Time Period		Real time: 6 months Intermediate: 6 months Accelerated: 6 months	
Frequency		Accelerated: 0, 3, 6 (Months) Intermediate: 3, 6, 9, 12 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)	
Batch No.		TR-643	TR-644	TR-645
Batch Size		4.0 L	4.0 L	4.0 L
Manufacturing Date		10-2020	10-2020	10-2020
Date of Initiation		29-10-2020	29-10-2020	29-10-2020
No. of Batches		03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The board approved Glyzia-XR Tablet 50/500m of M/s AGP limited B-23, SITE, Karachi in 285th meting held in October 2018. As per minutes, HPLC is 21 CFR compliant and have audit trails.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Cetirizine Hydrochloride:** Copy of GMP certificate No. S-GMP/21092927 issued by Food and Drug Control Administration, India, valid till 09th Oct 2023.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC Attested Karachi invoice no Ex/060 date 1-1-2020	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of 3 batches of 4 liter each with raw data sheets, COA, and chromatograms have been submitted.	

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing was submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Short coming	Replies
a) 2.3.P.8/ 3.2.P.8 Stability. The storage condition "Do not store above 25C " does not meet zone IV a condition. Please Justify.	The Rigix oral solution (Cherry flavour) is also a brand of innovator purchased by AGP few years back. The storage temperature conditions of Rigix oral solution (Cherry Flavour) is "Do not store above 25℃. Therefore, we have conducted the stability studies of Rigix Oral solution (Strawberry Flavour) at 30+- 2℃ / 65+-5% RH (real time for 12 months at initial, 6, 9th and 12month.) of 3 batches. 40+- 2℃ / 75+-5% RH (Accelerated for 6months) of 3 batches. The other brand of innovators "Zyrtec" in USA has also the same storage condition i.e. Between 20 ℃ to 25 ℃. We hereby revise the storage condition as "Store below 30'C." The firm did not submit fee for correction. The me-too product Zyrtec by GSK Pakistan has storage condition "Do not store above 30'C.
b) Approval of valid API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin is required.	Valid copy of GMP certificate of API manufacturer i.e. M/s PRAVEEN LABORATORIES PVT. LTD, India, Block No. 206, Village: Jolwa, Taluka: Palsana Dist.: Surat, Gujarat, INDIA. valid till 19-9-2023. Certificate is issued b Food and Drug Control Administration.

Decision of 316th: Deferred for justification of not performing long term stability studies testing at 3rd month time point.

Evaluation: The firm has submitted:

- We have conducted stability studies of our product on Zone IV-A (30°C ± 2°C / 65 ± 5% RH) and by mistake we have skipped 3rd month stability testing point but we have performed 6th month, 9th month and 12th months stability studies and results shows that the product is stable.
- We have also performed accelerated stability studies for 0, 3 & 6 months, the results are also in compliance with specifications.

	• We assure you that we will continue the stability studies up to the shelf life of 24 months i.e. 18th months, 24months and submit the data at DRAP.	
	Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**	
451.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Shazal's Pharmaceuticals, 41/A-1, Phase-1, Industrial Estate Hattar**
	Name, address of Manufacturing site.	**M/s Shazal's Pharmaceuticals, 41/A-1, Phase-1, Industrial Estate Hattar**
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1682: 13-01-2021
	Details of fee submitted	PKR 20,000/-: 29-10-2020
	The proposed proprietary name / brand name	**Zyacef 200mg/5ml suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml dry powder for suspension contains: Cefixime (as trihydrate)….200mg
	Pharmaceutical form of applied drug	Dry powder for suspension
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by MHRA
	For generic drugs (me-too status)	Cefiget 200mg / 5ml Suspension By GETZ Aventis Pharma
	GMP status of the Finished product manufacturer	13-2-2019 and 19-1-2020. The panel unanimously recommends resumption of production activites in all section of the firms.
	Name and address of API manufacturer.	M/s. Pharmagen Ltd Kot nabi Bukhsh wala, 34km ferozpur road Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.		
	Module-III (Drug Product):	Firm has submitted relevant information against the Module III, including, Process validation protocol, Finished product analytical method validation report & stability studies data.		
STABILITY STUDY DATA				
Manufacturer of API		M/s. Pharmagen Ltd Kot nabi Kuksh wala, 34km ferozpur road Lahore.		
API Lot No.		00244/043-2019		
Description of Pack (Container closure system)		Amber glass bottle		
Stability Storage Condition		Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 9 months Accelerated: 6 months		
Frequency		Accelerated: 0,3, 6 (Months) Real Time: 0, 3, 6, 9 (Months)		
Batch No.		Cef-T1	Cef-T2	Cef-T3
Batch Size		16kg	16kg.	16kg
Manufacturing Date		10-2019	11-2019	12-2019
Date of Initiation		10-2019	11-2019	12-2019
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	• N/A		

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate was issued to M/s Pharmagen Ltd based on evaluation conducted on 8-1-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	API source is local. Local Invoice is attached.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) (VI)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers

Observation	**Response**
Submit data of pharmaceutical equivalence in section 3.2.P.2.2.1. to comply the decision of 293rd meeting of Registration Board, which states that "Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product should be submitted and discussed".	Firm has performed comparative analysis of their developed formulation against the comparator product i.e. "Cefiget". Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator product. . The results depicts that the developed formulation is comparable to the comparator product.
Submit the data of verification of analytical method for drug substances in section 3.2.S.4.3 to comply the decision of 293rd meeting of Registration Board, which states that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as noncompendial drug substance(s) shall be submitted".	Firm has submitted protocols and results of verification of analytical method of drug substance based on recommendations of USP.

Decision of 308th : Deferred for following:

- Submission of details of stability chambers for conducting stability studies.
- **Batch size in units.**
- Pharmaceutical equivalence with innovator's product

Evaluation VI:

Short coming	**Replies**

a) Submission of details of stability chambers.	Details of stability chambers both long term of 400L and accelerated chambers of 500L of Organa international have been submitted.
b) Batch size in units	Batch Size is of 5000 bottles
c) Pharmaceutical equivalence with innovator product	Pharmaceutical equivalence has been done with Cefiget 200mg/5ml of Getz Pharma having batch number 954.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical equivalence studies against the innovator product i.e, Cefspan suspension.**

Case no 4: Registration of applications for
Exemption from onsite verification of stability data
Deferred case

452.	Name and address of manufacturer / Applicant	**"M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan.**
	Brand Name +Dosage Form + Strength	Indamac 85mcg +43mcg DPI Capsule
	Composition	Each DPI Capsule Contains: Indacaterol maleate eq to Indacterol……85mcg Glycopyrronium bromide eq to glycopyrronium …. 43 mcg
	Diary No. Date of R& I & fee	Dy. No: 9787 : date 24-07-17: Rs. 50,000 7-7-2017Slip No: 0313258
	Pharmacological Group	Bronchodilator
	Type of Form	Form 5D
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	10's, 20's, 30's /As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in EMA Ultibro Breezhaler
	Me-too status	Ultibro Breezhaler of Novartis Pharma
	GMP status	The firm was granted GMP certificate based on inspection conducted on 14-03-2017.
	Remarks of the Evaluator	

STABILITY STUDY DATA	
Drug	Indamac 85mcg +43mcg DPI Capsule
Name of Manufacturer	M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan.
Manufacturer of API	Glycopyrrolate U.S.P: M/s. Harman Finochem Ltd. Indacaterol maleate: Inke S.A Area Industrial Del Llobregat
API Lot No.	Glycopyrrolate U.S.P: GCP/004/2017-2018/A Indacaterol: PP-1 PR3
Description of Pack (Container closure system)	Alu-Alu blister
Stability Storage Condition	Real Time: 30^{o}C ± 2^{o}C / 65% ± 5%RH Accelerated:40^{o}C ±2^{o}C / 75% ± 5%RH

Time Period	Real Time: 24 Months Accelerated:06Months		
Frequency	Real Time: 0,1,3,6,9,12,18,24 Months(on going) Accelerated: 0,1,3,6 Months		
Batch No.	001P	002P	003P
Batch Size	10000 Capsules	10000 Capsules	10000 Capsules
Manufacturing Date	02-2018	02-2018	02-2018
Date of Initiation	26-02-18	26-02-18	26-02-18
No. of Batches	03		
Date of Submission	22/02/2019 Dy. No. 7826)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

The firm has submitted stability study data as per checklist of 14 points approved by Registration Board in its 293rd meeting.

1.	Reference of last onsite panel inspection for instant dosage form conducted during last two years.	Firm has referred to onsite inspection report of their products "Venticort Rotacaps 100mcg+6mcg, which were presented in 257th meeting of Registration board. Registration Board decided to approve registration of Venticort Rotacaps 100mcg+6mcg of M/s Macter International Limited F-216, S.I.T.E., Karachi-Pakistan. According to the report generated following points were confirmed a) The HPLC used for analysis of stability batches is Shimadzu 20 ATVP with auto sampler and gradient system and it was 21 CFR compliant. b) The firm has six stability chambers for real time and accelerated stability studies which are equipped with proper alarm system and data loggers
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has submitted copies of COA of drug substance from drug substance manufacturer and analytical report of their testing of raw material. Glycopyrrolate U.S.P of M/s. Harman Finochem Ltd, Batch No. GCP/004/2017-2018/A and Indacaterol of Inke S.A, Batch No. PP-1 PR3
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer.	Analytical method for testing of API as well as from API manufacturer was submitted
4.	Stability study data of API from API manufacturer.	The firm has submitted 6 months accelerated and 36 months real time stability study data of API as per zone IVA.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by regulatory authority of country of origin.	Copy of GMP certificate for Glycopyrrolate (Certificate#6087313) issued by Food and Drug Administration, Aurangabad division, Maharashtra state valid upto 10-04-2020. Copy of GMP certificate for Indacaterol (Certificate# NCF-II/1740/001/CAT) issued by Directorate General Ministry of Health of Govt of Catalonia – spain issued on 21-06-2017

<table>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoices to import Glycopyrrolate (0.010 kg) and Indacaterol (10 gm) attested by AD, I&E DRAP, Karachi has been submitted.
Detailed as under:
<table><tr><th>Batch No.</th><th>Invoice No.</th><th>Date of approval by DRAP</th></tr><tr><td>GCP/004/2017-2018/A
PP-1 PR3</td><td>P/E9/129/2017-18
Macter10102017</td><td>01-08-2017
06-10-2017</td></tr></table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>The firm has submitted protocols for conduction of stability studies.</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP.</td><td>Details of methods used for analysis of finished Product “Indamac 85mcg +43mcg DPI Capsule ” has submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Excipients are same as of innovators product.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>Photocopies of complete batch Manufacturing records of following 03 Batches:<table><tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr><tr><td>001P</td><td>10000 Capsules</td><td>02-2018</td></tr><tr><td>002P</td><td>10000 Capsules</td><td>02-2018</td></tr><tr><td>003P</td><td>10000 Capsules</td><td>02-2018</td></tr></table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>N/A</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>The firm has submitted stability study data of 03 batches along with chromatograms, raw data sheets, COA, and summary data sheet.</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>The HPLC software is 21CFR compliant
Registration Board in its 257th decided to approve registration of Venticort Rotacaps 100mcg+6mcg of M/s Macter International Limited Karachi.
According to the report generated following points were confirmed
a) The HPLC used for analysis of stability batches is Shimadzu 20 AT with auto sampler and gradient system and it was 21 CFR compliant.
The firm has also submitted audit trail reports of applied product.</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>The record of Digital data logger for temperature and humidity monitoring of stability chambers is submitted in soft copy as well as in hard copy</td></tr>
<tr><td colspan="3">• The firm has submitted 06 months Accelerated and 24 months Real Time Stability Data for 03 Batches.
Decision of 290th meeting of Registration Board:
Deferred for confirmation of manufacturing facility for DPIs.
Evaluation by PEC:
Firm has submitted following documents:</td></tr>
</table>

• The Central Licensing Board in its 277th meeting held on 15th -16th October 2020, has considered and approved the regularization of building layout in the name of M/s Macter International on the recommendation of panel of experts for the following sections:

Sr no.	Section
1	Capsule (General)
2	Capsule DPI (General)

Firm has submitted that we have our product DPI Capsule pilot batches were manufactured on 19-2-2018 in available area of DPI, at that time there is no steroidal and non-steroidal separate section policy available. Later CLB in its 277th meeting October 2020 has approved Capsule DPI General Section.

Firm has submitted following documents as per the decision of **290th** meeting of Registration Board regarding Manufacturing Requirements for Rotacaps (Dry Powder Inhaler).

• Evidence of approval of applied formulation in EMA. The label claim of EMA approved product Ultibro Breezhaler 85 micrograms/43 micrograms inhalation powder hard capsules is as follows: Each capsule contains 143 micrograms of indacaterol maleate equivalent to 110 micrograms of indacaterol and 63 micrograms of glycopyrronium bromide equivalent to 50 micrograms of glycopyrronium.

Each delivered dose (the dose that leaves the mouthpiece of the inhaler) contains 110 micrograms of indacaterol maleate equivalent to 85 micrograms of indacaterol and 54 micrograms of glycopyrronium bromide equivalent to 43 micrograms of glycopyrronium.

• Firm has submitted results of aerodynamic particle size distribution by cascade impactors for Indamac DPI, uniformity of delivered dose, results of delivered dose contents of both indacaterol as well as glycopyrronium

Decision: Approved with Innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of Pharmaceutical equivalence studies including test of "Aerodynamic particle size distribution test" & "Uniformity of delivered dose test" against the innovator/reference product.**

Agenda of Evaluator PEC-VII

Case no. 01 Registration applications for local manufacturing of (Human) drugs

a. New cases on Form 5

453.	Name and address of manufacturer / Applicant	M/s Medicon Pharmaceuticals Pvt Ltd.

		Industrial Estate, Jamrud Road, Peshawar, Pakistan
	Brand Name +Dosage Form + Strength	Clonamed 2mg Tablet
	Diary No. Date of R& I & fee	Form-5 Dy.No 38246 dated 20-11-2018 Rs.20,000/- Dated 20-11-2018 (Slip# 0749866)
	Composition	Each Tablet Contains: Clonazepam…2mg
	Pharmacological Group	Benzodiazepine derivatives
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	3x10's As per SRO
	Approval status of product in Reference Regulatory Authorities	KLONOPIN TABLETS (clonazepam) of Roche Pharma (USFDA)
	Me-too status	Clonazep 2 mg Tabletsof Roryan Pharma (Reg. 078589)
	GMP status	NA
	Remarks of the Evaluator.	GMP inspection report conducted on 14-12-2020 is also provided wherein it is concluded that the firm is considered to be operating at satisfactory level of compliance with cGMP guidelines as per Drug Act, 1976 and rules framed there under
	Decision: Deferred for confirmation of requisite manufacturing facility i.e Tablet Psychotropic Section.	
454.	Name and address of manufacturer / Applicant	M/s. Obsons Pharma, industrial state, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Tagalin capsules
	Composition	Each capsule contains:- Pregabalin……..150 mg
	Diary No. Date of R& I & fee	Dy. No.2260; 23-01-2017; Rs. 20,000/-
	Pharmacological Group	Antiepileptic
	Type of Form	Form-5
	Finished product Specifications	Innovators
	Pack size & Demanded Price	2x7's As per SRO
	Approval status of product in Reference Regulatory Authorities	Lyrica by Pfizer Prism CV (USFDA)
	Me-too status	Gabica by Getz Pharma
	GMP status	Latest GMP inspection report dated 22-02-2022 concluded as satisfactory in tablet general Capsule general. Oral liquid and dry powdered suspension section
	Remarks of Evaluator	
	Decision: Approved with innovator's specification. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021.	

b. Deferred cases on Form 5

455.	Name and address of manufacturer / Applicant	M/S Welwrd Pharmaceuticals, Plot No ; 3, Block A, Phase I– II, Industrial Estat, Hattar, Pakistan Contract manufacturing from M/s WinBrains Research Laboratories, Plot # 69/1, Phase I-II, Industrial Estate, Hattar.
	Brand Name +Dosage Form + Strength	Top-Dex eye drops
	Diary No. Date of R& I & fee	Form-5 Dy.No 26337 dated 28-12-2017 Rs. 50,000 Dated 28-12-2017
	Composition	Each Drop Tainer Dispenser Contains: Dexamethasone…… 0.1% Tobramycin ……0.3%
	Pharmacological Group	Corticosteroids and Aminoglycoside antibiotic
	Type of Form	Form-5
	Finished Product Specification	Innovator
	Pack Size & Demanded Price	5ml As per SRO
	Approval Status of Product in Reference Regulatory Authorities.	TOBRADEX by Novartis (USFDA Approved)
	Me-too Status	TOBRADEX by Novartis
	GMP status	M/S Winsbrain GMP Certificate of GMP, Date: 20-5-2019(Have eye drop general section)
	Remarks of the Evaluator.	Sections of welward: 8 Products on contract manufacturing: 4 (2 approved letter awaited) Clarification shall be submitted whether applied formulation is in solution form or suspension form, since reference product approved by USFDA is in suspension dosage form. Confirmation of container closure system whether as per innovator or otherwise and confirmation of manufacturing facility of Drop Tainer Dispenser
	Decision 293: Deferred for clarification of dosage form i.e. solution or suspension Remarks of evaluator Firm revised the formulation with 20,000 fees (#2028796) dated 06/07/2020 to Each ml suspension Contains: Dexamethasone…… 0.1% Tobramycin ……0.3% Decision of 296: Deferred for confirmation of separate dispensing booth for steroidal ingredients Remarks of evaluator Firm submitted that our inspection is conducted but no inspection report is provided	
	Decision: Approved with innovator's specification. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, showing evidence of separate dispensing booth	

456.	Name and address of manufacturer / Applicant	M/s. Winthrox Laboratories Plot # K-219-A, SITE, Super Highway Phase II, Karachi
	Brand Name +Dosage Form + Strength	Womic-D Tablet 830mg+400IU
	Diary No. Date of R& I & fee	Diary No: 521 , 17/11/2016 , Rs. 20,000/-
	Composition	Each Tablet contains: Ossein MineralComplex…830mg Vitamin D……..400 I.U
	Pharmacological Group	Mineral + Vitamin
	Type of Form	Form-5
	Finished Product Specification	Mfg.
	Pack size & Demanded Price	As per SRO / Pack size as per SRO
	Approval status of product in Reference Regulatory Authorities.	Wellese Calcium and Vitamin D3 Tablet by Botanical Laboratories, USA.
	Me-too status	Bonmin Tablet by M/s. S J & G Fazal Elahi, Karachi.
	GMP status	09-10-2018 Routine GMP Inspection "overall GMP compliance level is rated as good."
	Remarks of Evaluator	Evidence of international availability provided by firm could not be confirmed in reference regulatory authority.
	Previous Decision (M275)	Registration Board in its 275th meeting decided as under: Deferred for submission of following: Evidence of approval in reference regulatory authorities. Evidence of availability of atomic absorption spectrophotometer
	Remarks of Evaluator XIII	Firm provide the evidence of Me-Too product Bonmin Tablet Registered in the name of M/s. S J & G Fazal Elahi Pvt Ltd, Karachi. (Reg. No. 070532) Evidence of availability of atomic absorption spectrophotometer is required.
	Previous Decision (M295)	Deferred for confirmation of availability of Atomic absorption spectrophotometer
	Remarks of Evaluator VII	Firm provide the evidence of availability of atomic absorption spectrophotometer. In manufacturing license inspection report of winthrox Lab dated 1-01-2015 atomic absorption is verified by Federal inspector of drug in the list of equipment's.
	Previous Decision (M312)	Deferred for submission of complete composition of Ossein mineral complex and confirmation of avaialability of atomic absorption spectrophotometer for analysis of minerals.
	Remarks of Evaluator VII	Firm provide the evidence of availability of atomic absorption spectrophotometer. In GMP inspection report of winthrox Lab dated 31-01-2022 atomic absorption is verified by Federal inspector of drug in the list of equipment's.

		Complete composition is provided as Each film coating tablet contains Vitamin D……400IU Ossien Mineral complex…..830mg Corresponding to Calcium……177.6mg Phosphorous…….82.2mg Residual Mineral Salt……24.9mg Collagen…….224mg Other proteins……....66.4mg Trace elements F, Mg, Fe, Zn, Cu, Ni. Corresponding to approximately 440mg hydroxyapatite
	Decision: Approved with innovator's specification Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021.	
457.	Name and address of manufacturer / Applicant	M/s Lisko Pakistan Pvt Ltd. L-10-D, Block 21, Shaheed Rashid Minhas Road, F.B. Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Slim 120mg Capsule
	Diary No. Date of R& I & fee	Form-5 Dy.No 3588 dated 29-01-2018 Rs. 20,000 Dated 17-01-2018
	Composition	Each capsule contains: Orlistat IR pellets 50% equivalent to Orlistat……120mg Source of pellets: M/s Vision Pharmaceuticals, Islamabad
	Pharmacological Group	Lipase Inhibitor
	Type of Form	Form-5
	Finished Product Specification	USP Specs
	Pack Size & Demanded Price	Proposed packs: 10's, 20's, 30's, 84's Proposed price: 85 Rs. Per Capsule
	Approval Status of Product in Reference Regulatory Authorities.	XENICAL 120mg Hard Gelatin Capsule, CHEPLAPHARM Arzneimittel GmbH Ziegelhof 24 17489 Greifswald Germany
	Me-too Status	Orlifit by Getz (Reg# 058474)
	GMP status	Latest inspection dated 24-04-2018 Conclusion: "Based on current inspection, documents reviewed it was noted that firm is currently working under satisfactory level of cGMP compliance. (Show cause notice revoked on 27-04-2018)"
	Remarks of the Evaluator.	
	Previous Decision (M287)	Registration Board deferred the case for submission of accelerated stability study data of pellets by M/s Vision Pharmaceuticals, Islamabad
	Remarks of Evaluator VII	While quoting the decision of 296th meeting of Registration Board, firm has

		referred to previously submitted real time stability studies data of orlistat pellets from M/s Vision Pharmaceuticals.
	Previous Decision (M307)	Deferred for submission of source of pellets in which stability studies of the pellets have been conducted at real time conditions i.e., 30°C ± 2°C/65% RH ± 5% RH alongwith quantification of degradation products throughout the stability studies / assigned shelf life.
	Remarks of Evaluator VII	submission of stability study data of pellets by M/s Vision Pharmaceuticals, Islamabad
	Decision: Deferred for further deliberation upon stability data requirement for orlistat Pellets in which stability studies of the pellets have been conducted at real time conditions i.e., 30°C ± 2°C/65% RH ± 5% RH along with quantification of degradation products throughout the stability studies / assigned shelf life.	
458.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Aultolax 4mg Injection
	Composition	Each 2 ml Injection Contains: Thiocolchicoside…4mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 16521 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900766)
	Pharmacological Group	Muscle relaxants, centrally acting agents
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	2 ml glass ampoule As per SRO
	Approval status of product in Reference Regulatory Authorities	THIOCOLCHICOSIDE PHARMY II 4 mg/2 ml, solution injectable ampule. ANSM approved
	Me-too status	Myolax Injection. Reg. No. Reg. No. 69277
	GMP status	DML issued on 5th March, 2019.
	Remarks of the Evaluator VII	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specification Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
459.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan

	Brand Name +Dosage Form + Strength	Athancinol Injection
	Composition	Each 4ml Injection Contains: Phloroglucinol Hydrated…40mg Trimethylphloroglucinol….0.04mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14904 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902260)
	Pharmacological Group	Antispasmodic
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Spasfon injection by M/s Teva Health (ANSM) France Approved (4 ml glass ampoule)
	Me-too status	Spasrid Injection of Barrett Hodgson Pakistan (Pvt) Ltd (Reg.# 034744)
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	The firm revised there form 5 and method of manufacturer from Each 4ml Injection Contains: Phloroglucinol Hydrated…40mg Trimethylphloroglucinol….0.04mg To Each 4ml Injection Contains: Phloroglucinol dihydrated…40mg (eq to 31.12 mg anhydrous phloroglucinol) Trimethylphloroglucinol….0.04mg which is according to the reference product with fee of 5000/- (#2038551) dated 03/9/2020
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specification Firm shall submit the full fee for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
460.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Suxamethonium 50mg Injection (100mg/2ml)
	Composition	Each ml Injection Contains: Suxamethonium chloride …50mg (IV/IM)
	Diary No. Date of R& I & fee	Form-5 Dy. No 16548 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1900797)
	Pharmacological Group	Neuromuscular blocker
	Form	Form-5
	Finished product Specifications	BP
	Pack size & Demanded Price	2 ml ampoule As per SRO

	Approval status of product in Reference Regulatory Authorities	Suxamethonium chloride 100 mg/2 ml injection 2m1, clear glass ampoules, glass type I (MHRA approved)
	Me-too status	Suxal Injection 100mg/ 2ml of M/s Global Pharma (Reg. # 026629)
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator VII	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
461.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Transalta 250mg/5ml Injection
	Composition	Each 5ml Injection Contains: Tranexamic Acid…250mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14916 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902375)
	Pharmacological Group	Haemostatic/ Anti-Fibrinolytic
	Form	Form-5
	Finished product Specifications	JP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	PMDA approved
	Me-too status	Dravix 250mg/5ml Injection of Getz Pharma Karachi
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator VII	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
462.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Moxid 400mg Tablets
	Composition	Each Film Coated Tablet Contains: Moxifloxacin as Hcl…400mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14907 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902267)
	Pharmacological Group	Antibiotic
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	1x5's As per SRO
	Approval status of product in Reference Regulatory Authorities	AVELOX (moxifloxacin as hydrochloride) 400mg tablets, film-coated. USFDA approved

	Me-too status	G-Mox 400 mg Tablets by M/s Reliance Pharma, Reg. No. 72148
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator VII	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with USP specification Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
463.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Spas 40mg Tablets
	Composition	Each Film Coated Tablet Contains: Otilonium Bromide…40mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16508 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902374)
	Pharmacological Group	anticholinergic, quaternary ammonium compounds
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Spasmomen of Italy
	Me-too status	Spasmomen tablet 40mg of Pharmatech.
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator VII	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specification Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
464.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Levo 250mg Tablets
	Composition	Each Film Coated Tablet Contains: Levofloxacin as hemihydrate…250mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16526 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1900773)
	Pharmacological Group	Fluoroquinolones, Antibiotic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's As per SRO

	Approval status of product in Reference Regulatory Authorities	Levofloxacin Tablets 250mg By Actavis Group United Kingdom (MHRA)
	Me-too status	Leflox Tablets 250mg By Getz
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
465.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Tazo 2mg Tablets
	Composition	Each Film Coated Tablet Contains: Tizanidine HCL Eq. to…2mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16490 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1902355)
	Pharmacological Group	Muscle relaxant
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Tizanidine 2mg Tablets by M/s Actavis UK Ltd (MHRA)
	Me-too status	Musidin 2mg Tablet by M/s Martin Dow (Reg# 027218)
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
466.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Tazo 4mg Tablets
	Composition	Each Film Coated Tablet Contains: Tizanidine HCL Eq. to…4mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16567 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902373)
	Pharmacological Group	Muscle relaxant
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	Tizanidine 4mg Tablets by M/s Actavis UK Ltd (MHRA)
	Me-too status	Musidin 4mg Tablet by M/s Martin Dow (Reg#037105)

	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
467.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Aultaroxit CR 12.5mg Tablet
	Composition	Each Film Coated Tablet Contains: Paroxetine Hcl Eq. to Paroxetine…12.5mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16491 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1902356)
	Pharmacological Group	SSRI
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Paxil CR 12.5mg Tablet by M/s Apotex Technologies, USA.
	Me-too status	Paroxin CR 12.5mg Tablet by M/s Sharooq Pharmaceuticals
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	The firm revised there form 5 and method of manufacturer from Each Film Coated Tablet Contains: Paroxetine Hcl Eq. to Paroxetine to Each enteric film coated controlled release tablet contains Paroxetine (as hydrochloride) which is according to the reference product with fee of 5000/- (#1926488) dated 17/8/2020
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved, Firm shall submit the fee of Rs. 30,000 for revision of formulation from film coated tablet to control release tablet as per notification No.F.7-11/2012 B&A/DRAP dated 13-07-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
468.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Diclo K 50mg Tablets
	Composition	Each Film Coated Tablet Contains: Diclofenac potassium…50mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16549 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1900798)
	Pharmacological Group	NSAID
	Form	Form-5
	Finished product Specifications	USP

	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Diclofenac Potassium 50mg Film Coated Tablets by M/s Accord Healthcare Limited, MHRA
	Me-too status	NOREX TABLETS 50mg tablets by M/s Alen Pharmaceuticals (Pvt) Ltd, Reg. No. 3172
	GMP status	DML issued on 5th March, 2019.
	Remarks of evaluator	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
469.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Letro 2.5mg Tablets
	Composition	Each Film Coated Tablet Contains: Letrozole…2.5mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14896 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902385)
	Pharmacological Group	Non-Steroidal aromatase inhibitor
	Form	Form-5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	FEMARA letrozole 2.5mg coated tablet by Novartis Pharmaceuticals Australia Pty Ltd (TGA Approved)
	Me-too status	Femara 2.5mg Tablet by Novartis (Reg. No. 021129)
	GMP status	DML issued on 5th March, 2019.
	Remarks of evaluator	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with USP specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
470.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Piroxiwen 20mg Tablets
	Composition	Each Tablet Contains: Piroxicam Betacyclodextrin…20mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 16520 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900765)
	Pharmacological Group	Non-Steroidal aromatase inhibitor
	Form	Form-5

	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	PIROXICAM G GAM 20 mg, scored table (ANSM approved)
	Me-too status	Piroxibet 20mg Tablets of M/s Lawari International (Reg. # 054939)
	GMP status	DML issued on 5th March, 2019.
	Remarks of evaluator	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
471.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Soda 200mg Tablets
	Composition	Each Film Coated Tablet Contains: Sodium Valproate…200mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 16518 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900763)
	Pharmacological Group	Antiepileptic
	Form	Form-5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	10x10's As per SRO
	Approval status of product in Reference Regulatory Authorities	Epilim 200 Gastro-resistant tablets (MHRA)
	Me-too status	Epilim E.C 200mg Tablet by Sanofi (#058501)
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	The firm revised there form 5 and method of manufacturer from Each Film Coated Tablet Contains: Sodium Valproate to Each gastro resistant coated tablet contains Sodium Valproate which is according to the reference product with fee of 5000/- (#2038553) dated 03/9/2020
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovators specification, Firm shall submit the fee of Rs. 30,000 for revision of formulation from film coated tablet to each gastro resistant tablet as per notification No.F.7-11/2012 B&A/DRAP dated 13-07-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	

472.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Quepine 150mg Tablet
	Composition	Each Film Coated Tablet Contains: Quetiapine as Fumarate…150mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16515 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900760)
	Pharmacological Group	Antipsychotic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	SEROQUEL® (quetiapine fumarate). USFDA approved
	Me-too status	Ziapine XR150mg Oral Tablets Reg. No. 78755
	GMP status	DML issued on 5th March, 2019.
	Remarks of evaluator	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
473.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Pentrex 40mg Tablets
	Composition	Each gastro resistant Tablet Contains: Pantoprazole as Sodium Sesquihydrate…40mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16492 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902357)
	Pharmacological Group	Proton pump inhibitor
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Pantoprazole 40 mg gastro resistant Tablet (MHRA Approved)
	Me-too status	Pantopraz 40mg Tablet M/s Klifton Pharma,
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	In RRA its gastro resistant not enteric coated so firm revised their formulation from enteric coated to gastro resistant tablet by paying fee of 5000/- (#1926490) dated 20 aug 2020.
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved, Firm shall submit the fee of Rs. 30,000 for revision of formulation from enteric coated tablet to gastro resistant tablet as per notification No.F.7-11/2012 B&A/DRAP dated 13-07-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
474.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Leflunomalt 20mg Tablets
	Composition	Each Film Coated Tablet Contains: Leflunomide…20mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16550 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900799)
	Pharmacological Group	Immunosuppressant
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	ARAVA 20 mg film-coated tablet by Sanofi (ANSM approved)
	Me-too status	Lefluno Tablet of M/s Caraway Pharma 050063
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
475.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Cipro 500mg Tablets
	Composition	Each Film coated Tablet Contains: Ciprofloxacin HCL Eq. to Ciprofloxacin…500mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 16538 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1900787)
	Pharmacological Group	Fluoroquinolones, Antibiotic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	Ciprofloxacin tablets 500mg of M/s Special Concept Development (UK MHRA Approved)
	Me-too status	Axcin Tablets 500mg of M/s Novartis Pharmaceuticals
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
476.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Artho 75/200 mg Tablets
	Composition	Each Film Coated Tablet Contains: Diclofenac Sodium…75mg Misoprostol…200mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16500 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902366)
	Pharmacological Group	Anti-rheumatic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Arthrotec 75 modified-release tablets by M/s Pfizer, MHRA approved
	Me-too status	Arsofin Tablets by M/s Martin Dow Pharmaceuticals (Pakistan) Ltd, Reg. no. 48013
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	Firm initially applied as Each Film Coated Tablet Contains Diclofenac sodium…..75mg Misoprostol…….200mcg Moreover, Misoprostol requires special storage Conditions 2-80C. On communication firm submit revised formulation as per the composition of reference product given in the following along with the submission of requisite fee of 5000/- (#1926474) dated 20 aug 2020; Each Film Coated Tablet Contains: Diclofenac Sodium (enteric coated core)…….…75mg Misoprostol (1% HPMC Dispersion)…..……..…200mcg In RRA the product is approved as inner enteric coated layer of diclofenac sodium surrounded by misoprostol dispersion coating but the firm applied as film coated tablet.
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Deferred for confirmation of manufacturing facility of bilayered tablet	
477.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan

	Brand Name +Dosage Form + Strength	Ceflar 250mg Tablets
	Composition	Each Film Coated Tablet Contains: Clarithromycin…250mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14902 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902266)
	Pharmacological Group	Macrolide
	Form	Form-5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Clarithromycin 250 mg of Sandoz (USFDA Approved)
	Me-too status	Clarmark 250mg tablet Of M/S Wel Mark Pharmaceutical
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator VII	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with USP specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
478.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Aultopride 50mg Tablets
	Composition	Each Film Coated Tablet Contains: Itopride HCL…50mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14903 dated 07-03-2019 Rs.20,000/- Dated 07-03-201 (#1902255)
	Pharmacological Group	Prokinatic
	Form	Form-5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Ganaton 50mg Tablet by Abbott (PMDA approved)
	Me-too status	Itoguard Tablet of M/s Macter International Karachi (Reg.#055753)
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator VII	The firm revised there form 5 and method of manufacturer from Itopride to Itopride HCL which is according to the reference product with fee of 5000/- (#1926489) dated 17/8/2020
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved, Firm shall submit the fee of Rs. 30,000 for revision of formulation from Itopride to Itopride HCL as per notification No.F.7-11/2012	

	B&A/DRAP dated 13-07-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
479.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Cipro 250mg Tablets
	Composition	Each Film coated Tablet Contains: Ciprofloxacin HCL Eq. to Ciprofloxacin…250mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14925 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902384)
	Pharmacological Group	Fluoroquinolones, Antibiotic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Ciprofloxacin tablets 250mg of M/s Special Concept Development (UK MHRA Approved)
	Me-too status	Axcin Tablets 250mg of M/s Novartis Pharmaceuticals
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
480.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Levo 500mg Tablets
	Composition	Each Film Coated Tablet Contains: Levofloxacin as hemihydrate…500mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14923 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902382)
	Pharmacological Group	Fluoroquinolones, Antibiotic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Levofloxacin Tablets 500mg of M/s Actavis Group United Kingdom (MHRA Approved)
	Me-too status	Leflox Tablets 500mg of M/s Getz Pharma
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	

481.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Stowel 10mg Tablets
	Composition	Each Film coated Tablet Contains: Escitalopram as Oxalate…10mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 14931 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902274)
	Pharmacological Group	Antidepressant (SSRIs)
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10, 14's As per SRO
	Approval status of product in Reference Regulatory Authorities	Escitalopram by cresent pharma Approved by MHRA of UK
	Me-too status	Zavesca tablet 10mg of Getz Pharma. (Reg.#045279)
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
482.	Name and address of manufacturer / Applicant	M/s Athan Pharmaceuticals. Plot 84/1, Block B, Phase 5, Industrial Estate, Hattar, Kpk, Pakistan
	Brand Name +Dosage Form + Strength	Dimecrotic Acid 50mg Tablets
	Composition	Each Film Coated Tablet Contains: Dimecrotic Acid…50mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 16539 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#1900788)
	Pharmacological Group	Gastrointestinal drugs Cholagogues & hepatic preparations
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed
	Me-too status	Hepadial 50mg TABLETS (Hilton Pharma), Reg. No. 16850
	GMP status	DML issued on 5th March, 2019.
	Remarks of Evaluator [VII]	Reference in RRA needed, provided reference of fisiobil spain can't be verified and in ANSM HEPADIAL 50 mg, coated tablet contains magnesium dimecrotate
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Deferred for Evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.	

483.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Osicare Plus Tablet
	Composition	Each Tablet Contains: Glucosamine sulphate…500mg Chondrotoin sulphate…400mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13374 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0845203)
	Pharmacological Group	Other antiinflammatory and antirheumatic agents, nonsteroids
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	2x10's As per SRO
	Approval status of product in Reference Regulatory Authorities	TGA; Australia Approved
	Me-too status	Gevolox Ch Tablets of M/s Hilton Pharma (Reg. # 039688)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	Previously firm applied as each Tablet Contains: Glucosamine sulphate…750mg Chondrotoin sulphate…600mg which is not present in RRA so firm revised its formulation as Each Tablet Contains: Glucosamine sulphate…500mg Chondrotoin sulphate…400mg according to RRA with due fee of 20,000/- (#1983273) dated 26 aug 2020. Firm also requested to change its brand name to "Jovecare tablets"
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved, Firm shall submit the remaining fee of Rs. 10,000 for revision of formulation as per notification No.F.7-11/2012 B&A/DRAP dated 13-07-2021 Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
484.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Afexdine 120mg Tablet
	Composition	Each Film Coated Tablet Contains: Fexofenadine Hcl…120mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13364 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900441)
	Pharmacological Group	Antihistamines for systemic use
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO

	Approval status of product in Reference Regulatory Authorities	Fexotabs 120 mg tablet Approved in TGA
	Me-too status	Epodin 120mg Tablet M/s Epoch Pharma (#52778)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
485.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Andreprol 100mg Tablet
	Composition	Each Film Coated Tablet Contains: Metoprolol Tartrate…100mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13378 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0845207)
	Pharmacological Group	Beta blocking agents, selective
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Metoprolol Tartrate 100 mg Film-coated Tablets. MHRA approved
	Me-too status	Dronic 100mg Tablets, film coated. Reg. No. 81425
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
486.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Alpharich 0.5mcg Tablet
	Composition	Each Tablet Contains: Alfacalcidol…0.5mcg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13362 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588348)
	Pharmacological Group	Beta blocking agents, selective
	Form	Form-5
	Finished product Specifications	Manufacturer
	Pack size & Demanded Price	As per SRO

	Approval status of product in Reference Regulatory Authorities	Alfacalcidol tablet 0.5mcg PMDA Japan approved
	Me-too status	Alfasta Tablet 0.5mcg by M/s Star Labs, Reg. No. 81398
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
487.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arremide 50mg Tablet
	Composition	Each Film Coated Tablet Contains: Lacosamide…50 mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13355 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588341)
	Pharmacological Group	Antiepilaptic
	Form	Form-5
	Finished product Specifications	Manufacture specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	VIMPAT® (lacosamide) Tablet, Film Coated USFDA Approved.
	Me-too status	Atcomid 50mg Tablet Atco Lab. Karachi. (Reg. # 075947)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
488.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arremide 100mg Tablet
	Composition	Each Film Coated Tablet Contains: Lacosamide…100mg

	Diary No. Date of R& I & fee	Form-5 Dy. No 13354 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588340)
	Pharmacological Group	Antiepileptic
	Form	Form-5
	Finished product Specifications	Manufacture specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Vimpat tablet of UCB Inc, USFDA Approved.
	Me-too status	Lacolep tablet of Hilton Pharma (Reg. No# 073858).
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
489.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arremide 150mg Tablet
	Composition	Each Film Coated Tablet Contains: Lacosamide…150mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13356 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588342)
	Pharmacological Group	antiepileptic
	Form	Form-5
	Finished product Specifications	Manufacture specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	VIMPAT® (lacosamide) Tablet, Film Coated USFDA Approved.
	Me-too status	Atcomid 150mg Tablet Atco Lab. Karachi. (Reg.#075949)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	

490.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Thioside 4mg Capsule
	Composition	Each Capsule Contains: Thiocolchicoside…4mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13346 dated 07-03-2019 Rs.20,000/- Dated 07-03-2 (#0846646)
	Pharmacological Group	Muscle Relaxants, Centrally Acting Agents
	Form	Form-5
	Finished product Specifications	Manufacture specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	MYOPLEGE 4 mg hard capsule of M/s GENEVRIER SA Laboratories approved by ANSM of France
	Me-too status	Muscodid 4mg Capsule M/s Regal Pharmaceuticals, Rawat (Reg #081968)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
491.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Afexdine 60mg Tablet
	Composition	Each Film Coated Tablet Contains: Fexofenadine Hcl…60mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13363 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588349)
	Pharmacological Group	Other antihistamines for systemic use
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	FEXOTABS fexofenadine hydrochloride 60mg tablet blister pack.TGA approved
	Me-too status	Vigil Tablets by Tabros Pharma. (Reg. No. 39776)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
492.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Andreprol 50mg Tablet
	Composition	Each Film Coated Tablet Contains: Metoprolol Tartrate…50mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13377 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902392)
	Pharmacological Group	Beta blocking agents, selective
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Metoprolol Tartrate 50 mg Film-coated Tablets. MHRA approved
	Me-too status	Mepresor 50mg Tablets, film-coated. Reg. No. 36124
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
493.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Afexdine 180mg Tablet
	Composition	Each Film Coated Tablet Contains: Fexofenadine Hcl…180mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13365 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900442)
	Pharmacological Group	H1 receptor antagonist
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Fexofenadine hydrochloride film coated tablet 180mg by M/s Cipla (MHRA Approved)
	Me-too status	Epodin 180mg Tablet by M/s Epoch Pharmaceutical, Reg. No. 58058
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
494.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Misonac Tablet
	Composition	Each Tablet Contains: Paracetamol…500mg Caffeine…65mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13349 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0846648)
	Pharmacological Group	Analgesic and CNS Stimulent
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	30's, 100's, and 200's As per SRO
	Approval status of product in Reference Regulatory Authorities	Panadol Extra Advance 500 mg/65 mg Film Coated Tablets by M/s GSK, MHRA Approved. Paracetamol and caffeine 500mg/65mg soluble tablets (MHRA Approved)
	Me-too status	Cafimol Extra Tablets uncoated. Zinta Pharmaceutical Industry (038898) Me-too Status Paratol Extra tablet by M/s Highnoon (Reg.# 13346)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
495.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Siliptin-M 50/500 mg Tablet
	Composition	Each Film Coated Tablet Contains: Sitagliptin as Sitagliptin Phosphate Monohydrate…50mg Metformin Hcl…500mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13365 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0845204)
	Pharmacological Group	Antidiabetic
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Janumet film coated tablet (50mg/500mg & 50mg/1000mg) by M/s MSD, USFDA Approved.

	Me-too status	Sitaglip-Plus Tablet 50/500 by M/s Maple Pharmaceuticals (Pvt) Ltd, Reg. No. 53403
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
496.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Siliptin-M 50/1000 mg Tablet
	Composition	Each Film Coated Tablet Contains: Sitagliptin as Sitagliptin Phosphate Monohydrate…50mg Metformin Hcl…1000mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13375 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0845205)
	Pharmacological Group	Anti diabetic
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Janumet film coated tablet (50mg/500mg & 50mg/1000mg) by M/s MSD, USFDA Approved.
	Me-too status	Sitaglip-Plus Tablet 50/1000 by M/s Maple Pharmaceuticals (Pvt) Ltd, Reg. No. 53404
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
497.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Utrobin 10mg Tablet
	Composition	Each Film Coated Tablet Contains: Solifenacin as Succinate…10mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13369 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900446)

	Pharmacological Group	Muscarinic antagonist
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Vesicare® (5mg& 10mg) film-coated tablet by M/s Astellas Pharma Ltd, MHRA Approved.
	Me-too status	Solifen Tablet 10mg by M/s GetzPharma, Reg. No. 61203
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
498.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Nebilol 5mg Tablet
	Composition	Each Film Coated Tablet Contains: Nebivolol as Hcl…5mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13338 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0846638)
	Pharmacological Group	Beta-1 receptor blocker
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Bystolic 5 mg Tablet (USFDA Approved)
	Me-too status	Nabil Tablets 5mgM/s. Getz Pharma
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
499.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi

	Brand Name +Dosage Form + Strength	Klomifen 50mg Tablet
	Composition	Each uncoated Tablet Contains: Clomifene Citrate…50mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13373 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900450)
	Pharmacological Group	Beta-1 receptor blocker
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	GENRX CLOMIPHENE clomifene citrate 50mg Uncoated TGA Approved.
	Me-too status	Florid 50mg Tablet M/s Opal Labs, Karachi 075806
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
500.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arecrip 2.5mg Tablet
	Composition	Each Tablet Contains: Bromocriptine as Mesylate…2.5mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13370 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900447)
	Pharmacological Group	Prolactine inhibitor/ Dopamine Receptor Agonist
	Form	Form-5
	Finished product Specifications	BP
	Pack size & Demanded Price	3x10's As per SRO
	Approval status of product in Reference Regulatory Authorities	Bromocriptine 2.5mg Tablets by M/s. Meda Pharma, MHRA approved
	Me-too status	Parlodel 2.5 mg tablet by M/s Novartis (Reg#004714)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Deferred for the evidence of required manufacturing facility. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
501.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arrizin 4mg Tablet
	Composition	Each Tablet Contains: Tizanidine as Hcl…4mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13336 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0846636)
	Pharmacological Group	Muscle relaxant
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's as per SRO
	Approval status of product in Reference Regulatory Authorities	Zanaflex® (tizanidine hydrochloride) uncoated tablets, USFDA Approved
	Me-too status	Tizax 4mg Tablet by Searle (#076022)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
502.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arractam 250 mg Tablet
	Composition	Each Film Coated Tablet Contains: Levetiracetam…250mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13360 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588343)
	Pharmacological Group	Anti-Epileptic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	Levetiracetam zentiva 250 mg of MHRA Approved
	Me-too status	Levep 250mg Tablet by Hilton Pharma (Reg. No. 053348
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
503.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arractam 750mg Tablet
	Composition	Each Film Coated Tablet Contains: Levetiracetam…750mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13358 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588345)
	Pharmacological Group	Anti-Epileptic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	KEPPRA tablets USFDA Approved
	Me-too status	Lepsira 750mg tablets by Scilife Pharma (Reg. 100439)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
504.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Arractam 1000mg Tablet
	Composition	Each Film Coated Tablet Contains: Levetiracetam…1000mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13359 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0588346)
	Pharmacological Group	Anti-Epileptic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's As per SRO
	Approval status of product in Reference Regulatory Authorities	KEPPRA (250mg, 500mg, 750mg, 1000mg) film coated tablets USFDA Approved
	Me-too status	Elicia 1000mg Tablet of Martin Dow (Reg.#081157)
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
505.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Utrobin 5mg Tablet
	Composition	Each Film Coated Tablet Contains: Solifenacin as Succinate…5 mg
	Diary No. Date of R& I & fee	Form-5 Dy. No 13368 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1900445)
	Pharmacological Group	Muscarinic antagonist
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Vesicare (5mg& 10mg) film-coated tablet by M/s Astellas Pharma Ltd, MHRA Approved.
	Me-too status	Solifen Tablet 5mg by M/s GetzPharma, Reg. No. 61202
	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovators specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
506.	Name and address of manufacturer / Applicant	M/s Arreta Pharmaceuticals Pvt Ltd. Plot No. 13, Street N-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Misonac plus Tablet
	Composition	Each Tablet Contains: Paracetamol…500mg Caffeine…65mg Chlorpheniramine (Maleate)…….2 mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 13349 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#1902392)
	Pharmacological Group	Analgesic and CNS Stimulent
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status	Hesmol Extra tablets of Wisdom Pharmaceuticals

	GMP status	Last inspection report dated 22-05-2018 concluded that the firm was found to be GMP compliant.
	Remarks of Evaluator [VII]	Evidence in RRA
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Deferred for evidence of approval of the applied product in reference regualtory authorities/agencies which were declared/approved by Registrtaion Board in its 275th meeting.	
507.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Gentasis 80mg/2ml Ampoule
	Composition	Each 2ml Vial Contains: Gentamicin as Gentamicin Sulphate…80mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 10765 dated 05-03-2019 Rs.20,000/- Dated 05-03-2019 (#0703856)
	Pharmacological Group	Aminoglycoside Antibacterial
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	25's As per SRO
	Approval status of product in Reference Regulatory Authorities	Cidomycin 80mg/2ml Solution for Injection (5 x 2ml colourless glass ampoules (Type I) by M/s Aventis Pharma Limited (MHRA Approved)
	Me-too status	Refobacin 80mg/2ml Injection by AD Marker Quetta (Reg. #006473)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
508.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Lexus 20 mg
	Composition	Each 2ml Vial Contains: Furosemide…20mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17387 dated 07-03-2019 Rs.20,000/- Dated 05-03-2019 (#0826527)
	Pharmacological Group	Loop Diuretics
	Form	Form-5
	Finished product Specifications	JP
	Pack size & Demanded Price	2 ml As per SRO

	Approval status of product in Reference Regulatory Authorities	Furosemide 20mg /2ml solution for Injection (MHRA approved)
	Me-too status	Lasix Injection of Sanofi Aventis (Reg#000230)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
509.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Metolide 10mg/2ml Ampoule
	Composition	Each 2ml Ampoule Contains: Metoclopramide as Metoclopramide Hcl…10mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17392 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0761625)
	Pharmacological Group	Antiemetic
	Form	Form-5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in US-FDA
	Me-too status	Vominor 10mg Injection of Nortech Pharmaceuticals
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021.Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
510.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Atropine 1mg/ml Injection
	Composition	Each ml Ampoule Contains: Atropine Sulphate…1mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17388 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0761616)
	Pharmacological Group	Anti- cholinergic

	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Atropine Sulfate Injection 1mg in 1 ml (MHRA)
	Me-too status	Atropine Injection By M/s. Alina: 049677
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
511.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	D-Spa 40mg/2ml Injection
	Composition	Each 2ml Ampoule Contains: Drotaverine Hcl…40mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17396 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019 (#0839015)
	Pharmacological Group	Antispasmodic
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in 3 European countries
	Me-too status	NO-SPA INJECTION. Reg No. 08296
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021.Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
512.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Ketamile 500mg/10ml Ampoule
	Composition	Each 10ml Vial Contains: Ketamine as Ketamine Hcl…500mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17395 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826521)
	Pharmacological Group	General anesthetics (N01AX03)

	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10ml glass ampoule, As per SRO
	Approval status of product in Reference Regulatory Authorities	Ketalar USFDA Approved 10-mL multi-dose vial
	Me-too status	Ketarol Injection 50mg/ml M/s Global Pharmaceuticals, Islamabad; 026630
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	In RRA its in Vial
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
513.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Avebion Ampoule
	Composition	Each 3ml Ampoule Contains: Thiamine Hcl…100mg Pyridoxine Hcl…100mg Cyanocobalamin…1000mcg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17379 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826520)
	Pharmacological Group	B-complex vitamin
	Form	Form-5
	Finished product Specifications	Manufacturer specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Neurobion Injection by M/s Merck (Germany) Merck
	Me-too status	Neurobion Injection by Merck (Reg. No. 001485)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications with shelf life of 12 Months. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021.Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
514.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan

	Brand Name +Dosage Form + Strength	Gravisis 50mg/ml Injection
	Composition	Each 1ml Ampoule Contains: Dimenhydrinate …50mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17383 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826524)
	Pharmacological Group	Antiemetic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Dimenhydrinate Injection of Fresenius Kabi, USFDA Approved.
	Me-too status	Corinate 50mg/ml Inj. of Asian continental (Reg#057863).
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of Formulation for nine sections:
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
515.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Piromax 20mg/ml Injection
	Composition	Each ml Ampoule Contains: Piroxicam…20mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17389 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0761613)
	Pharmacological Group	Anti-rheumatic
	Form	Form-5
	Finished product Specifications	Manufacturers specification
	Pack size & Demanded Price	5's As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved by ANSM of France
	Me-too status	Salden 20mg Injection of M/s Danas Pharma (Reg.#080373)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. **Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years**	

516.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Transit 500mg/5ml Injection
	Composition	Each 5ml Ampoule Contains: Tranexamic Acid…500mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17373 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826522)
	Pharmacological Group	Antifibrinolytic
	Form	Form-5
	Finished product Specifications	BP
	Pack size & Demanded Price	5's, 10's, 20's as per SRO
	Approval status of product in Reference Regulatory Authorities	CYKLOKAPRON 500mg Solution for Injection by M/s Pfizer Limited, MHRA
	Me-too status	Tremic -500 Injection of M/s M/s Fynk Pharmaceuticals,
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. **Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years**	
517.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Transit 250 mg/5ml Injection
	Composition	Each 5ml Ampoule Contains: Tranexamic Acid…250mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17374 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826523)
	Pharmacological Group	Antifibrinolytic
	Form	Form-5
	Finished product Specifications	JP
	Pack size & Demanded Price	5's, 10's, 20's As per SRO
	Approval status of product in Reference Regulatory Authorities	PMDA approved
	Me-too status	Dravix 250mg/5ml Injection of Getz Pharma Karachi
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
518.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Ketrolav 30mg/ml Ampoule
	Composition	Each ml Ampoule Contains: Ketrolac Trometamol…30mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17382 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826526)
	Pharmacological Group	Anti-inflammatory and Anti-rheumatic Products, Non-Steroids
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	5's, 25's As per SRO
	Approval status of product in Reference Regulatory Authorities	Tora-Dol 30 mg/ml AIFA Approved
	Me-too status	Orkit Injection IV Aulton Pharmaceuticals (080560)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
519.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Kinza 20mg/ml Ampoule
	Composition	Each 1ml Ampoule Contains: Nalbuphine Hcl…20mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17390 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0841037)
	Pharmacological Group	Potent analgesic.
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	5's, 25's As per SRO
	Approval status of product in Reference Regulatory Authorities	NUBAIN – (nalbuphine hydrochloride) injection (1ml ampule), for intramuscular, subcutaneous, or intravenous (USFDA).
	Me-too status	Nalfy Injection 20mg. Reg. No. 81911
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn

	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
520.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	D-Fenac 75mg/3ml Injection
	Composition	Each 3ml Ampoule Contains: Diclofenac Sodium…75mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17380 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0826525)
	Pharmacological Group	NSAID
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	5's, 25's As per SRO
	Approval status of product in Reference Regulatory Authorities	NUBAIN – (nalbuphine hydrochloride) injection for intramuscular, subcutaneous, or intravenous (USFDA).
	Me-too status	Nalfy Injection 20mg. Reg. No. 81911
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
521.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Adrenaline 0.1% Injection
	Composition	Each Ampoule Contains: Adrenaline…1mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17378 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0761617)
	Pharmacological Group	adrenergic
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	100's As per SRO
	Approval status of product in Reference Regulatory Authorities	Adrenaline solution for ijection (MHRA)
	Me-too status	Adrenaline injection by Elite (#026237)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant

		of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021.Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
522.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Codomax 500/15 mg Tablet
	Composition	Each Tablet Contains: Paracetamol…500mg Codeine phosphate hemihydrate…15mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17385 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0841047)
	Pharmacological Group	Opioid analgesic
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	100's As per SRO
	Approval status of product in Reference Regulatory Authorities	Co-codamol 15/500 Tablets of Zentiva Pharma UK Limited
	Me-too status	Lowmol Tablets (Reg. 040426) of Lowit Pharma (Pvt) Ltd
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	In RRA Codeine phosphate hemihydrate not just codien No master formulation and method of manufacturer
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Deferred for the following; • **Submission of method of manufacturign and master formulation.** • **Submission of correct label claim since the reference product contains Codeine Phosphate Hemihydrate while you have applied for Codiene (base) only.**	
523.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Montysis 4mg Sachet
	Composition	Each Sachet Contains: Montelukast as Montelukast Sodium oral granules …4mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17385 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0841018)

	Pharmacological Group	Leukotriene antagonist
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's, 14's As per SRO
	Approval status of product in Reference Regulatory Authorities	Singulair Sachet 4mg Granules of Merck, USFDA
	Me-too status	Montiget Sachet of M/s Getz Pharma (Reg.# 044046
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	
524.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Estern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Stilmix 10mg Tablet
	Composition	Each Film Coated Tablet Contains: Zolpidem Tartrate…10mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17385 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0813648)
	Pharmacological Group	Sedative
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	10's, 14's As per SRO
	Approval status of product in Reference Regulatory Authorities	Stilnoct (5mg, 10mg) film-coated Tablets by M/s Sanofi, MHRA Approved.
	Me-too status	Olida 10mg Tablets of M/s Glitz Pharmaceuticals, Islamabad (Reg.# 081418)
	GMP status	Inspection dated 28-11-2018 for DML, CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Deferred for confirmation of requisite manufacturing facility that is Tablet Psychotropic Section.	
525.	Name and address of manufacturer / Applicant	M/s Avensis Pharmaceuticals. F-24/1, Eastern Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Kinza 10mg/ml Ampoule
	Composition	Each 1ml Ampoule Contains:

		Nalbuphine Hcl…10mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 17391 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019 (#0841036)
	Pharmacological Group	Potent analgesic.
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	5's, 25's As per SRO
	Approval status of product in Reference Regulatory Authorities	NUBAIN – (nalbuphine hydrochloride) injection for intramuscular, subcutaneous, or intravenous (USFDA).
	Me-too status	Sonotic injection of M/s Brookes Pharma (Reg. # 057729)
	GMP status	CLB in its 267th meeting held on 31st Dec, 2018 has considered and approved the grant of DML to Avensis Pharmaceuticals by way of formulation for nine sections
	Remarks of Evaluator [VII]	
	Previous Decision (M296)	Deferred for consideration on its turn
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500 for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012- B&A/DRAP dated 07-05-2021. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years	

Case no. 02 Registration applications of drugs for which stability study data is submitted
Registration applications for Form 5F

a) newly granted DML or New section (Human)

Case No. 01: M/s Sayyed Pharmaceutical (Pvt) Ltd,67/2, Phase 3, Industrial estate, hattar, Haripur. M/s M/s Sayyed Pharmaceutical (Pvt) Ltd,67/2, Phase 3, Industrial estate, hattar, Haripur has been granted additional section Tablet section (Psychotropic) section) dated 07-04-2020 by Licensing division DRAP. Now the firm has submitted following applications as per the details mentioned in the table below: Tablet section (Psychotropic): 01 Molecules / 01 Products		
526.	Name, address of Applicant / Marketing Authorization Holder	M/s Sayyed Pharmaceutical (Pvt) Ltd,67/2,Phase 3,Industrial estate,hattar,Haripur.
	Name, address of Manufacturing site.	M/s Sayyed Pharmaceutical (Pvt) Ltd,67/2,Phase 3,Industrial estate, hattar, Haripur.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 6512859933 dated 17/09/2021
	Details of fee submitted	PKR 30,000/-: dated 31/08/2021
	The proposed proprietary name / brand name	Zolsyd 10mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film Coated tablet contains: Zolpidem tartrate…….10mg
	Pharmaceutical form of applied drug	White, Round shaped, bisect film coated tablet
	Pharmacotherapeutic Group of (API)	Imidazopyridine
	Reference to Finished product specifications	USP
	Proposed Pack size	2×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ambien 10mg tablet (USFDA Approved).
	For generic drugs (me-too status)	Somnia 10 mg Tablet by M/s Wilshire
	GMP status of the Finished product manufacturer	New Section approved on 09/04/2020 Tablet (Psychotropic)
	Name and address of API manufacturer.	M/s Cambrex Profarmaco Milano S.R.L Via Curiel,34-20067 Paullo-Milano, Italy.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Zolpidem tartrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A & related substance, (N,N-Dimethyl-2-(7-methyl-2-p-tolylimido[1,2-a]pyridine-3-yl)acetamide specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies of API	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (010101), (010202), (010303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Comparator product that is Downox 10mg tablet by Martin Dow by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Downox 10mg tablet by Martin Dow in Acid media (pH 1.2) (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
	Remarks: The formulation is same as innovator 2.3.P.5.2 In USP the time of dissolution is 15 minutes but firm mentioned time as 45 minutes and at some places 30 minutes Injection volume 10 ul instead of pharmacopeia 100 ul In 3.2.S.4.2 analytical procedure no details of dissolution is there	

STABILITY STUDY DATA			
Manufacturer of API	M/s Cambrex Profarmaco Milano S.R.L Via Curiel,34-20067 Paullo-Milano, Italy.		
API Lot No.	188439		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial-01	Trial-02	
Batch Size	5000 tab	5000 tab	
Manufacturing Date	03-2021	03-2021	
Date of Initiation	31-03-2021	31-03-2021	

No. of Batches		02
Administrative Portion		
31.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
32.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. II-API/44/H/2019 issued by Italian Medicine Agency.
33.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No. F.5-4/2020-CD (M-71)dated 11/11/2020 for the purpose of test/analysis and stability studies is granted. • Invoice No.1000002020 dated 18/12/2020
34.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
35.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
36.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S No	Section #.	Deficiencies	Reply
1.	1.6.5	Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin is needed as the provided one is valid till January 2021	GMP Certificate valid till 30-1-2022 was provided
2.	3.2.P.4.5	Regarding query that Excipients of Human or Animal Origin shall be addressed for the use of "Magnesium stearate" in the applied formulation For excipients of human or animal origin, a certificate shall be provided, confirming that the excipient(s) are free from BSE and TSE. the firm provided the certificate from "Peter geven" that this magnesium stearate is from plant source	COA of magnesium stearate attached. No contamination with TSE/BSE –Rist materials

<table>
<tr><td>3.</td><td>3.2.P.4.5</td><td>The detailed analytical procedure of active pharmaceutical ingredient details of dissolution is provided in 3.2.P.5.2 in the analysis procedure of finished product</td><td>Provided</td></tr>
<tr><td>4.</td><td>3.2.P.5</td><td>In USP the time of dissolution is 15 min but firm mentioned time as 45 minutes and at some places 30 minutes. Justification is needed</td><td>Firm has following USP dissolution test 1 in which dissolution time is 15 minutes. firm as followed same dissolution time as 15 minutes as per USP throughout the stability study till now and same 15 minutes in mentioned as analytical reports. Also 15 minutes mentioned in analytical procedure</td></tr>
<tr><td>5.</td><td>3.2.P.5</td><td>In assay the injection volume prescribed inn USP is 25 ul but firm used 100 ul. justification is needed</td><td>100 µl injection loop is fixed from the manufacturer with our HPLC. By using 100ul injection volume concentration of standard and sample increased 4 time to injection volume mentioned in USP i.e 25 ul and proportionally area also increased of standard and sample which obey beer lambert law, which states that there is linear relation between concentration and absorbance of a solution.
By Using 100 µl, RSD of standard in the assay is less than 2%, which is within the limit
In method verification of linearity, study was conducted on increased concentration (Data submitted)</td></tr>
<tr><td>6.</td><td></td><td>• As per relevant guidelines & structure of Form 5F, Comparative Dissolution profile and comparative assay has to be performed at the time of formulation development, while according to your submitted data, Comparative Dissolution profile studies and comparative assay have been performed after commencing stability studies. Justification shall be submitted.</td><td>As analysis of formulation development was finished before two days of CDP end date, that’s why that date on which formulation development analysis was finished, was considered as initial stability date
<table>
<tr><th>Strength</th><th>Formulation development analysis finished date</th><th>CDP end date</th></tr>
<tr><td>0.5 mg</td><td>01/03/2021</td><td>03/03/2021</td></tr>
<tr><td>0.25 mg</td><td>17/03/2021</td><td>19/03/2021</td></tr>
<tr><td>1 mg</td><td>24/03/2021</td><td>25/03/2021</td></tr>
</table></td></tr>
</table>

7.		Letter of approval for import of narcotic/psychotropic substance for manufacturing of trial batches and conduction of stability studies	Firm provides the Letter # 5-1/2021-CD(M73) of approval for import of narcotic/psychotropic substance (Clonazepam) for manufacturing of trial batches and conduction of stability studies

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of Pharmaceutical equivalence and Comparative Dissolution Profile against innovator drug product.**

Case No. 01: M/s Shaigan Pharmaceuticals Limited, Post Office Dahgal, 14-Km Adyala Road Rawalpindi.
has been granted additional facility of dry powder section dated 13 january 2022 by Licensing division DRAP. Now the firm has submitted following applications as per the details mentioned in the table below:
01 Molecules / 01 Products

527.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Shaigan Pharmaceuticals Limited, Post Office Dahgal, 14-Km Adyala Road Rawalpindi.**
	Name, address of Manufacturing site.	M/s Shaigan Pharmaceu9 36ticals (Pvt.) Ltd. 14-Km Adyala road, Post office Dahgal, Rawalpindi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	GMP certificate issued on 8/12/2021
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 13-01-2022 which specifies Oral Dry powder suspension (general) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No: 5413 25/02/2022
	Details of fee submitted	PKR 30,000/-: 25/02/2022 (#255776532)

	The proposed proprietary name / brand name	Famot Dry Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml (after reconstitution) contains: Famotidine……40mg
	Pharmaceutical form of applied drug	Dry suspension
	Pharmacotherapeutic Group of (API)	H_2 Receptors antagonists
	Reference to Finished product specifications	USP specification
	Proposed Pack size	50ml, 60ml, 90ml, 120ml
	Proposed unit price	As per S.R.O
	The status in reference regulatory authorities	"PEPCID" Approved by Merck & CO.,INC,USA
	For generic drugs (me-too status)	APSIN (Reg. No.: 046460) manufactured by Safron Pharmaceuticals (19 km Sheikhupura Road Faisalabad Pakistan.)
	Name and address of API manufacturer.	**Famotidine** Vaasavaa Pharamceuticals Pvt. Ltd Plot NoC-216,MIDC,Chincholi,Solapur-413 255,Maharashtra India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions duration of Stability studies)	**Famotidine:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 60 months.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence Profile	Pharmaceutical Equivalence Studies Profile has been done against reference product of Zapsin Dry Suspension

STABILITY STUDY DATA

Manufacturer of APIs	**Famotidine** Vaasavaa Pharmaceuticals Pvt. Ltd plot NoC-216,MIDC,Chincholi,Solapur-413 255,Maharashtra India		
API Lot No.	**Famotidine:** 2002475		
Description of Pack (Container closure system)	Amber color bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-0003
Batch Size	1000	1000	1000
Manufacturing Date	05.2019	05.2019	05.2019
Date of Initiation	05.2019	05.2019	05.2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to their last inspection report for Emdagan 10mg & 20mg Tablets conducted on 10-06-2021, approved in 307th meeting of Registration Board. Following are details of few points; • The HPLC software is 21CFR Compliant. • Audit trail reports were available and physically checked by the inspection team. • Firm has adequate monitoring and controls for stability chambers. • Software is installed for continuous monitoring of chambers.

<table>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Famotidine:
Copy of GMP issued in the name of Vaasavaa Pharamceuticals Pvt. Ltd Plot NoC-216,MIDC,Chincholi,Solapur-413 255,Maharashtra India., valid upto 19-07-2022</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API
with approval from DRAP (in case of
Import).</td><td>Copy of commercial invoice attested by AD I&E DRAP has been submitted.
Famotidine:
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>FAM-1120183</td><td>EPY20-21/335</td><td>200 Kg</td><td>04/12/2020</td></tr>
</table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with Chromatograms, raw data sheets, COAs and summary data sheets.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Firm has submitted 21 CFR evidence and audit trail reports of product testing.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature & humidity monitoring of stability chambers
(real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
</table>

Remarks OF Evaluator:
Analysis is according to USP

S.No	Section	Deficiency/Remarks	Reponses
1.		Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Famotidine: Copy of GMP issued in the name of Vaasavaa Pharamceuticals Pvt. Ltd Plot NoC-216,MIDC,Chincholi,Solapur-413 255,Maharashtra India., valid upto 19-07-2022
2.	3.2.P.2.5	The microbial attributes and preservative effectiveness study is required	Submitted
3.	3.2.P.8.3	Submission of Volume of diluent for reconstitution along with justification (weight/ml calculation) with reference to innovator/reference product.	Details of Volume of diluent (45 ml) for reconstitution along with justification with reference to innovator/reference product is submitted
4.	3.2.P.	Submission of Stability data of reconstituted suspension up to proposed shelf life is submitted	Stability data of reconstituted suspension up to proposed shelf life of 30 days is submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of Pharmaceutical equivalence with either innovator or brand leader if innovator is not available in Pakistan.**

Enzon Pharma Labs Pvt Ltd, 5 km off Raiwind Manga Road, Lahore
CLB in its 273 meeting held on 15th January 2020 has considered and approved the grant of DML by way of
Formulation. Now firm has applied for following products.

528.	Name, address of Applicant / Marketing Authorization Holder	Enzon Pharma Labs Pvt Ltd 5 km off Raiwind Manga Road, Lahore
	Name, address of Manufacturing site.	Enzon Pharma Labs Pvt Ltd 5 km off Raiwind Manga Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 396 dated 5/01/2022
	Details of fee submitted	PKR 30,000/-: dated 09/08/2021
	The proposed proprietary name / brand name	Ensol- Metro 0.5% IV Infusion 100 mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100 mL contains: Metronidazole…….....0.5% w/v
	Pharmaceutical form of applied drug	Intravenous Injection
	Pharmacotherapeutic Group of (API)	Other IV Solution Additives ATC CODE: J01XD01
	Reference to Finished product specifications	BP
	Proposed Pack size	100 mL LDPE bottle **w/ Eurocap**
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Metronidazole 500 mg / 100 ml Intravenous Infusion Baxter Healthcare Ltd. Caxton Way Thetford Norfolk IP24 3SE, UK

	For generic drugs (me-too status)	Flagyl Injection **Sanofi- aventis Pakistan Limited** Plot 23, Sector 22 Korangi Industrial Area, Karachi
	GMP status of the Finished product manufacturer	New DML Approved. Last inspection conducted on 15 & 16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Name and address of API manufacturer.	Hubei Hongyuan Pharmaceutical Technology Co., Ltd., No.428, Yishui North Road, Fengshan Town, Luotian County, Hubei Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted relevant information against the Module III, including Process validation protocol, Finished product analytical method validation report & stability studies data of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (031201, 031202 and 031203)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted Pharmaceutical equivalence study of their product with Flagyl injection". Batch # AH324 of M/S Sanofi Aventis Comparative dissolution studies are not applicable

	Analytical method validation/verification of product	Method verification studies has been submitted including accuracy, precision, specificity and robustness.	
STABILITY STUDY DATA			
Manufacturer of API	Hubei Hongyuan Pharmaceutical Technology Co., Ltd., No.428, Yishui North Road, Fengshan Town, Luotian County, Hubei Province, China		
API Lot No.	0182007017		
Description of Pack (Container closure system)	100 mL LDPE Bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	A	B	C
Batch Size	100 L	100 L	100 L
Manufacturing Date	29-07-2020	29-07-2020	29-07-2020
Date of Initiation	30-07-2020	30-07-2020	30-07-2020
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Certificate (Certificate No. # HB20180424) for Hubei Hongyuan Pharmaceutical Technology Co., Ltd., No.428, Yishui North Road, Fengshan Town, Luotian County, Hubei Province, China issued by China food & Drug Administration valid up to 30-07-2023 is submitted	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy invoice (invoice# HTIE20-155SQ) dated: 04-07-2020 from for Hubei Hongyuan Pharmaceutical Technology Co., Ltd., No.428, Yishui North Road, Fengshan Town, Luotian County, Hubei Province, China cleared by DRAP Lahore office dated 19-07-2020.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks Of Evaluator:

S. No	Sections	Observations/Deficiencies/ Short-comings	Response by the Firm
1.	3.2.P.8	Commercial invoice of Metronidazole was provided by Shaoxing Hantai import and export Co Ltd. not Hubei Hongyuan Pharmaceutical Technology Co., Ltd. Clarification is needed	The commercial invoice of Metronidazole being issued by Shaoxing Hantal Import & Export Co, Ltd because they are the importer and material is procured with approval from DRAP
2.	1.5.9	Reference of previous approval of applications with stability study data of the firm (if any)	Ensol- NS 0.9% (25ml, 100ml, 500ml, 1000ml) Ensol- WFI (5ml, 10ml, 20ml) Ensol- 5% (100ml, 500ml, 1000ml) Ensol- DS (500ml, 1000ml) Ensol- RL (500ml, 1000ml)
3.	3.2. P.2.2.1	Justify why the pharmaceutical equivalence was established against comparator product instead of using innovator / reference product.	The comparison of the developed formulation is against the comparator product because CTD guidelines clearly mentioned that the applicant may compare their product with the innovator / reference / comparator product
4.	3.2.P.2.3	Scientific justification is required regarding the temperature and duration of sterilization in autoclave, sterilization of applied product has been done at 106 °C for 1 hour while the conventional condition is 121°C for 15min.	Relevant Guidelines for terminal sterilization allow the performance of steam sterilization by applying reduce temperature and time other than that of reference condition i.e., ≥ 121°C, ≥ 15 min, while considering the nature of product and container closure system Following two conditions shall be ensured while applying steam sterilization other than that of the reference conditions. Minimum sterilization cycle of F° ≥ 8 minutes. Sterility assurance level (SAL) of 10-6 is achieved. As evident form of the submitted data, the SAL of

			10-6 has been achieved while applying temperature of 106°C for 60 minutes, hence fulfilling the mandatory requirements of guidelines
5.	3.2. P.5.2	Provide detailed analytical procedure of Bacterial Endotoxin Testing test and sterility test of drug product	The detailed analytical procedure of sterility test of drug product is submitted
6.		Analysis is by UV spectrophotometer as per BP requirements	The detailed of Analytical procedure of metronidazole infusion as per BP requirements is submitted

Decision: Approved.

• Manufacturer will place first three production batches on long term stability studies throughout
proposed shelf life and on accelerated studies for six months as per the commitment submitted in
the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

529.	Name, address of Applicant / Marketing Authorization Holder	Enzon Pharma Labs Pvt Ltd 5 km off Raiwind Manga Road, Lahore
	Name, address of Manufacturing site.	Enzon Pharma Labs Pvt Ltd 5 km off Raiwind Manga Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1008 dated 11/01/2022
	Details of fee submitted	PKR 30,000/-: dated 09/08/2021
	The proposed proprietary name / brand name	Ensol- 25% IV Infusion 1000 mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each mL contains: Glucose Anhydrous…….250mg
	Pharmaceutical form of applied drug	Intravenous Injection
	Pharmacotherapeutic Group of (API)	Other IV Solution Additives ATC CODE: V06DC01
	Reference to Finished product specifications	BP

	Proposed Pack size	1000 mL LDPE with Eurocap
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose 25% Intravenous Infusion BP of **Baxter Healthcare Pty Ltd.** 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA
	For generic drugs (me-too status)	Sterifluid- 25 (Intravenous Infusion BP) **Frontier Dextrose Ltd.** Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan
	GMP status of the Finished product manufacturer	New DML Approved. Last inspection conducted on 15 & 16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Name and address of API manufacturer.	Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted relevant information against the Module III, including Process validation protocol, Finished product analytical method validation report & stability studies data of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (W20150514, W20150515 and W20150516)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pledex 25% dextrose solution by Otsuka Pakistan (1000 ml) verified by section.
	Analytical method validation/verification of product	Method verification studies has been submitted including accuracy, precision, specificity and robustness.

STABILITY STUDY DATA			
Manufacturer of API	Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China.		
API Lot No.	20200427-2		
Description of Pack (Container closure system)	1000 mL LDPE Bottle with eurocap		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	A	B	C
Batch Size	100 L	100 L	100 L
Manufacturing Date	24-07-2020	24-07-2020	24-07-2020
Date of Initiation	25-07-2020	25-07-2020	25-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Certificate (Certificate No. # SD20180787) for Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China issued by China food & Drug Administration valid up to 14-10-2023 is submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy invoice (invoice# WFST312) dated: 28-04-2020 from Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China cleared by DRAP Lahore office dated 01-06-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks Of Evaluator:

Me too Pledex 25% dextrose solution by Otsuka Pakistan (1000 ml) was verified by section.

S. No	Sections	Observations/Deficiencies/ Short-comings	Reply
1.	1.5.9	Evidence of approval / registration / marketing status of the applied formulation in the same composition, salt form and dosage form in one of the reference regulatory authority specified by Registration Board.	The product is registered in same composition, salt and dosage form in TGA Australia Glucose 25% 1000 ml by Baxter healthcare Australia
2.	1.5.9	Reference of previous approval of applications with stability study data of the firm (if any)	Ensol-///ns 0.9% (25 ml, 100ml, 500ml, 1000ml) Ensol-RL (500ml,1000ml)
3.	3.2. S.4.3	• Submitted Analytical Method Verification report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter for Glucose anhydrous. • Describe sample preparation procedure for performance of precision parameter for Glucose anhydrous.	Submitted Analytical Method Verification report
4.	3.2. S.4.4	• COA of drug substance Glucose anhydrous from drug substance manufacturer include pyrogen Testing and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but same test has not been included in the COA of drug substance from drug product manufacturer. • Evidence of availability of HPLC equipped with refractometer and column oven to maintained the temperature at 85°C as per the chromatographic condition given in BP.	The updated COA of drug substance from drug product manufacturer is provided along with supporting documents
5.	3.2. S.5	COA of reference standard of anhydrous glucose is submitted,	Firm has submitted that the COA of reference standard of Glucose

		while according to BP glucose hydrous chemical reference standard is used to analyze the quality of glucose anhydrous. Justification is required for using glucose anhydrous reference standard for the assay.	anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.
6.	3.2.P.2.3	Scientific justification is required regarding the temperature and duration of sterilization in autoclave, sterilization of applied product has been done at 106 °C for 1 hour while the conventional condition is 121°C for 15min.	Relevant Guidelines for terminal sterilization allow the performance of steam sterilization by applying reduce temperature and time other than that of reference condition i.e., ≥ 121°C, ≥ 15 min, while considering the nature of product and container closure system .Following two conditions shall be ensured while applying steam sterilization other than that of the reference conditions. Minimum sterilization cycle of F° ≥ 8 minutes. Sterility assurance level (SAL) of 10-6, is achieved. As evident form of the submitted data, the SAL of 10-6 has been achieved while applying temperature of 106°C for 60 minutes, hence fulfilling the mandatory requirements of guidelines
7.	3.2. P.5.2	Provide detailed analytical procedure of Bacterial Endotoxin Testing test and sterility test of drug product	Provided
8.		Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard.	Firm submitted the separate stability data for 1000ml volume with the statement that "Same stability data was submitted for 500ml &1000ml erroneously by our analyst, hence we are submitting the actual stability data results for each pack size separately. We regret the Inconvenience caused in this regard."
9.	3.2. P.5.3	• Submitted Analytical Method Verification report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter for glucose anhydrous	Firm has submitted the following reply: • The details of accuracy parameter of drug product is given below. • ACCURACY/ RECOVERY • Prepared the three replicates of ENSOL- 25% INFUSION with the active • drug from 95% to 105% of the label claim by taking 4.75g for 95%, 5.0g for

			• 100% and 5.25g for 105% in each 100ml volumetric flasks. Recover the • spiked amount by analyzing these samples as per analytical procedure. The • figure No.2 will be help full in this regard. • Acceptance Criteria: -The recovery should be 100 ± 2.0% across 95–105% • of target concentrations

Decision: Approved.

• Manufacturer will place first three production batches on long term stability studies throughout
proposed shelf life and on accelerated studies for six months as per the commitment submitted in
the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

530.	Name, address of Applicant / Marketing Authorization Holder	Enzon Pharma Labs Pvt Ltd 5 km off Raiwind Manga Road, Lahore
	Name, address of Manufacturing site.	Enzon Pharma Labs Pvt Ltd 5 km off Raiwind Man ga Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 6638 dated 10 March/2022 (New license)
	Details of fee submitted	PKR 30,000/-: dated 22 February 2022
	The proposed proprietary name / brand name	Ensol- Cipro 0.2% IV Infusion 100mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100mL contains: Ciprofloxacin as Ciprofloxacin Lactate …….....0.2%w/v
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Antibacterial agents ATC CODE: J01MA02
	Reference to Finished product specifications	BP
	Proposed Pack size	100mL

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	CIPROFLOXACIN 2MG/ML INFUSION by Pfizer Limited. (MHRA)
	For generic drugs (me-too status)	Reflox Infusion of M/s Regal Pharmaceutical
	GMP status of the Finished product manufacturer	New DML Approved. Last inspection conducted on 15 & 16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Name and address of API manufacturer.	Zhejiang Guobang Pharmaceutical Co., Ltd. No.06, Weiwu Road, Hangzhou Zhejiang China
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted relevant information against the Module III, including Process validation protocol, Finished product analytical method validation report & stability studies data of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (110504-1, 110505-1 and 110506-1)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence Bacip Inf 200mg /100 ml by surge pharma batch # AH324

	Analytical method validation/verification of product	Method verification studies has been submitted including accuracy, precision, specificity and robustness.		
STABILITY STUDY DATA				
Manufacturer of API		Zhejiang Guobang Pharmaceutical Co., Ltd. No.06, Weiwu Road, Hangzhou Zhejiang China		
API Lot No.		190707		
Description of Pack (Container closure system)		100mL LDPE bottle w/ Eurocap		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		A	B	C
Batch Size		100 L	100 L	100 L
Manufacturing Date		14-07-2020	14-07-2020	14-07-2020
Date of Initiation		15-07-2020	15-07-2020	15-07-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Ensol- NS 0.9% (25ml, 100ml, 500ml, 1000ml) Ensol- WFI (5ml, 10ml, 20ml) Ensol- 5% (100ml, 500ml, 1000ml) Ensol- DS (500ml, 1000ml) Ensol- RL (500ml, 1000ml)		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Certificate (Certificate No. # ZJ20190170) for Zhejiang Guobang Pharmaceutical Co., Ltd. No.06, Weiwu Road, Hangzhou Zhejiang China issued by China food & Drug Administration valid up to 29-11-2024 is submitted		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy invoice (invoice# 20NVT-183) dated: 16-04-2020 from Shanghai Nuvit bio- tech co ltd china cleared by DRAP Lahore office dated 29-04-2020.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted		

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks Of Evaluator:

 USP-Injection monograph
 BP-Infusion monograph
Firm use same analytical method according to BP
Master formula has ciprofloxacin lactate and lactic acid while BP monograph states that ciprofloxacin infusion is a sterile solution prepared by the interaction of ciprofloxacin and lactic acid.
Excipients change as compare to RRA
Documents for the procurement of API with approval from DRAP (in case of import)

S. No	Sections	Observations/Deficiencies/ Short-comings	Reply
1.	1.5.9	Evidence of approval / registration / marketing status of the applied formulation in the same composition, salt form and dosage form in one of the reference regulatory authority specified by Registration Board.	The link is attached for your kind attention. https://mhraproducts4853.blob.core.windows.net /docs/78150360f4c25d036caca70cb71988061dbd6efd
2.		Master formula has ciprofloxacin lactate and lactic acid while BP monograph states that ciprofloxacin infusion is a sterile solution prepared by the interaction of ciprofloxacin and lactic acid.	Packaging material of the applied formulation is LDPE and is different from the reference product which is PVC bag contained in a polypropylene/polyester aluminium/polyester pouch. No explanations regarding method of manufacturing
3.	1.33	The address of manufacturer on invoice is Shanghai Nuvit bio- tech co ltd china instead of Zhejiang Guobang Pharmaceutical clarification is needed in this regard.	The reason for the commercial invoice of Ciprofloxacin Lactate being issued by shanghai Nuvit biotech co ltd china is provided
4.	(2.3.S.4.3)	Provide summarized tabulated results of verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer	Submitted
5.	***2.3.P.4***	The excipients are different from the reference product in MHRA. Justification n is needed	The reference having same excipients is provided https://mhraproducts4853.blob.core.windows.net /docs/78150360f4c25d036caca70cb71988061dbd6efd

6.	3.2. P.2.2.1	Justify why the pharmaceutical equivalence was established against comparator product instead of using innovator / reference product.	The comparison of the developed formulation is against the comparator product because CTD guidelines clearly mentioned that the applicant may compare their product with the innovator / reference / comparator product. The reference of CTD guidelines is given
7.	3.2.P.2.3	Scientific justification is required regarding the temperature and duration of sterilization in autoclave, sterilization of applied product has been done at 106 °C for 1 hour while the conventional condition is 121°C for 15min.	Relevant Guidelines for terminal sterilization allow the performance of steam sterilization by applying reduce temperature and time other than that of reference condition i.e., ≥ 121°C, ≥ 15 min, while considering the nature of product and container closure system. Following two conditions shall be ensured while applying steam sterilization other than that of the reference conditions. • Minimum sterilization cycle of F° ≥ 8 minutes. • Sterility assurance level (SAL) of 10-6 , is achieved. As evident form of the submitted data, the SAL of 10-6 has been achieved while applying temperature of 106°C for 60 minutes, hence fulfilling the mandatory requirements of guidelines Reference: EMA guidelines on the sterilization of the medicinal product, active substance, excipient and primary container. (EMA/CHMP/CVMP/QWP/850374/2015)
8.	3.2. P.5.2	Provide detailed analytical procedure of Bacterial Endotoxin Testing test and sterility test of drug product	Submitted

Decision: Approved.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

- **Registration letter will be issued after submission of Pharmaceutical equivalence against innovator drug product.**

Case No.01. Correction in Label Claim/ Strength of Approved Products of M/s Adamjee Pharmaceuticals (Pvt) Ltd., Plot 39, Sector 15, Korangi Industrial Area Karachi (DML No. 000236)

Registration Board in its 308th meeting held on 21st-22nd June, 2021 approved the following products of M/s Adamjee Pharmaceuticals Pvt Ltd. Plot 39, Sector 15, Korangi Industrial Area, Karachi (DML No. 000236) as per below mentioned details:

1.	Name and address of manufacturer / Applicant	Applicant: M/s Adamjee Pharmaceuticals Pvt Ltd. Plot 39, Sector 15, Korangi Industrial Area, Karachi Manufactured By: M/s Safe Pharmaceuticals Pvt Ltd. Plot No. C.I-20, Sector 6-B, Industrial Area, North Karachi
	Brand Name +Dosage Form+ Strength	Adpime Injection **500mg** (IV/IM)
	Diary No. Date of R& I & fee	Dy.No 41935 dated 07-12-2018 Rs.50,000/- Dated 07-12-2018
	Composition	Each vial of dry substance contains: Cefepime as HCL (with L-Arginine)…**1000mg**
	Pharmacological Group	Cephalosporin
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Cefipime hydrochloride 1gm Injection M/s Hospira, Inc. (USFDA approved)
	Me-too Status	Nuxipim 1gm Injection by M/s Bosch, Reg. No. 44357
	GMP Status	Same as stated above
	Remarks of the Evaluator.	
	Decision of 295th meeting: Deferred for following: a. Submission of details of products which are already being manufactured on contract. b. Capacity assessment report of M/s safe Pharma, Karachi by already constituted panel **Decision: Approved.**	
2.	Name and address of manufacturer / Applicant	Applicant: M/s Adamjee Pharmaceuticals Pvt Ltd. Plot 39, Sector 15, Korangi Industrial Area, Karachi Manufactured By: M/s Safe Pharmaceuticals Pvt Ltd. Plot No. C.I-20, Sector 6-B, Industrial Area, North Karachi
	Brand Name +Dosage Form+ Strength	Adpime Injection **500mg** IM Powder for injection
	Diary No. Date of R& I & fee	Dy.No 41931 dated 07-12-2018 Rs.50,000/- Dated 07-12-2018
	Composition	Each vial of dry substance contains: Ceftriaxone Sodium eq to Ceftriaxone…**250mg**
	Pharmacological Group	Cephalosporin
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Ceftriaxone powder for injection (250mg, 500mg, 1000mg, 2000mg) by M/s Bowmed limited, MHRA Approved.
	Me-too Status	Trimark 250mg Injection IM by M/s WelMark Reg. No. 69750

	GMP Status	Same as stated above
	Remarks of the Evaluator.	
	Decision of 295th meeting: Deferred for following: a. Submission of details of products which are already being manufactured on contract. b. Capacity assessment report of M/s safe Pharma, Karachi by already constituted panel **Decision: Approved.**	

Registration letter could not be issued due to disparity in strengths mentioned in composition and alongside the brand name.

In this context original dossier could not be retrieved from available record, however, the firm has submitted copies of DRAP's acknowledged receipts & fee challans of 250mg and 500mg strengths of both formulations. Furthermore, approval for registration of Cefepime Injection 1000mg and Ceftriaxone Injection 250mg have also been issued by the Registration Board in its 308th meeting.

Accordingly, the case has been placed for correction in strengths of above-mentioned products which appears to be due to cut-paste/ typographical error.

Proceedings of 320th Meeting:

Registration Board was further apprised regarding correction required in composition/ label claim of product at S.No.1 as the reference/ standard formulation approved by RRA contains "Cefepime (as Hydrochloride Monohydrate) 1000mg"

Decision: Registration Board decided as under:

i. **Approved correction in strength and composition of product at S.No.1 as per following detail:**

   Adpime Injection 500mg
   Each vial contains:
   Cefepime as Hydrochloride Monohydrate (with L-Arginine)……500mg
   (USP Specifications)

ii. **Approved correction in strength/ label claim of product at S.No.2 as per following detail:**

   Adpime Injection 250mg IM
   Each vial contains:
   Ceftriaxone Sodium Eq. to Ceftriaxone……250mg
   (USP Specifications)

iii. **Furthermore, for product at S.No.1, the applicant shall submit fee of Rs. 75,000/- in the light of notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 for pre-registration correction in composition/label claim.**

Case No.02. Correction in Label Claim/ Dosage Form of Approved Products of M/s Swiss Pharmaceuticals (Pvt) Ltd., A-159, S.I.T.E Super Highway Karachi (DML No. 000438).

Registration Board in its 295th meeting held on 08th-11th June, 2020 approved the following products of M/s Swiss Pharmaceuticals Pvt Ltd., A-159, S.I.T.E Super Highway, Karachi (DML No. 000438) as per below mentioned details:

1.	Name and address of manufacturer Applicant	M/s Swiss Pharmaceuticals Pvt Ltd. A-159, S.I.T.E Super Highway, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Letam 100mg/ml **Oral Solution**
	Composition	Each 1 ml **ampoule** contains: Levetiracetam…100 mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 9264 dated 28-02-2019 Rs.20,000/- Dated 28-02-2019 (#0621840)
	Pharmacological Group	Antiepilaptic
	Form	Form-5
	Finished product Specifications	USP

	Pack size & Demanded Price	5 ml (**vial**) As per SRO
	Approval status of product in Referen Regulatory Authorities	KEPPRA (levetiracetam) **injection**, for intravenous use. (USFDA)
	Me-too status	Lerace **Injection** 500mg/5ml/ Reg. No. 66949
	GMP status	M/s: Swiss Pharma Last GMP inspection conducted on 18-10-2018.and report concludes overall current GMP compliance level is rated as good.
	Remarks of Evaluator [VII]	
	Decision: Approved.	

Registration letter could not be issued due to disparity in dosage form mentioned alongside the brand name and as evident from label claim/ demanded pack/ RRA reference and generic product reference.

In this context original dossier could not be retrieved from available record, however, the firm has informed that they applied for complete range of "Levetiracetam" containing dosage forms including:

- 250mg & 500mg Tablets (approved and registered vide M-293),
- 100mg/ml Oral Solution (approved and registered vide M-295) and
- 100mg/ml Injection which was mistakenly quoted under the name of Oral Solution with same diary No. However, deposit slip No., applied pack, RRA and generic status are correctly mentioned in minutes.

As evidence, the firm has also submitted copies of acknowledgement receipts, fee challans of both applications (i.e., Oral solution and Injection) & duplicate dossier of "Letam 100mg/ml Injection" and requested for issuance of registration letter with following details:

Svetri Injection 100mg/ml (Already registered name for Levetiracetam)
Each ml contains:
Levetiracetam……..100 mg
(USP Specifications)

Accordingly, the case has been placed for correction in dosage form of above-mentioned product which appears to be due to cut-paste/ typographical error.

Decision: **Registration Board approved correction in label claim/ dosage form of above-mentioned product as per following detail:**
Letam Injection 100mg/ml
Each ml contains:
Levetiracetam……..100 mg
(USP Specifications)

Case No.03. Correction in Decision of 316th Meeting of Registration Board

Registration Board in its 316th meeting held on 15th-18th March, 2022 approved the following product of The Searle Company Limited F-319, S.I.T.E., Karachi as per below mentioned details. However, below-mentioned product was not included in the decision recorded.

592.	**Name, address of Applicant / Marketing Authorization Holder**	**The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.**
	Name, address of Manufacturing site.	The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 17245 dated 21-06-2021
	Details of fee submitted	Rs.50,000/- dated 29-03-2021
	The proposed proprietary name / brand name	**Emsyn-Met XR 5mg + 1000mg Tablets**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Emsyn-Met XR Tablets Each Film coated tablet contains: Empagliflozin……...5mg Metformin hydrochloride (Extended Release)…….1000mg
	Pharmaceutical form of applied drug	Apple Green colored, Oblong shaped, Biconvex, Film coated Tablets, Plain from both sides
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	In-House
	Proposed Pack size	1×14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by US FDA and marketed in USA, with the name of Synjardy XR Tablets
	For generic drugs (me-too status)	Xenglu-Met XR Manufactured by Hilton Pharma (Pvt.) Ltd **Strength:** Empagliflozin 5mg + Metformin 1000mg **Reg. No**.105268
	GMP status of the Finished product manufacturer	New license granted on 13/08/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** Anhui Youcare Kaiyue Pharmaceutical Co., Ltd. Industrial Avenue area A, Economic Development Zone, Taihe County, Anhui Province, China **Metformin HCL** Aarti Drugs Limited Mahendra Industrial Estate Plot No. – 109 –D Road No.29, Sion (East), Mumbai – 400 022. INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Empagliflozin** Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20151116, 20151208, 20160104) Stability study conditions: **Metformin HCL** Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(MEF/1510145, MEF/1510146, MEF/1510147)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Synjardy XR Tablet US FDA Approved by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Synjardy XR Tablet US FDA Approved in Acid media (pH 1.2) & Phosphate Buffer (PH 4.5) And (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.
STABILITY STUDY DATA		
Manufacturer of API	Emagliflozin:	

	Anhui Youcare Kaiyue Pharmaceutical Co., Ltd. Industrial Avenue area A, Economic Development Zone, Taihe County, Anhui Province, China		
Manufacturer of API	**Metformin HCl** Aarti Drugs Limited Mahendra Industrial Estate Plot No. – 109 –D Road No.29, Sion (East), Mumbai – 400 022. INDIA		
API Lot No. (Emagliflozin)	20190501001		
API Lot No: (Metformin HCL)	MEF/10020674		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0,3, 6, 9, 12, 18 & 24m (Months)		
Batch No.	20PD-088	20PD-089	20PD-090
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	April 2020	April 2020	April 2020
Date of Initiation	Jun 2020	Jun 2020	Jun 2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted documents for Reference of Previous Approval
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**EMPAGLIFLOZIN** **GMP Certificate** of Empagliflozin Manufacturer: Anhui Youcare Kaiyue Pharmaceutical Co., Ltd Valid Till: 5-3-2023 **METFORMIN HCL:** **GMP Certificate** of Metformin HCl from Aarti Drugs Limited Valid Till: 19-3-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**EMPAGLIFLOZIN** **Invoice** From Timesnow international Co.Ltd Quantity: 1 Bag Batch: 20190501001 Mfg Date: 14-May-2019 Exp: 13 May 2021 **METFORMIN HCL:** **Invoice** From Arti Drug Ltd Quantity: 3000Kg Batch: MEF/ 1002067 MEF/10020674

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator[II]:

Section #	Observations	Firm's response
	Empagliflozin	
3.2. S.4.1	• Analytical procedure and specifications applied by the drug product manufacturer shall be submitted. • The specifications and analytical procedure submitted from the drug substance manufacturer does not contain test for Assay.	• Firm has submitted analytical procedure as per the method applied by the drug substance manufacturer. • Complete analytical method including test of Assay has been submitted from drug substance manufacturer.
3.2. S.4.3	Analytical method verification studies shall be submitted performed by the drug product manufacturer.	Firm has submitted analytical method verification report, performed by M/s Searle.
3.2. S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture.	Submitted as per following details. **Drug substance** — **Batch#** Emagliflozin — 20190501001
3.2. S.5	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted.
	Metformin HCl	
3.2. S.4.1	• Analytical procedure and specifications applied by the drug product manufacturer shall be submitted. • The specifications and analytical procedure submitted from the drug substance manufacturer does not contain test for Assay.	• Firm has submitted analytical procedure as per the method applied by the drug substance manufacturer. • Complete analytical method including test of Assay has been submi

3.2. S.4.3	Analytical method verification studies shall be submitted performed by the drug product manufacturer.	Firm has submitted analytical method verification report, performed by M/s Searle.
3.2. S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture.	Submitted as per following details. **Drug substance** — **Batch#** Metformin HCl — MEF/10020674
3.2.S.5	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted.
3.2.P.1	• Role of each excipient shall be submitted. • Innovator product formulation includes Polyethylene oxide, whereas it is not included in the applied formulation.	With the reference of query, this is to inform you that Polyethylene Oxide is highly sensitive to oxidation leading to chain cleavage of reduction of viscosity during storage. High temperature speeds up the autooxidation of Polyethylene Oxide and can impact its stability. Due to these properties of Polyethylene Oxide and its short shelf life, Hypromellose was taken in EmsynMet XR tablet and dissolution profile has been achieved by a single polymer. Polyethylene Oxide and Hypromellose are both hydrophilic extended-release matrices and use as the rate-controlling polymer. The benchmark of the innovator product, Janumet XR 1000mg tablet also includes only Hypromellose as a rate-controlling polymer.
3.2.P.2	Drug excipient compatibility study shall be submitted since composition of Metformin core tablet is different from that of the innovator product.	The above excipients had been chosen on the basis of core formulation of Metformin HCl XR tablet of innovator product, Janumet XR tablet which shows these excipients are compatible with Metformin HCl.
3.2.P.5.2	Submitted analytical procedure does not include the details for the test of "Content Uniformity" for Empagliflozin.	Drug product analytical method has been submitted including test of content uniformity.
3.2.P.5.3	Specificity parameter has been performed by injecting the placebo, diluent, mobile phase & standard solution. Whereas USP chapter <1225> & ICH Q2 (R1) guidelines suggests spiking the drug substance with appropriate levels of impurities or exposing the drug product sample to relevant stress conditions (e.g.,	Firm has submitted data for stress conditions i.e., heat, acid hydrolysis, base hydrolysis and oxidation as per ICH guidelines and USP chapter 1225 to demonstrate that the method is capable to identify and quantify the degraded compounds.

	light, humidity, acid or base hydrolysis, oxidation). Justification shall be submitted for this variation in method. Clarification shall be submitted for this variation.	
3.2. P.6	Working standard of Empagliflozin has been standardized against the reference standard from M/s Beijing Huikang Boyuan, whereas the drug substance has been procured from the M/s Anhui Youcare Kaiyue Pharmaceutical Co., Ltd. Justification shall be submitted in this regard.	We, The Searle Company Limited has been manufacturing the Empagliflozin Tablets 10mg and Empagliflozin Tablets 25mg since 2019. Beijing Huikang Boyuan is one the approved source for Empagliflozin that's why trail of standardization include the reference standard from the source other than Anhui Youcare Kaiyue.
	• Justification of 10% extra amount of Empagliflozin in master formulation (which is required to be based on study/scientific rationale) for which firm has stated that it was taken to compensate the loss during coating. • Quantity of batch after active coating, mentioned in the product development record is not correct. • The submitted product development record does not reflect performance of dissolution for Metformin HCl before proceeding for seal & active coating step. Justification shall be submitted for proceeding further without establishing the Dissolution profile of Metformin HCl. • The submitted product development record does not reflect performance of Uniformity of dosage units test by way of Assay for Empagliflozin before proceeding for final film coating step. Justification shall be submitted for proceeding further without establishing the content of Empagliflozin.	• In normal routine coating process, there is always some loss of coating dispersion as 100% coating material doesn't reach the tablet rather some quantity gets loss during spraying of coating due to continuous coating air blowing and exhaust. This loss is compensated by taking extra coating material and same is the case with Empagliflozin. It is coated over the tablets in the form of coating dispersion. That's why 10% extra quantity of API coating material has been taken. • In correct quantity of batch after active coating is a typographical error. Firm has submitted product development record with correct quantity. • We, The Searle Company Limited has established dissolution profile during trial that's why we perform dissolution testing at final stage. • We, The Searle Company Limited, performed content uniformity test as per routine practice at final stage i.e., after film coating.

Decision: Registration Board approved the applications of "Emsyn-Met XR 12.5mg + 1000mg Tablets", "Emsyn-Met XR 10mg + 1000mg Tablets", "Emsyn-Met XR 25mg + 1000mg Tablets" & "Emsyn-Met XR 25mg + 1000mg Tablets" with Innovator's specifications.

- Firm shall submit fee of Rs. 7,500 for each product for correction/pre-approval change in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
- Manufacturer will place first three commercial batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.
- Manufacturer will perform process validation of first three commercial batches as per the commitment submitted in the registration application.

Keeping in view the complete details of the case presented in 316th meeting, registration letter was issued, however, the case has been placed for information and record of Registration Board.

Decision: Registration Board noted the correction in minutes of 316th meeting regarding approval of Emsyn-Met 5mg + 1000mg Tablet which could not be recorded in decision.

Case No.04. Request of M/s GSK Consumer Healthcare Pakistan Limited, Jamshoro (DML No. 000010) for De-Registration of Paradon Tablets (Reg. No. 083992)

M/s GSK Consumer Healthcare Pakistan Limited, Petaro Road, Jamshoro (DML No. 000010) has requested for de-registration of Paradon Tablets (Reg. No. 083992) as per following details:

S/N	Reg. No.	Brand name and composition	Justification	Date of Reg. & Last Renewal Status
I	II	III	IV	V
1.	083992	Paradon 500mg Tablet Each tablet contains:- Paracetamol …….. 500 mg (BP Specification)	The product is similar in nature to one of our already registered products. Therefore, considering local regulations and requirements, we would like to apply for the de-registration of this product.	DOR: 20-04-2017 (in the name of M/s GSK OTC (Pvt) Ltd., Petaro Road, Jamshoro) Last Renewal Submission: 28-03-2022

Decision: Keeping in view the current need of paracetamol containing formulations, Registration Board did not accede to the request regarding de-registration of Paradon (Paracetamol) 500mg Tablet. The Board further advised the firm to ensure market availability of the product.

Case No.05. Request of M/s Abbott Laboratories (Pakistan) Limited, Opposite Radio Pakistan Transmission Centre Hyderabad Road Landhi, Karachi (DML No. 000001) for Withdrawal of Application for Discontinuation of Brufen Plus Tablet (Reg. No.044415)

M/s Abbott Laboratories (Pakistan) Limited, Opposite Radio Pakistan Transmission Centre Hyderabad Road Landhi, Karachi (DML No. 000001) has requested for withdrawal of their previously submitted application for discontinuation of Brufen Plus Tablet (Reg. No.044415) due to commercial reason.

Previously submitted application for discontinuation of Brufen Plus Tablet was presented before the Board in its 313th meeting as per following detail:

Intimation for Discontinuation of Registered Product of M/s Abbott Laboratories (Pakistan) Limited, Opposite Radio Pakistan Transmission Center, Hyderabad Road, Landhi, Karachi

S/N	Reg. No.	Brand Name and Composition	Justification	Date of Reg. & Last Renewal Status
1.	044415	Brufen Plus Tablet 200mg/20 Each tablet contains: Ibuprofen……..……200mg Codeine…….20mg	The firm has Ibuprofen range in Market and also the brand leader under the same segment, therefore due to commercial reasons we are discontinuing marketing of this combination.	DOR: 30-11-2006 Last Renewal Submission: 19-09-2016
Documents submitted by the firm in the light of SOP approved vide 283rd meeting of Registration Board		a. Copy of Registration Letter & Last Renewal Status. b. List of alternate brands available in the country (**Not Provided**). c. Justification. d. An Undertaking that (**Not Provided**): i. No case is pending at any forum/ court of law regarding above mentioned products. ii. Provided information/ documents are true/ correct.		
Decision of M-313:		***Registration Board deferred the case and advised to further deliberate the matter with availability committee and share the outcome with Registration Board for consideration.***		

The firm has further informed that they have also submitted renewal of registration dated 28-03-02022.

Decision: **Registration Board acceded to the request of M/s Abbott Laboratories (Pakistan) Limited, Opposite Radio Pakistan Transmission Centre Hyderabad Road Landhi, Karachi (DML No. 000001) regarding withdrawal of their previously submitted application for discontinuation of Brufen Plus Tablet (Reg. No.044415) and the Board further advised the firm to ensure market availability of the product.**

Case No.06. **Request of M/s Fedro Pharmaceutical Labs (Pvt.) Ltd. 149-Industrial Estate Jamrud Road Peshawar (DML No. 000238) for Withdrawal of Registrations of Cephalosporin Tablet Section.**

M/s Fedro Pharmaceutical Labs (Pvt.) Ltd. 149-Industrial Estate Jamrud Road Peshawar (DML No. 000238) has requested for withdrawal of registrations of Cephalosporin Tablet Section as per following details:

S/N	Reg. No.	Brand name and composition	Justification	Date of Reg. & Last Renewal Status
I	**II**	**III**	**IV**	**V**
1.	068494	Fedixime Tablets 100mg Each tablet contains:- Cefixime Trihydrate Eq. to Cefixime ……100mg (USP Specification)	Certain changes have been made in premises layout by replacing "Cephalosporin Tablet Section" with "Ware House (Cephalosporin)". Same layout has been approved by	DOR: 26-03-2011 Last Renewal Submission: 04-04-2016
2.	068495	Fedixime Tablets 200mg Each tablet contains:- Cefixime Trihydrate Eq. to Cefixime …….200mg		DOR: 26-03-2011 Last Renewal Submission:

		(USP Specification)	Licensing Division vide letter dated 22-09-2021. Therefore, the firm do not have requisite manufacturing facility.	04-04-2016
3.	068496	Fedixime Tablets 400mg Each tablet contains:- Cefixime Trihydrate Eq. to Cefixime …….400mg (USP Specification)		DOR: 26-03-2011 Last Renewal Submission: 24-03-2021
4.	073334	Cephdro Tablets 250mg Each tablet contains:- Cephradine ……..…250mg (USP Specification)		DOR: 06-09-2012 Last Renewal Submission: 11-09-2017
5.	073335	Cephdro Tablets 500mg Each tablet contains:- Cephradine ……..…500mg (USP Specification)		DOR: 06-09-2012 Last Renewal Submission: 11-09-2017

Decision: Registration Board acceded to the request of M/s Fedro Pharmaceutical Labs (Pvt.) Ltd. 149-Industrial Estate Jamrud Road Peshawar (DML No. 000238) and decided to cancel the registration of following products due to non-existence of requisite manufacturing facility [i.e., Tablet (Cephalosporin) Section]:

S/N	Reg. No.	Brand Name and Composition
I	**II**	**III**
1.	**068494**	**Fedixime Tablets 100mg Each tablet contains:- Cefixime Trihydrate Eq. to Cefixime ……100mg (USP Specification)**
2.	**068495**	**Fedixime Tablets 200mg Each tablet contains:- Cefixime Trihydrate Eq. to Cefixime …….200mg (USP Specification)**
3.	**068496**	**Fedixime Tablets 400mg Each tablet contains:- Cefixime Trihydrate Eq. to Cefixime …….400mg (USP Specification)**
4.	**073334**	**Cephdro Tablets 250mg Each tablet contains:- Cephradine ……..…250mg (USP Specification)**
5.	**073335**	**Cephdro Tablets 500mg Each tablet contains:- Cephradine ……..…500mg (USP Specification)**

Case No.07. Request of M/s GlaxoSmithKline Pakistan Limited, Karachi for De-Registrations of Products.

M/s GlaxoSmithKline Pakistan Limited, Karachi has requested for de- registrations of their following products which are registered for local manufacturing at their different sites:

Request For De- Registration of Local Products By M/s GlaxoSmithKline Pakistan Limited, F-268, S.I.T.E, Karachi (DML No.000233)

S/N	Reg. No.	Brand Name and Composition [Fee Detail]	Justification	Alternate Brands	Date of Reg. & Renewal Status
I	II	III	IV	V	VI
1.	038906	Grivin Oral Suspension Each 5ml contains:- Griseofulvin micronized USP….125mg [Fee of Rs.7500/- (DS#22844021924)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market. ➢ Better/ new molecules to cater the same portfolio are also available in the market. ➢ Virtually there is no demand of this product in local market.	➢ Fonaz by M/s Atco ➢ Icon by M/s Ferozsons ➢ Grisol by M/s Lisko	DOR: 04-07-2005 (M/s Martin Dow, Lahore) Transfer of Registration: **No evidence submitted** Last Renewal Submission: 18-08-2016
2.	000400	Dependal-M Tablets Each tablet contains: Furazolidone……100 mg Metronidazole……300 mg [Fee of Rs.7500/- (DS#58136242233)]		➢ Furamid of M/s Satnley ➢ Mefudol of M/s Hizat ➢ Metric of M/s Polyfine	DOR: 22-11-1984 (M/s Smith Kline & French of Pakistan, Karachi) Last Renewal Submission: 04-09-2018
3.	003709	Dependal-M Suspension Each 5ml contains: Furazolidone……25 mg Metronidazole…..…75 mg Pection……..50 mg Kaolin……1gm [Fee of Rs.7500/- (DS#41413795)]		➢ Furamid of M/s Satnley ➢ Mefudol of M/s Hizat ➢ Metric of M/s Polyfine	DOR: 22-11-1984 (M/s Smith Kline & French of Pakistan, Karachi) Last Renewal Submission: 04-09-2018
4.	008382	Marzine syrup Each 5ml contains: Cyclizine HCl B...12.5mg [Fee of Rs.7500/- (DS#29964802684)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market.	➢ Medizine of M/s Mediceena **Similar Anti-emetic:** ➢ Gravinate of M/s Searle ➢ Hydrinate of M/s Lisko	DOR: 18-06-1985 (M/s Wellcome Pakistan, Karachi) Last Renewal Submission: 20-07-2018

5.	027800	Acti fen Tablets 200mg Each tablet contains:- Ibuprofen……..200mg [Fee of Rs.7500/- (DS#35609524)]	➢ Better/ new molecules to cater the same portfolio are also available in the market. ➢ Virtually there is no demand of this product in local market.	➢ Brufen of M/s Abbott ➢ Ibugesic of M/s Wilsons ➢ Amrofen of M/s Amros	DOR: 05-09-2002 Last Renewal Submission: 04-09-2018
6.	027801	Acti fen Tablets 400mg Each tablet contains:- Ibuprofen……..400mg [Fee of Rs.7500/- (DS#7257793003)]		➢ Brufen of M/s Abbott ➢ Ibugesic of M/s Wilsons ➢ Amrofen of M/s Amros	DOR: 05-09-2002 Last Renewal Submission: 04-09-2018
7.	027802	Acti fen Tablets 600mg Each tablet contains:- Ibuprofen……..600mg [Fee of Rs.7500/- (DS#19855017810)]		➢ Brufen of M/s Abbott ➢ Ibugesic of M/s Wilsons ➢ Amrofen of M/s Amros	DOR: 05-09-2002 Last Renewal Submission: 04-09-2018
8.	027803	Acti fen Suspension Each 5ml contains:- Ibuprofen……..100mg [Fee of Rs.7500/- (DS#8435862281)]		➢ Brufen of M/s Abbott ➢ Ibugesic of M/s Wilsons ➢ Amrofen of M/s Amros	DOR: 05-09-2002 Last Renewal Submission: 04-09-2018
9.	000301	Cytacon Liquid [Fee of Rs.7500/- (DS#447547949772)]		➢ Vitacon-12 of M/s Polyfine	DOR: 20-04-1976 Last Renewal Submission: 20-07-2018
10.	015027	Atarax Syrup Each 5ml contains: Hydroxyzine Dihydrochloride….10 mg [Fee of Rs.7500/- (DS#2495238877)]		➢ Artosin of M/s Paramount	DOR: 29-04-2015 Last Renewal Submission: 17-08-2020
11.	006662	Wellcosine Syrup Triamine HCl…5mg Riboflavin ……1.66mg Pyridoxine HCl….1mg Nicotinamide…..20mg D-Panthenol…….2.5mg Cyanocobalamin..10mcg		➢ Vidaylin L of M/s Abbott. ➢ Unicap of M/s Johnson & Johnson	DOR: 17-01-1985 (M/s Wellcome Pakistan, Karachi)

		Inositol…….5mg Lysine Mono-HCl..35mg Ascorbic Acid….75mg [Fee of Rs.7500/- (DS#21864836712)]		➢ Camovit L of M/s Mendoza	<u>Last Renewal Submission:</u> 04-09-2018
12.	000395	Stelabid Tablets [Fee of Rs.7500/- (DS#33885803)]		**<u>Similar Therapeutic Class</u>** ➢ Librax of M/s Martin Dow ➢ No-Spa of M/s Sanof-Aventis ➢ Buscopan of M/s Martin Dow	<u>DOR:</u> 22-03-1976 (M/s Smith Kline & French, Karachi) <u>Last Renewal Submission:</u> 03-08-2018
13.	075850	Coarbid 80/480mg Tablets Each tablet contains:- Artemether …….80mg Lumefantrine …….480mg (Manufacturer's Specification) [Fee of Rs.7500/- (DS#47566764966)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market. ➢ Better/ new molecules to cater the same portfolio are also available in the market. ➢ Virtually there is no demand of this product in local market.	➢ Defal of M/s Abbott. ➢ MalEra of M/s Barret Hodgson ➢ Qmetem of M/s Bosch	<u>DOR:</u> 10-04-2013 <u>Last Renewal Submission:</u> 15-02-2018
14.	013321	Nemazole Suspension Each 5ml contains: Mebendazole…….100 mg [Fee of Rs.7500/- (DS#22670025150)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market.	➢ Vermox of M/s Aspin ➢ Vermin of M/s Adamjee ➢ Vermol of M/s Woodward s	<u>DOR:</u> 25-05-1992 <u>Transfer of Reg.</u> From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi: 30-08-2003

			➢ Better/ new molecules to cater the same portfolio are also available in the market. ➢ Virtually there is no demand of this product in local market.		Last Renewal Submission: 20-07-2018
15.	017306	Nemazole-500 Chewable Tablets Each tablet contains: Mebendazole…….500 mg [Fee of Rs.7500/- (DS#27602172255)]			DOR: 21-06-1995 Transfer of Reg. From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi: 30-08-2003 Last Renewal Submission: 20-07-2018
16.	013320	Neamzole Tablets Each tablet contains: Mebendazole…….100 mg [Fee of Rs.7500/- (DS#369542115677)]			DOR: 25-05-1992 Transfer of Reg. From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi: 30-08-2003 Last Renewal Submission: 20-07-2018
17.	000219	Orbenin Syrup 125mg/ml [Fee of Rs.7500/- (DS#89493492)]		➢ Aksopril by M/s Akson Pharma	DOR: 16-04-1976 Transfer of Reg. From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi: 30-08-2003 Last Renewal Submission: 20-07-2018
18.	000217	Penbritin Paediatric Drops 100mg/ml [Fee of Rs.7500/- (DS#9951636180)]		➢ Omnipen of M/s Pfizer ➢ Standacillin by M/s Novartis. ➢ Arpicillin by M/s Sanofi.	DOR: 16-04-1976 Transfer of Reg. From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi:

					30-08-2003 Last Renewal Submission: 03-08-2018
19.	000216	Penbritin Syrup 125mg/5ml [Fee of Rs.7500/- (DS#9132609697)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market. ➢ Better/ new molecules to cater the same portfolio are also available in the market. ➢ Virtually there is no demand of this product in local market.		DOR: 16-04-1976 Transfer of Reg. From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi: 30-08-2003 Last Renewal Submission: 03-08-2020
20.	024305	Zeatin Tablets Each tablet contains:- Cetirizine Dihydrochloride...10mg [Fee of Rs.7500/- (DS#421396041)]		➢ Zyrtec by M/s Gsk ➢ Rigix by M/s AGP ➢ Gixer by M/s Barret Hodgson.	DOR: 20-03-2002 Transfer of Reg. From M/s Stiefel Laboratories Pakistan Pvt. Ltd., Lahore to M/s GSK Pakistan Ltd., 35, Dockyard Road, West Wharf, Karachi: 13-01-2013 Last Renewal Submission: 24-11-2017
Request For De- Registration of Local Products By M/s GlaxoSmithKline Pakistan Limited, 35-Dockyard Road West Wharf Karachi (DML No.000017)					
1.	015519	Fongitar Liquid Contains: Zinc Pyrithoine 1% w/w Polytar 1% w/w [Fee of Rs.7500/- (DS#8493683971)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market.	Not provided	DOR: 14-06-1994 in the name of M/s Stiefel Laboratories, Lahore. Transfer of Reg. From Import to Local manufacturing at GSK West Wharf dated 23-08-2011 Last Renewal Submission:

			➢ Better/ new molecules to cater the same portfolio are also available in the market. ➢ Virtually there is no demand of this product in local market.		18-08-2016
2.	015718	Panoxyl Aqua Gel 2.5% Each 10gm contains: Benzoyl peroxide 2.5%w/w [Fee of Rs.7500/- (DS#56369419695)]		➢ Acnesan 10% Gel by M/s Sante ➢ Benoxyl 5% Gel by M/s Glitz ➢ Brevoxyl 4% Cream by M/s GSK	<u>DOR:</u> 05-09-1994 in the name of M/s Stiefel Laboratories, Lahore. <u>Transfer of Reg.</u> From Import to Local manufacturing at GSK West Wharf dated 23-08-2011 <u>Last Renewal Submission:</u> 18-08-2016
3.	007791	Panoxyl Acnegel-10 Contains: Benzoyl peroxide 10% [Fee of Rs.7500/- (DS#1365549450)]			<u>DOR:</u> 10-03-1995 in the name of M/s Stiefel Laboratories, Lahore. <u>Transfer of Reg.</u> From M/s Fazal Din & Sons (Pvt.) Ltd., Lahore to M/s Stiefel, Lahore dated 23-10-1993 <u>Transfer of Reg.</u> From Import to Local manufacturing at GSK West Wharf dated 23-08-2011 <u>Last Renewal Submission:</u> 18-08-2016
4.	005034	Panoxyl Acnegel 5% [Fee of Rs.7500/- (DS#907699337)]			<u>DOR:</u> 05-09-1994 in the name of M/s Stiefel Laboratories, Lahore.

					Transfer of Reg. From M/s Fazal Din & Sons (Pvt.) Ltd., Lahore to M/s Stiefel, Lahore dated 23-10-1993 Transfer of Reg. From Import to Local manufacturing at GSK West Wharf dated 23-08-2011 Last Renewal Submission: 18-08-2016
Documents submitted by the firm in the light of SOP approved vide 283rd meeting of Registration Board	a. Copy of Registration Letter & Last Renewal Status. b. List of alternate brands available in the country. c. Justification. d. An Undertaking that: i. No case is pending at any forum/ court of law regarding above mentioned products. ii. Provided information/ documents are true/ correct.				

Request For De- Registration of Local Products By M/s GlaxoSmithKline Pakistan Limited, Plot No.5, Sector 21, Korangi Industrial Area, Karachi (DML No.000248).

S/N	Reg. No.	Brand Name and Composition [Fee Detail]	Justification	Alternate Brands	Date of Reg. & Last Renewal Status
I	II	III	IV	V	VI
1.	009574	Capozide Tablets 50/25mg Each tablet contains: Captopril……50mg Hydrochlorothiazide.25 mg [Fee of Rs.7500/- (DS#3336254167)]	➢ Suitable therapeutic alternatives and advanced therapies are available in the market. ➢ Better/ new molecules to cater the same portfolio are also	➢ Cortec Plus by M/s Nabiqasim ➢ Co-Renitec by M/s OBS ➢ Cardace-H by M/s Zafa	DOR: 26-02-1987 Transfer of Reg. From M/s Bristol Myers Squibb (Pvt.0 Ltd. to GSK Pakistan Ltd.: 01-10-2010 Last Renewal Submission: 18-09-2020
2.	013816	Monopril 10mg Tablets Each tablet contains: Fosinopril Sodium…10mg		Aksopril by M/s Akson Pharma	DOR: 17-11-1992 Transfer of Reg.

		[Fee of Rs.7500/- (DS#3239246115)]	available in the market. ➢ Virtually there is no demand of this product in local market.		From M/s Bristol Myers Squibb (Pvt.0 Ltd. to GSK Pakistan Ltd.: 01-10-2010 Last Renewal Submission: 18-09-2020
Documents submitted by the firm in the light of SOP approved vide 283rd meeting of Registration Board	a. Copy of Registration Letter & Last Renewal Status. b. List of alternate brands available in the country. c. Justification. d. An Undertaking that: i. No case is pending at any forum/ court of law regarding above mentioned products. ii. Provided information/ documents are true/ correct.				

Decision: **Registration Board deferred the case and advised to further deliberate the matter with availability committee and share the outcome with Registration Board for consideration.**

Case No.08. **Request of M/s Novartis Pharma (Pakistan) Limited, 15 West Wharf Dockyard Road, Karachi (DML No.000193) for De- Registrations of Pharmaceutical Products.**

M/s Novartis Pharma (Pakistan) Limited, 15 West Wharf Dockyard Road, Karachi (DML No.000193) for de- registrations of their following products:

S/N	Reg. No.	Brand Name and Composition [Fee Detail]	Justification	Alternate Brands	Date of Reg.
I	II	III	IV	V	VI
1.	026361	Nimaran Tablets Each tablet contains: Nimesulide……100mg [Fee of Rs.7500/- (DS#09434319)]	Due to global directives the firm has divested this portfolio in Pakistan.	Emsulide by M/s Bosch Pharmaceutical	12-09-2000
2.	055852	Dorivel 500mg Tablet Each tablet contains: Valaciclovir……..500mg [Fee of Rs.7500/- (DS#55105458)]		➢ Viro by M/s CCL, Lahore ➢ Valavir by M/s Hilton	29-04-2009
3.	048407	Glory 1mg Tablet Each tablet contains: Glimepride ……..….1mg (USP specification) [Fee of Rs.7500/- DS#8520136893]	Due to global directives the firm has divested this portfolio in Pakistan.	➢ Gempride by M/s Atco ➢ Evopride by M/s. Pharmevo ➢ Hilpride by M/s. Hilton	22-02-2020
4.	048408	Glory 2mg Tablet Each tablet contains: Glimepride ……..…..2mg (USP specification)		➢ Gpride by M/s Sami ➢ Gliride by M/s Pfizer	22-02-2020

		[Fee of Rs.7500/- DS#2326813907]		➢ Glow by M/s Adamjee	
5.	048409	Glory 3mg Tablet Each tablet contains: Glimepride …….3mg (USP Specification) [Fee of Rs.7500/- DS#75762696502		➢ Glow by M/s Adamjee ➢ Gempride by M/s Atco ➢ Evopride by M/s. Pharmevo	22-02-2020
6.	048410	Glory 4mg Tablet Each tablet contains: Glimepride ……...4mg (USP Specification) [Fee of Rs.7500/- DS#51599263945]		➢ Evopride by M/s. Pharmevo ➢ Glow by M/s Adamjee ➢ Gempride by M/s Atco	22-02-2020
Documents submitted by the firm in the light of SOP approved vide 283rd meeting of Registration Board		a. Copy of Registration Letters. b. List of alternate brands available in the country. c. Justification. d. An Undertaking that: i. No case is pending at any forum/ court of law regarding above mentioned products. ii. Provided information/ documents are true/ correct.			

Decision: **Registration Board deferred the case and advised to further deliberate the matter with availability committee and share the outcome with Registration Board for consideration.**

Case No.09. **Request of M/s Sanofi-Aventis Pakistan Limited, Plot No.23, Sector 22, Korangi Industrial Area, Karachi (DML No. 000007) for License Withdrawal of Stemetil Injection (Reg.No.001233)**

M/s Sanofi-Aventis Pakistan Limited, Plot No.23, Sector 22, Korangi Industrial Area, Karachi (DML No. 000007) has requested for license withdrawal of Stemetil Injection (Reg.No.001233)

S/N	Reg. No.	Brand name and composition	Justification	Alternate Brands	Date of Reg. & Last Renewal Status
I	II	III	IV	V	VI
1.	001233	Stemetil Injection	The product has no demand and better molecules are available in market. Furthermore,	➢ Gencate (Fluphenazine) by M/s Genetics Pharma ➢ Clopixol (Zuclopenthixol)	DOR: 14-07-1976 (M/s May & Baker Ltd, Mandviwallas Chambers, Karachi)

			the decision is not related to safety, quality and efficacy.	by M/s. Lundbeck Pharma. ➢ Serenance (Haloperidol) by M/s. TheSearle Company	<u>Transfer of Reg:</u> 25-10-1993 (M/s Rhone-Poulance Pakistan (Pvt) Ltd, Wah Cantt) 21-01-2004 (M/s Aventis Ltd, Karachi) 28-07-2006 (M/s Sanofi-Aventis (Pakistan)Ltd, Karachi. <u>Last Renewal Submission:</u> 25-07-2016
Documents submitted by the firm in the light of SOP approved vide 283rd meeting of Registration Board	a. Copy of Registration Letter and Last Renewal Status. b. List of alternate brands available in the country. c. Justification. d. An Undertaking that: i. No case is pending at any forum/ court of law regarding above mentioned products. ii. Provided information/ documents are true/ correct.				

Decision: Registration Board deferred the case and advised to further deliberate the matter with availability committee and share the outcome with Registration Board for consideration.

Case No.10. Request for Change in Registration Status of Products from M/s The Searle Company Limited, Plot No. F-319, S.I.T.E., Karachi (DML No. 000016) to M/s Searle Pakistan Limited (Formerly OBS Pakistan Private Limited), C-14, Manghopir Road, S.I.T.E, Karachi (DML # 000012).

M/s. OBS Pakistan (Pvt.) Ltd., C-14, Manghopir Road, S.I.T.E, Karachi has requested vide letter No. RA/AA/07/2K20/LO-96 dated 06th July, 2020 and subsequent correspondence no. RA/SA/01/2K22/LOC-004 dated 7th Jan, 2022 RA/SA/04/2K22/LOC-038 dated 5th April, 2022 RA/SA/04/2K22/LOC-046 dated 19th April, 2022 for change in registration of their below mentioned products from M/s The Searle Company Ltd., F-319, S.I.T.E Karachi to their name.

During the evaluation process, the name of applicant firm M/s OBS Pakistan (Pvt.) Ltd., C-14, Manghopir Road, S.I.T.E, Karachi was changed to M/s Searle Pakistan Limited with the approval of Central Licensing Board dated 23rd November, 2021 along with change in firm's management. The firm has submitted pre-registration variation fee Rs. 150,000/- for each application.

The detail of cases is as following:

Administrative Documents Submitted in the light of SOP approved by the Registration Board in its 283rd meeting
i. Copy of GMP certificate dated 16th December, 2020 on the basis of inspection conducted on 07-10-2020.
ii. Copy of DML (000012) of M/s OBS renewed w.e.f. 31-03-2020.
iii. Approval of "Capsule (General) Section" confirmed from copy of letter dated 07-10-2020 issued by Licensing Division for renewal of licensed section.
iv. NOC from M/s. The Searle Company Ltd; Karachi for transfer of Zenbar 20mg, 30mg and 60mg on the name of M/s The Searle Pakistan Limited (Formerly OBS Pakistan Pvt. Ltd.,) Karachi dated 01-04-2022.
v. Relevant undertakings & commitments.

The cases were referred to Pharmaceutical Evaluation Cell / QMS for scrutinization/evaluation. Detail of submitted documents remarks of evaluators have been mentioned as under:

I	II	III	IV
S.No.	**Reg. No.**	**Product Name & Composition (As per initial Registration letter)**	**Registration Trail**
1.	055608	Zenbar 20mg Capsule Each capsule contains: - Doulexetine HCl enteric coated pellets eq. to Doluxetine……20mg	Initial Reg. Date**:** **01-04-2009** Change of Registration to new title of firm: **19-03-2018** Renewal of registered drugs (under SRO 1005(I)/2017 dated 5th Oct 2017 communicated vide RRR's letter dated **09-05-2018** in following terms: "Registration Board acceded to request of firm and decided to grant/regularize the renewal till 31-03-2019" Last renewal submitted on: **01-03-2019 with fee of Rs.10000/- and differential fee of Rs.10000/- was submitted on 14-04-2021**
	Name, address of Applicant / Marketing Authorization Holder		**M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700,,Sindh, Pakistan**
	Name, address of Manufacturing site.		M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700, Sindh, Pakistan. **(DML 000012)** ***(Transfer of Registration from M/s Searle Pakistan to M/s OBS Pakistan Pvt. Ltd Karachi,*** ***[NOC attached dated 15-06-2021]***
	Status of the applicant		☒Manufacturer ☐ Importer ☐Is involved in none of the above (contract

		giver)
	GMP status of the firm	**For transfer of registration:** GMP certificate of M/s OBS Pakistan (Pvt Ltd, C-14, Manghopir Road, S.I.T.E , Karachi-75700, based on inspection dated 07.10.2020.
	Evidence of approval of manufacturing facility	Applicant has provided copy of letter of renewal of Capsule General section dated 12th Mar, 2020.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy.No.28019 (R&I) dated 11-10-2021
	Details of fee submitted	**For transfer of registration:** PKR (100,000/- + 50,000) = 150,000/- DS# 1940944 dated 14-07-2020 DS# 17608640341 dated 08-07-2021 **Pre-registration variation:** PKR (75000/- + 142,500/-) = 150,000/- DS# 74955414098 dated 12.01.2022 DS# 055044403 dated 30.03.2022
	The proposed proprietary name / brand name	**Zenbar 20 mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Delayed release capsule contains: Duloxetine Hydrochloride 20% w/w equivalent to 20mg of Duloxetine
	Pharmaceutical form of applied drug	White to off white pellets encapsulated in hard gelatin capsule size #3 with light pink opaque color cap and body.
	Pharmacotherapeutic Group of (API)	Serotonin Norepinephrine reuptake Inhibitor
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	2x 7s
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Cymbalta 20mg Capsule Eli Lily & Co.(FDA)
	For generic drugs (me-too status)	Cymbalta 20mg Capsule, Eli lily Company Limited (Reg#021427)
	Name and address of API manufacturer.	Alphamed Formulations Pvt Ltd. Sy.No. 225, Sampanbole village, shamirpet Mandal, Medchal-Malkajgiri District Telanganad, India.
	1.5.11-Proposed Label	Submitted

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to general properties, structure, elucidation, polymorphism, solubility, physical forms, manufacturing site, impurities characterizations, specifications based on USP, analytical procedures, analytical method validation, batch analysis, container closure and stability of Duloxetine pellets at both real time and accelerated conditions. Similarly, information summaries for drug product (Zenbar) including its description, composition, pharmaceutical development, pharmaceutical equivalence against Cymbalta, comparative dissolution profile, in-process controls, analytical procedure and its validation, specification based on USP, batch analysis and specification, reference(working) standard, container closure system and stability studies has been provided.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, character elucidation, impurities structures, physical form, manufacturer, raw material specifications by DS and DP manufacturer, analytical method and its verification performed drug product manufacturer, batch analysis, certificate of analysis by drug product manufacturer, pellets specification, reference standard an CoA of working standard, container closure system used for pellets, specification and test methods for packing materials, and stability studies.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches (each of 25kg) drug substance at both accelerated as well as real time conditions**.** The accelerated stability data was conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months and the long-term stability data was conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months. Pellets were packed in LDPE transparent bag with 2 Poly bags in HDPE container. The pellets remained within specified limits as tested on defined intervals.
	Module-III Drug Product:	Firm has submitted data of drug product including its composition, selection of excipients, drug excipient compatibility studies, manufacturing procedure, in-process controls and validation protocol, pharmaceutical equivalence against Cymbalta 20mg Capsules, excipients testing methods, dissolution method verification of USP Test 1, microbial limits test validation, specifications, analytical procedures

<table>
<tr><td></td><td></td><td>and its verification, dissolution method verification, batch analysis for 3 trial batches, specifications as per USP monograph, working standard and its CoA, container closure system and stability studies.</td></tr>
<tr><td></td><td>Pharmaceutical Equivalence and Comparative Dissolution Profile</td><td>Pharmaceutical equivalence was performed against Cymbalta 20mg Capsule which shows comparable results within specified limits.
The comparative dissolution profile was performed for Zenbar 20mg Capsules against the Cymbalta 20mg Capsule, manufactured by Eli Lily. Comparison was performed using 12 samples at acidic stage for 2 hours and buffer stage at pH 6.8 for 60min. Calculation of the obtained values are as under:
<table>
<tr><th>Mediums</th><th>Time interval</th><th>Zenbar 20mg Cap</th><th>Cymbalta 20mg Cap</th></tr>
<tr><td rowspan="7">Acidic stage</td><td>10 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>20 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>30 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>40 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>50 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>60 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td colspan="3"></td></tr>
<tr><td rowspan="8">Buffer (pH 6.8)</td><td>10 min</td><td>74 %</td><td>67 %</td></tr>
<tr><td>20 min</td><td>88 %</td><td>85 %</td></tr>
<tr><td>30 min</td><td>93 %</td><td>92 %</td></tr>
<tr><td>40 min</td><td>94 %</td><td>96 %</td></tr>
<tr><td>50 min</td><td>94 %</td><td>96 %</td></tr>
<tr><td>60 min</td><td>96 %</td><td>98 %</td></tr>
<tr><td colspan="3">f1 = 3
f2= 74</td></tr>
</table>
</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Firm has claimed USP specifications and performed verification of analytical method for the drug product. DS manufacturers has also provided validation of analytical methods for Duloxetine.</td></tr>
<tr><td colspan="3">STABILITY STUDY DATA</td></tr>
<tr><td colspan="2">Manufacturer of API</td><td>Alphamed Formulations Pvt Ltd.
Sy.No. 225, Sampanbole village, shamirpet Mandal, Medchal-Malkajgiri District Telangana, India.</td></tr>
<tr><td colspan="2">API Lot No.</td><td>DP5A9005</td></tr>
<tr><td colspan="2">Description of Pack (Container closure system)</td><td>Alu/PVC blister in unit carton</td></tr>
<tr><td colspan="2">Stability Storage Condition</td><td>Real time: 30°C ± 2°C / 75% ± 5%RH
Accelerated: 40°C ± 2°C / 75% ± 5%RH</td></tr>
</table>

Time Period	Real time: 18 months (Continue for 36 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	041DT01	041DT02	041DT03
Batch Size	3000 Capsules	3000 Capsules	3000 Capsules
Manufacturing Date	05-09-2020	05-09-2020	05-09-2020
Date of Initiation	02-10-2020	02-10-2020	02-10-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	-
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Drugs Control Administration, Govt of Telangana, dated 30-08-2019. (Valid up to 29-08-2022).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	5Kg of API purchased from M/s Alphamed Formulations Pvt Ltd, Telagana, India invoice dated 15-07-2020, cleared 12-08-2020 from DRAP, Karachi.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail of stability batches.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

The drug substance for Zenbar 20 mg Capsule is manufactured by M/s Alphamed Formulations Pvt Ltd, Telagana, India (GMP certified by Drugs Control Administration, Govt of Telangana, dated 30-08-2019). Pellets specification has been verified according to pharmacopeia specification. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) and verification of analytical method of DS according to provided specifications.

The finished pharmaceutical product is hard gelatin capsule containing 100mg Duloxetine Hydrochloride 20% w/w equivalent to 20mg of Duloxetine manufactured by Ms/ Searle Pakistan Ltd. (Formerly M/s OBS Pakistan (Pvt.) Ltd. Karachi (DML 000012; Formulation). The method of manufacturing is encapsulation with adequate in process controls. Submitted regulatory specifications are verified according to USP monograph. Dissolution method is also verified

according to USP test method 1. Stability data shows compliance to the specification range at specified time points during 06 months accelerated and 18-month real time stability studies.

M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) is GMP complaint as per certificate issued by DRAP, Karachi office on 16-12-2020 based on the inspection conducted on 07-10-2020.

Zenbar 20mg Capsules' pharmaceutical equivalence has been established against the Cymbalta 20mg Capsule (Eli Lilly) approved by the FDA. The clinical particulars and pharmacological properties of the Duloxetine, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the treatment of major depressive disorder.

Conclusion:

The applicant shall maintain consistency in clinical particulars and pharmacological properties with the current version of the reference medicinal product (cymbalta 20mg Cap) as approved by reference regulatory authority and this information shall be updated regularly when the new information becomes available for reference medical product in accordance with the post registration variation procedures.

I	II	III	IV
S.No.	**Reg. No.**	**Product Name & Composition (As per initial Registration letter)**	**Registration Trail**
2.	055609	Zenbar 30mg Capsule Each capsule contains: - Doulexetine HCl enteric coated pellets eq. to Doluxetine……30mg	Initial Reg. Date**:** **01-04-2009** Change of Registration to new title of firm: **19-08-2016** Last renewal submitted on: **01-07-2021**
	Name, address of Applicant / Marketing Authorization Holder		**M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700,,Sindh, Pakistan**
	Name, address of Manufacturing site.		M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700, Sindh, Pakistan. **(DML 000012)** ***(Transfer of Registration from M/s Searle Pakistan to M/s OBS Pakistan Pvt. Ltd Karachi, [NOC attached dated 15-06-2021]***
	Status of the applicant		☒Manufacturer ☐ Importer ☐Is involved in none of the above (contract giver)
	GMP status of the firm		**For transfer of registration:** GMP certificate of M/s OBS Pakistan (Pvt Ltd, C-14, Manghopir Road, S.I.T.E , Karachi-75700, based on inspection dated 07.10.2020.

	Evidence of approval of manufacturing facility	Applicant has provided copy of letter of renewal of Capsule General section dated 12th Mar, 2020.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy.No.28020 (R&I) dated 11-10-2021
	Details of fee submitted	**For transfer of registration:** PKR (100,000/- + 50,000) = 150,000/- DS# 1940945 dated 14-07-2020 DS# 408151479909 dated 08-07-2021 **Pre-registration variation:** PKR (75000/- + 142,500/-) = 150,000/- DS# 285043056894 dated 12.01.2022 DS# 981344701871 dated 30.03.2022
	The proposed proprietary name / brand name	**Zenbar 30 mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Delayed release capsule contains: 150mg of Duloxetine Hydrochloride 20% w/w equivalent to 30mg of Duloxetine
	Pharmaceutical form of applied drug	White to off white pellets encapsulated in hard gelatin capsule size #2 with opaque light blue color cap and body.
	Pharmacotherapeutic Group of (API)	Serotonin Norepinephrine reuptake Inhibitor
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	1x 10s
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Cymbalta 30mg Capsule Eli Lily & Co.(FDA)
	For generic drugs (me-too status)	Cymbalta 30mg Capsule, Eli lily Company Limited (Reg#066173)
	Name and address of API manufacturer.	Alphamed Formulations Pvt Ltd. Sy.No. 225, Sampanbole village, shamirpet Mandal, Medchal-Malkajgiri District Telanganad, India.
	1.5.11-Proposed Label	Submitted
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to general properties, structure, elucidation, polymorphism, solubility, physical forms, manufacturing site, impurities characterizations, specifications based on USP,

		analytical procedures, analytical method validation, batch analysis, container closure and stability of Duloxetine pellets at both real time and accelerated conditions. Similarly, information summaries for drug product (Zenbar) including its description, composition, pharmaceutical development, pharmaceutical equivalence against Cymbalta, comparative dissolution profile, in-process controls, analytical procedure and its validation, specification based on USP, batch analysis and specification, reference(working) standard, container closure system and stability studies has been provided.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, character elucidation, impurities structures, physical form, manufacturer, raw material specifications by DS and DP manufacturer, analytical method and its verification performed drug product manufacturer, batch analysis, certificate of analysis by drug product manufacturer, pellets specification, reference standard an CoA of working standard, container closure system used for pellets, specification and test methods for packing materials, and stability studies.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches (each of 25kg) drug substance at both accelerated as well as real time conditions**.** The accelerated stability data was conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months and the long-term stability data was conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months. Pellets were packed in LDPE transparent bag with 2 Poly bags in HDPE container. The pellets remained within specified limits as tested on defined intervals.
	Module-III Drug Product:	Firm has submitted data of drug product including its composition, selection of excipients, drug excipient compatibility studies, manufacturing procedure, in-process controls and validation protocol, pharmaceutical equivalence against Cymbalta 20mg Capsules, excipients testing methods, dissolution method verification of USP Test 1, microbial limits test validation, specifications, analytical procedures and its verification, dissolution method verification, batch analysis for 3 trial batches, specifications as per USP monograph, working standard and its CoA, container closure system and stability studies.
	Pharmaceutical Equivalence and	Pharmaceutical equivalence was performed

<table>
<tr><td></td><td>Comparative Dissolution Profile</td><td>against Cymbalta 30mg Capsule which shows comparable results within specified limits.
The comparative dissolution profile was performed for Zenbar 30mg Capsules against the Cymbalta 30mg Capsule, manufactured by Eli Lily. Comparison was performed using 12 samples at acidic stage for 2 hours and buffer stage at pH 6.8 for 60min. Calculation of the obtained values are as under:
<table>
<tr><th>Mediums</th><th>Time interval</th><th>Zenbar 20mg Cap</th><th>Cymbalta 20mg Cap</th></tr>
<tr><td rowspan="7">Acidic stage</td><td>10 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>20 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>30 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>40 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>50 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td>60 min</td><td>0 %</td><td>0 %</td></tr>
<tr><td colspan="3"></td></tr>
<tr><td rowspan="8">Buffer (pH 6.8)</td><td>10 min</td><td>60 %</td><td>57 %</td></tr>
<tr><td>20 min</td><td>85 %</td><td>82 %</td></tr>
<tr><td>30 min</td><td>85 %</td><td>94 %</td></tr>
<tr><td>40 min</td><td>90 %</td><td>100 %</td></tr>
<tr><td>50 min</td><td>95 %</td><td>104 %</td></tr>
<tr><td>60 min</td><td>96 %</td><td>105 %</td></tr>
<tr><td colspan="3">f1 = 8
f2= 53</td></tr>
</table>
</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Firm has claimed USP specifications and performed verification of analytical method for the drug product. DS manufacturers has also provided validation of analytical methods for Duloxetine.</td></tr>
</table>

STABILITY STUDY DATA

Manufacturer of API	Alphamed Formulations Pvt Ltd. Sy.No. 225, Sampanbole village, shamirpet Mandal, Medchal-Malkajgiri District Telangana, India.		
API Lot No.	DP5A9005		
Description of Pack (Container closure system)	Alu/PVC blister in unit carton		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 75% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 18 months (Continue for 36 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	042DT01	042DT02	042DT03

Batch Size	3000 Capsules	3000 Capsules	3000 Capsules
Manufacturing Date	05-09-2020	05-09-2020	05-09-2020
Date of Initiation	02-10-2020	02-10-2020	02-10-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	-
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Drugs Control Administration, Govt of Telangana, dated 30-08-2019. (Valid up to 29-08-2022).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	5Kg of API purchased from M/s Alphamed Formulations Pvt Ltd, Telagana, India invoice dated 15-07-2020, cleared 12-08-2020 from DRAP, Karachi.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail of stability batches.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

The drug substance for Zenbar 30 mg Capsule is manufactured by M/s Alphamed Formulations Pvt Ltd, Telagana, India (GMP certified by Drugs Control Administration, Govt of Telangana, dated 30-08-2019). Pellets specification has been verified according to pharmacopeia specification. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) and verification of analytical method of DS according to provided specifications.

The finished pharmaceutical product is hard gelatin capsule containing 150mg Duloxetine Hydrochloride 20% w/w equivalent to 30mg of Duloxetine manufactured by Ms/ Searle Pakistan Ltd. (Formerly M/s OBS Pakistan (Pvt.) Ltd. Karachi (DML 000012; Formulation). The method of manufacturing is encapsulation with adequate in process controls. Submitted regulatory specifications are verified according to USP monograph. Dissolution method is also verified according to USP test method 1. Stability data shows compliance to the specification range at specified time points during 06 months accelerated and 18-month real time stability studies.

M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) is GMP complaint as per certificate issued by DRAP, Karachi office on 16-12-2020 based on the inspection conducted on 07-10-2020.

Zenbar 30mg Capsules' pharmaceutical equivalence has been established against the Cymbalta 30mg Capsule (Eli Lilly) approved by the FDA. The clinical particulars and pharmacological properties of the Duloxetine, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the treatment of major depressive disorder.

Conclusion:

The applicant shall maintain consistency in clinical particulars and pharmacological properties with the current version of the reference medicinal product (cymbalta 30mg Cap) as approved by reference regulatory authority and this information shall be updated regularly when the new information becomes available for reference medical product in accordance with the post registration variation procedures.

I	II	III	IV
S.No.	**Reg. No.**	**Product Name & Composition (As per initial Registration letter)**	**Registration Trail**
3.	055610	Zenbar 60mg Capsule Each capsule contains: - Doulexetine HCl enteric coated pellets eq. to Doluxetine……60mg	Initial Reg. Date**:** **01-04-2009** Change of Registration to new title of firm: **19-08-2016** Last renewal submitted on: **01-07-2021**
	Name, address of Applicant / Marketing Authorization Holder		**M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700,,Sindh, Pakistan**
	Name, address of Manufacturing site.		M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700, Sindh, Pakistan. **(DML 000012)** ***(Transfer of Registration from M/s Searle Pakistan to M/s OBS Pakistan Pvt. Ltd Karachi,*** ***[NOC attached dated 15-06-2021]***
	Status of the applicant		☒Manufacturer ☐ Importer ☐Is involved in none of the above (contract giver)
	GMP status of the firm		**For transfer of registration:** GMP certificate of M/s OBS Pakistan (Pvt Ltd, C-14, Manghopir Road, S.I.T.E , Karachi-75700, based on inspection dated 07.10.2020.
	Evidence of approval of manufacturing facility		Applicant has provided copy of letter of renewal of Capsule General section dated 12th Mar, 2020.
	Status of application		☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product		☐Domestic sale

		☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy.No.28021 (R&I) dated 11-10-2021
	Details of fee submitted	**For transfer of registration:** PKR (100,000/- + 50,000) = 150,000/- DS# 1940946 dated 14-07-2020 DS# 93814218620 dated 08-07-2021 **Pre-registration variation:** PKR (75000/- + 142,500/-) = 150,000/- DS# 51456142 dated 12.01.2022 DS# 03547820 dated 30.03.2022
	The proposed proprietary name / brand name	**Zenbar 60 mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Delayed release capsule contains: 300mg of Duloxetine Hydrochloride 20% w/w equivalent to 30mg of Duloxetine
	Pharmaceutical form of applied drug	White to off white pellets encapsulated in hard gelatin capsule size #0 with opaque light green color cap and body.
	Pharmacotherapeutic Group of (API)	Serotonin Norepinephrine reuptake Inhibitor
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	1x 10s
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Cymbalta 60mg Capsule Eli Lily & Co.(FDA)
	For generic drugs (me-too status)	Cymbalta 60mg Capsule, Eli lily Company Limited
	Name and address of API manufacturer.	Alphamed Formulations Pvt Ltd. Sy.No. 225, Sampanbole village, shamirpet Mandal, Medchal-Malkajgiri District Telanganad, India.
	1.5.11-Proposed Label	Submitted
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to general properties, structure, elucidation, polymorphism, solubility, physical forms, manufacturing site, impurities characterizations, specifications based on USP, analytical procedures, analytical method validation, batch analysis, container closure and stability of Duloxetine pellets at both real time and accelerated conditions. Similarly, information summaries for drug product (Zenbar) including its description, composition, pharmaceutical development,

		pharmaceutical equivalence against Cymbalta, comparative dissolution profile, in-process controls, analytical procedure and its validation, specification based on USP, batch analysis and specification, reference(working) standard, container closure system and stability studies has been provided.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, character elucidation, impurities structures, physical form, manufacturer, raw material specifications by DS and DP manufacturer, analytical method and its verification performed drug product manufacturer, batch analysis, certificate of analysis by drug product manufacturer, pellets specification, reference standard an CoA of working standard, container closure system used for pellets, specification and test methods for packing materials, and stability studies.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches (each of 25kg) drug substance at both accelerated as well as real time conditions**.** The accelerated stability data was conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months and the long-term stability data was conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 36 months. Pellets were packed in LDPE transparent bag with 2 Poly bags in HDPE container. The pellets remained within specified limits as tested on defined intervals.
	Module-III Drug Product:	Firm has submitted data of drug product including its composition, selection of excipients, drug excipient compatibility studies, manufacturing procedure, in-process controls and validation protocol, pharmaceutical equivalence against Cymbalta 20mg Capsules, excipients testing methods, dissolution method verification of USP Test 1, microbial limits test validation, specifications, analytical procedures and its verification, dissolution method verification, batch analysis for 3 trial batches, specifications as per USP monograph, working standard and its CoA, container closure system and stability studies.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence was performed against Cymbalta 60mg Capsule which shows comparable results within specified limits. The comparative dissolution profile was performed for Zenbar 60mg Capsules against the Cymbalta 60mg Capsule, manufactured by Eli Lily. Comparison was performed using 12 samples at acidic stage for 2 hours and buffer stage at pH 6.8 for 60min. Calculation of the

		obtained values are as under: **Mediums** / **Time interval** / **Zenbar 20mg Cap** / **Cymbalta 20mg Cap** Acidic stage: 10 min 0 % 0 %; 20 min 0 % 0 %; 30 min 0 % 0 %; 40 min 0 % 0 %; 50 min 0 % 0 %; 60 min 0 % 0 % Buffer (pH 6.8): 10 min 73 % 62 %; 20 min 81 % 78 %; 30 min 86 % 88 %; 40 min 92 % 97 %; 50 min 99 % 103 %; 60 min 100 % 103 % f1 = 5 f2= 61
	Analytical method validation/verification of product	Firm has claimed USP specifications and performed verification of analytical method for the drug product. DS manufacturers has also provided validation of analytical methods for Duloxetine.

STABILITY STUDY DATA

Manufacturer of API	Alphamed Formulations Pvt Ltd. Sy.No. 225, Sampanbole village, shamirpet Mandal, Medchal-Malkajgiri District Telangana, India.		
API Lot No.	DP5A9005		
Description of Pack (Container closure system)	Alu/PVC blister in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 18 months (Continue for 36 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	042DT01	042DT02	042DT03
Batch Size	3000 Capsules	3000 Capsules	3000 Capsules
Manufacturing Date	05-09-2020	05-09-2020	05-09-2020
Date of Initiation	02-10-2020	02-10-2020	02-10-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	-
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by Drugs Control Administration, Govt of Telangana, dated 30-08-2019. (Valid up to 29-08-2022).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	5Kg of API purchased from M/s Alphamed Formulations Pvt Ltd, Telagana, India invoice dated 15-07-2020, cleared 12-08-2020 from DRAP, Karachi.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail of stability batches.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

The drug substance for Zenbar 60 mg Capsule is manufactured by M/s Alphamed Formulations Pvt Ltd, Telagana, India (GMP certified by Drugs Control Administration, Govt of Telangana, dated 30-08-2019). Pellets specification has been verified according to pharmacopeia specification. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) and verification of analytical method of DS according to provided specifications.

The finished pharmaceutical product is hard gelatin capsule containing 300mg Duloxetine Hydrochloride 20% w/w equivalent to 60mg of Duloxetine manufactured by Ms/ Searle Pakistan Ltd. (Formerly M/s OBS Pakistan (Pvt.) Ltd. Karachi (DML 000012; Formulation). The method of manufacturing is encapsulation with adequate in process controls. Submitted regulatory specifications are verified according to USP monograph. Dissolution method is also verified according to USP test method 1. Stability data shows compliance to the specification range at specified time points during 06 months accelerated and 18-month real time stability studies.

M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) is GMP complaint as per certificate issued by DRAP, Karachi office on 16-12-2020 based on the inspection conducted on 07-10-2020.

Zenbar 60mg Capsules' pharmaceutical equivalence has been established against the Cymbalta 60mg Capsule (Eli Lilly) approved by the FDA. The clinical particulars and pharmacological properties of the Duloxetine, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the treatment of major depressive disorder.

Conclusion:

The applicant shall maintain consistency in clinical particulars and pharmacological properties with the current version of the reference medicinal product (cymbalta 60mg Cap) as approved

by reference regulatory authority and this information shall be updated regularly when the new information becomes available for reference medical product in accordance with the post registration variation procedures.

Proceedings of M-320:

Registration Board was apprised that Legalized GMP certificate of M/s Alphamed Formulations (Pvt) Ltd., India (issued by Drugs Control Administration, Govt of Telangana, dated 30-08-2019) was valid up to 29-08-2022. The firm has now provided copy of GMP certificate (L.Dis.No:9342/TS/2022) valid until 15-08-2023 which can be verified online at Drugs Control Adminstration(DCA) (telangana.gov.in)

Decision: Registration Board decided as under:

i. **Cancelled registration of following products from the name of M/s The Searle Company Limited, Plot No. F-319, S.I.T.E., Karachi (DML No. 000016)**

S. No.	Reg. No.	Product Name & Composition
1.	055608	Zenbar 20mg Capsule Each capsule contains: - Doulexetine HCl enteric coated pellets eq. to Doluxetine……20mg
2.	055609	Zenbar 30mg Capsule Each capsule contains: - Doulexetine HCl enteric coated pellets eq. to Doluxetine……30mg
3.	055610	Zenbar 60mg Capsule Each capsule contains: - Doulexetine HCl enteric coated pellets eq. to Doluxetine……60mg

ii. **Approved registration of following products in the name of M/s Searle Pakistan Limited (Formerly OBS Pakistan Private Limited), C-14, Manghopir Road, S.I.T.E, Karachi (DML # 000012).**

a) **Manufacturer will place first three production batches of both products on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

b) **Manufacturer will perform process validation of first three batches of both products as per the commitment submitted in the registration application.**

S. No.	Product Name & Composition
1.	Zenbar 20mg Capsule Each Delayed release capsule contains: Duloxetine Hydrochloride 20% w/w equivalent to 20mg of Duloxetine (USP Specifications)
2.	Zenbar 30mg Capsule Each delayed release capsule contains: 150mg of Duloxetine Hydrochloride 20% w/w equivalent to 30mg of Duloxetine (USP Specifications)
3.	Zenbar 60mg Capsule Each delayed release capsule contains: 300mg of Duloxetine Hydrochloride 20% w/w equivalent to 30mg of Duloxetine (USP Specifications)

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.11: Request for Change in Registration Status of Product(s) From M/s GSK Pakistan Limited, 35-Dockyard Road, West Wharf, Karachi (DML #000017) to M/s. GlaxoSmithKline Consumer Healthcare Pakistan Ltd, Petaro Road Jamshoro (DML #000010)

Registration Board in its 291st meeting held on 02nd-04th September, 2019 considered the following application of M/s. GlaxoSmithKline Consumer Healthcare Pakistan Ltd [Formerly M/s GSK OTC (Pvt) Ltd.], Petaro Road Jamshoro (DML #000010) regarding change in registration status of below-mentioned product from M/s. GlaxoSmithKline Pakistan Ltd, Karachi to their name. Detail has been reproduced as under:

S/ N	Reg. No.	Brand Name & Composition of Registered Products	Initial letter of registration with renewal status.	Registration Holder/ Manufacturer	Dy. No. & Date/ Remarks
I	II	III	IV	V	VI
1.	016868	ENO Lemon Powder Contains: Sodium Bicarbonate …….34.16%w/w Sodium Bicarbonate Fine…..11.39%w/w Citric Acid (anhydrous)…… …….43.10%w/w Sodium Carbonate (anhydrous)… …….10.00%w/w Sodium Carbonate Decahydrate… …….0.25%w/w	1- F.No.3-1/95-Reg-II (M-112) dated 18-04-1995 in the name of M/s Beecham Pakistan (Pvt) Ltd, Karachi. 2- Transfer from M/s Galxowellcome to M/s GSK Pakistan Ltd., D/43, Textile Avenue, SITE, Karachi vide Letter No.3-3/2003-Reg-II (M-179) dated 30thAugust, 2003. 3- Last Renewal Application Dated 13-06-2018 **Remarks of RRR Section** Registration Board granted the renewal w.e.f 30-08-2018 to 29-08-2023 (Ref. F.No.3-10/2019-RRR (M-288 Dated 26-06-2019)	M/s GSK Pakistan Limited, 35-Dockyard Road, West Wharf, Karachi (DML#000017)	Duplicate Applications on From-5 along with photocopy fee challan of Rs.360,000/- (06-06-2016) and Rs.900,000/- (27-06-2016) received on 17-06-2019 (Dy. No.560) Label claim as applied on Form-5: ENO Fruit Salt Lemon Each 5gm contains: Sodium Bicarbonate ….2.277gm Sodium Carbonate.0.5gm Citric Acid ….2.155gm Label claim needs to be standardized/ corrected as per UK MHRA

The firm has provided following documents:-

1. Applications on From-5 along with fee of Rs.360,000/- (06-06-2016) and Rs.900,000/- (27-06-2016) (Duplicate)
2. Copies of initial letter of registration and renewal status.
3. Copy of last inspection report of M/s GlaxoSmithKline Pakistan Ltd, 35- Dockyard Road, West Wharf Karachi.
4. Evidence of approval for change in title from "GSK OTC (Pvt) Ltd Jamshoro" to "M/s. GlaxoSmithKline Consumer Healthcare Pakistan Ltd., Petaro Road Jamshoro (DML #000010)" dated 14-05-2019.
5. NOC from M/s. GlaxoSmithKline Pakistan Ltd, Karachi dated 25-06-2019.
6. Consent from contract manufacturers dated 03-07-2019 and 04-07-2019.

Decision of M-291:

Registration Board decided as follows:

[…Deferred the products at S.No. 5-13 for confirmation of approval status of required manufacturing facilities from Licensing Division. Furthermore, w.r.t products at S.No. 5, 6, 9 & 10, the Board also advised the firm for submission of evidence of approval status of applied formulations in Reference Regulatory Authorities.]

The firm has now submitted the following information/ documents:

1. Fee of Rs.75000/-(S#63313501456) and Rs.30000/-(S#7147148718).
2. Form-5 with following composition i.e., revised as per reference product approved by RRA (MHRA):

   ENO Lemon Powder
   Each 5gm contains:
   Sodium Bicarbonate …….2.32gm
   Sodium Carbonate……...0.5gm
   Citric Acid ……2.18gm

3. Panel Inspection Report for regularization & renewal of DML for M/s GSK Pakistan Limited, 35-Dockyard Road, West Wharf, Karachi (DML#000017), dated 05-09-2019 stating recommendation for renewal of DML for following sections:

   i. Ointment (General)
   ii. **Oral Powder Eno (General) Section.**
   iii. Eye/Ophthalmic Ointment Section.
   iv. Ear/ Otic Drops.
   v. Capsule/ Spansule (General)
   vi. Non-Pareil Seeds (NPS)- In house use only.

4. Copy of DML of M/s GSK CHC Pakistan Ltd., Jamshoro (renewed w.e.f. 31-03-2020).
5. Copy of DML of M/s GSK Pakistan Limited, West Wharf, Karachi (renewed w.e.f. 31-03-2020).
6. NOC from M/s. GlaxoSmithKline Pakistan Ltd, 35- Dockyard Road, West Wharf Karachi dated 10-08-2022.

Decision: Registration Board decided as under:

i. Cancelled registration of following product from the name of M/s GSK Pakistan Limited, 35-Dockyard Road, West Wharf, Karachi (DML#000017).

S. No.	Reg. No.	Product Name & Composition
1.	**016868**	**ENO Lemon Powder** **Contains:** **Sodium Bicarbonate …….34.16%w/w** **Sodium Bicarbonate Fine…..11.39%w/w**

		Citric Acid (anhydrous)…….43.10%w/w Sodium Carbonate (anhydrous)……..10.00%w/w Sodium Carbonate Decahydrate…….0.25%w/w

ii. Approved registration of following product in the name of M/s. GlaxoSmithKline Consumer Healthcare Pakistan Ltd, Petaro Road Jamshoro (DML #000010) by way of contract manufacturing at M/s GSK Pakistan Limited, 35-Dockyard Road, West Wharf, Karachi (DML#000017).

S. No.	Product Name & Composition
1.	**ENO Lemon Powder Each 5gm contains: Sodium Bicarbonate …….2.32gm Sodium Carbonate……...0.5gm Citric Acid ……2.18gm (As per Innovator's Specifications)**

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.12. Request for Change in Registration Status of Product from M/s The Searle Company Limited, Plot No. F-319, S.I.T.E., Karachi (DML No. 000016) to M/s Searle Pakistan Limited (Formerly OBS Pakistan Private Limited), C-14, Manghopir Road, S.I.T.E, Karachi (DML # 000012)

M/s. Searle Pakistan Limited (Formerly OBS Pakistan Pvt Ltd.), C-14, Manghopir Road, S.I.T.E, Karachi has requested for change in registration of below mentioned products from M/s The Searle Company Ltd., F-319, S.I.T.E Karachi to their name.

The detail of cases is as following:

Administrative Documents Submitted in the light of SOP approved by the Registration Board in its 283rd meeting
i. Copy of GMP certificate on the basis of inspection conducted on 15-02-2022.
ii. Copy of DML (000012) of M/s OBS renewed w.e.f. 31-03-2020.
iii. Copy of panel inspection report of M/s OBS for renewal of DML dated 08-10-2021 confirming "Tablet (General) Section"
iv. NOC from M/s. The Searle Company Ltd; Karachi for transfer of Morcet 5mg on the name of M/s. Searle Pakistan Limited (Formerly OBS Pakistan Pvt Ltd.), C-14, Manghopir Road, S.I.T.E, Karachi
v. Relevant undertakings & commitments.

The cases were referred to Pharmaceutical Evaluation Cell / QMS for scrutinization /evaluation. Detail of submitted documents remarks of evaluators have been mentioned as under:

I	II	III	IV
S.No.	**Reg. No.**	**Product Name & Composition (As per initial Registration letter)**	**Registration Trail**

1.	082242	Morcet 5mg Tablets Each tablet contains: - Escitalopram oxalate eq. to Escitalopram……5mg (USP Specification)	Initial Reg. Date: 26-09-2017 Last renewal submission dated: 08-04-2022
	Name, address of Applicant / Marketing Authorization Holder		**M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700,,Sindh, Pakistan**
	Name, address of Manufacturing site.		M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) Address: C-14, Manghopir Road, S.I.T.E , Karachi- 75700, Sindh, Pakistan. **(DML 000012)** ***(Transfer of Registration from M/s Searle Pakistan attached dated 18-02-2022***
	Status of the applicant		☒Manufacturer ☐ Importer ☐Is involved in none of the above (contract giver)
	GMP status of the firm		**For transfer of registration:** GMP certificate of M/s OBS Pakistan (Pvt Ltd, C-14, Manghopir Road, S.I.T.E , Karachi- 75700, based on inspection dated 07.10.2020.
	Evidence of approval of manufacturing facility		Applicant has provided copy of letter of renewal of DML mentioning Tablet (General) section among Formulation sections.
	Status of application		☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product		☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission		Dy.No.8560 (R&I) dated 04-04-2022 Dy.No 312 AD(Reg-I) dated 05-04-2022
	Details of fee submitted		**For transfer of registration:** PKR (20,000/- + 10,000) = 30,000/- DS# 1940930 dated 13-04-2020 DS# 601196719822 dated 24-02-2021
	The proposed proprietary name / brand name		**Morcet 5 mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit		Each film coated tablet contains: 6.390 mg of Escitalopram Oxalate is equivalent to 5mg of Escitalopram
	Pharmaceutical form of applied drug		Light green colored, round concave shaped, film coated tablet with break line on one side and plain from other side.
	Pharmacotherapeutic Group of (API)		Selective serotonin reuptake inhibitor (SSRI) antidepressant

	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	1 x 14's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Lexapro 5mg Tablet Oral Forest Laboratories, Inc (FDA)
	For generic drugs (me-too status)	Citanew 5mg Tablet, Hilton Pharma Pakistan (Pvt) Ltd. (Reg#037707)
	Name and address of API manufacturer.	Zhejiang Huahai Pharmaceutical Co, Ltd, Xunqiao, Linhai, Zhejiang, China.
	1.5.11-Proposed Label	Submitted
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information of Escitalopram oxalate (DS) related the structure, solubilities, and other general properties, manufacturing site, character elucidation, impurities characterizations, specifications based on USP, analytical procedures and its validation, batch analysis, refence standard, container closure and stability studies summaries of Escitalopram oxalate. Similarly, information summaries for drug product (Morcet) including its description, composition, pharmaceutical development, pharmaceutical equivalence against Cipralex, Lundbeck, comparative dissolution profile, justification for selection of manufacturing process and in-process controls, analytical procedure and its verification, batch analysis and specification, reference standard, container closure system and stability studies has been provided.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, character elucidation, physical form, manufacturer, a brief on manufacturing process, polymorphism (Form-I is DS), structure elucidation, impurities, specifications, analytical method, its validation, analytical method verification performed by DP manufacturer, certificate of analysis, impurities, specifications based on USP, analytical procedures, batch analysis, reference standard and its CoA , container closure system, specification and test methods for packing materials, and stability studies with study protocol.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches (64.54 kg each) of drug substance at both accelerated as well as real time conditions**. The accelerated stability data was conducted at**

<table>
<tr><td></td><td></td><td>40ºC ± 2ºC / 75% ± 5% RH for 6 months and the long-term stability data was conducted at 30°C ± 2°C / 75% ± 5% RH for 36 months. DS was packed in a polyethylene bag, sealed using a polyethylene tie, and packaged again in complex aluminium bag sealed with heat and placed in an aluminium tin. The DS remained within specified limits as tested on defined intervals.</td></tr>
<tr><td></td><td>Module-III Drug Product:</td><td>Firm has submitted data of drug product including its composition, manufacturing process and process control, manufacturing process validation protocol, excipients testing methods, pharmaceutical equivalence, specifications, analytical procedures and its verification, dissolution method verification, batch analysis, justification of specifications, USP procedure for organic impurities, reference standard or materials, container closure system and stability. The Specifications and control tests comply to USP.</td></tr>
<tr><td></td><td>Pharmaceutical Equivalence and Comparative Dissolution Profile</td><td>Pharmaceutical equivalence was performed against Cipralex 5mg Tablet which shows comparable results within specified limits.
The comparative dissolution profile was performed for Morcet 5mg Tablet against the Citanew 5mg, manufactured by Hilton Pharma, Pakistan. Comparison was performed using 12 samples at pH 1.2, pH 4.5 and pH 6.8 for 20min. Calculation of value is as under:
<table>
<tr><th>Sr</th><th>Mediums</th><th>Time interval</th><th>Morcet 5mg Tab</th><th>Citanew 5mg Tab</th></tr>
<tr><td rowspan="4"></td><td rowspan="4">Acidic buffer (pH 1.2)</td><td>10 min</td><td>103 %</td><td>101 %</td></tr>
<tr><td>15 min</td><td>105 %</td><td>103 %</td></tr>
<tr><td>20 min</td><td>105 %</td><td>104 %</td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td rowspan="4">ii</td><td rowspan="4">Acetate buffer (pH 4.5)</td><td>10 min</td><td>100 %</td><td>97%</td></tr>
<tr><td>15 min</td><td>102 %</td><td>100%</td></tr>
<tr><td>20 min</td><td>102 %</td><td>100%</td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td rowspan="4"></td><td rowspan="4">Phosphate Buffer (pH 6.8)</td><td>10 min</td><td>87 %</td><td>95 %</td></tr>
<tr><td>15 min</td><td>92 %</td><td>99 %</td></tr>
<tr><td>20 min</td><td>92 %</td><td>99 %</td></tr>
<tr><td></td><td></td><td></td></tr>
</table>
f1 and f2 value has not been calculated because both reference and test sample achieved 85% dissolution within 15 minutes.</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Firm has claimed USP specifications for which report of verification of analytical method for the drug product has been provided. Dissolution method verification protocol and study report were also provided.</td></tr>
</table>

STABILITY STUDY DATA			
Manufacturer of API	Zhejiang Huahai Pharmaceutical Co, Ltd, Xunqiao, Linhai, Zhejiang, China.		
API Lot No.	5356-19-004M		
Description of Pack (Container closure system)	Alu/PVC blister in unit carton		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 75% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 12 months (Continue for 36 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	018DT01	018DT02	018DT03
Batch Size	3000 Tablets	3000 Tablets	3000 Tablets
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	04-2020	04-2020	04-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	-
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued by China Food and Drug Administration, dated 26-06-2018. (Valid up to 25-06-2023).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	API purchased from Zhejiang Huahai Pharmaceutical Co, Ltd, Xunqiao, Linhai, Zhejiang, China. invoice dated 18-07-2019, cleared 12-08-2019 from DRAP, Karachi.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail of stability batches.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

The drug substance for Morcet 5 mg Tablet is manufactured by Zhejiang Huahai Pharmaceutical Co, Ltd, Xunqiao, Linhai, Zhejiang, China.(License and GMP certified by China Food and Drug Administration, on USP specifications. Polymorphic form of DS is Form-I. The impurity profiling of DS is also carried out including the potential genotoxic impurity Ethyl p-tosylate which was also tested by DS manufacturer using GC method and not detected in three batches. Manufacturing and controls, comparability protocols, structural characterization, and stability protocol has been submitted. Specification is considered adequate with respect to USP monograph. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications.

The drug product is film coated tablet of 5 mg manufactured by Searle Pakistan Ltd (Formerly OBS Pakistan (Pvt.) Ltd. Karachi DML 000012 (Formulation) (light green colored, round enclave film coated tablet). The method of manufacturing is granulation, direct compression and film coating with adequate in process controls. Submitted regulatory specifications are as per USP monograph and submitted stability data shows no degradation product at specified time points.

M/s Searle Pakistan Limited, (Formerly M/s OBS Pakistan (Pvt.) Ltd.) is a GMP complaint unit as per certificate issued by DRAP, Karachi office based on the inspection conducted on 15-02-2022.

Morcet 5mg Tablets' pharmaceutical equivalence has been established against the Cipralex 5mg Tablets approved by the Health Canada, however the comparative dissolution profile was studied against the Citanew 5mg Tablets manufactured by Hilton Pharma Karachi. The clinical particulars and pharmacological properties of the Escitalopram, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for Major depressive disorder, panic disorder with or without agoraphobia, social anxiety disorder, generalized anxiety, obsessive compulsive disorder.

Conclusion:

The applicant shall maintain consistency in clinical particulars and pharmacological properties with the current version of the reference medicinal product as approved by reference regulatory authority and this information shall be updated regularly when the new information becomes available for reference medical product in accordance with the post registration variation procedures.

The firm shall also ensure black boxed information on "Suicidality and Antidepressant Drugs" in the beginning of the leaflet.

Decision: Registration Board decided as under:

i. Cancelled registration of following product from the name of M/s The Searle Company Limited, Plot No. F-319, S.I.T.E., Karachi (DML No. 000016)

S. No.	Reg. No.	Product Name & Composition
1.	082242	**Morcet 5mg Tablets** **Each tablet contains: -** **Escitalopram oxalate eq. to Escitalopram……5mg** **(USP Specification)**

ii. Approved registration of following product in the name of M/s Searle Pakistan Limited (Formerly OBS Pakistan Private Limited), C-14, Manghopir Road, S.I.T.E, Karachi (DML # 000012).

a) Manufacturer will place first three production batches of both products on long term stability studies throughout proposed shelf

life and on accelerated studies for six months as per the commitment submitted in the registration application.

b) Manufacturer will perform process validation of first three batches of both products as per the commitment submitted in the registration application.

S. No.	Product Name & Composition
1.	**Morcet 5mg Tablet** **Each film coated tablet contains:** **6.390mg of Escitalopram Oxalate is equivalent to 5mg of Escitalopram** **(USP Specifications)**

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.13. Correction in Label Claim/ Strength of Approved Products of M/s High-Q Pharmaceuticals, Plot No. 224, Sector-23, Korangi Industrial Area, Karachi (DML No.000597).

a. Registration Board in its 283rd meeting held on 27th -29th June, 2018 approved the following product of M/s High-Q Pharmaceuticals, Plot No. 224, Sector-23, Korangi Industrial Area, Karachi (DML No.000597) as per below mentioned details:

1.	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals, Plot No. 224, Sector-23, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form+ Strength	Co-Mesart **40mg+5mg** Tablet
	Diary No. Date of R& I & fee	Diary No:15799, 21/09/2017, Rs: 20,000/-
	Composition	Each film-coated tablet contains: Olmesartan medoxomil …**20mg** Amlodipine as besilate …**5mg**
	Pharmacological Group	Angiotensin II antagonists and calcium channel blockers
	Type of Form	Form 5
	Finished Product Specification	Innovator's specifications
	Pack Size & Demanded Price	10's, 14's, 20's, 28's, 30's / As per SRO
	Approval Status of Product in Reference Regulatory Authorities	Sevikar 40 mg/5 mg film-coated tablets by M/s Daiichi Sankyo UK Ltd (MHRA Approved)
	Me-too Status	Comcarb 5/40mg tablet by M/s Maple Pharmaceuticals (Pvt) Ltd (Reg#061882)
	GMP Status	Last GMP inspection conducted on 19-07-2017 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator.	
	Decision: Approved with innovator's specification.	

Registration letter could not be issued due to disparity in strengths mentioned in composition and alongside the brand name.

In this context original dossier could not be retrieved from available record, however, the firm has submitted copies of DRAP's acknowledged receipts & fee challans of both strengths i.e., 40/5mg and 20/5mg. Furthermore, the firm has also submitted copy of registration letter of 20/5mg strength of above-mentioned formulation (R#091209) and copy of form-5 of 40/5mg strength stating correct label claim.

Accordingly, the case has been placed for correction in strength/label claim of above-mentioned product which appears to be due to typographical (cut-paste) error.

Submitted for consideration of Registration Board.

b. Registration Board in its 283rd meeting held on 27th -29th June, 2018 approved the following product of M/s High-Q Pharmaceuticals, Plot No. 224, Sector-23, Korangi Industrial Area, Karachi (DML No.000597) as per below mentioned details:

2.	Name and Address of Manufacturer / Applicant	M/s High-Q Pharmaceuticals, Plot No. 224, Sector-23, Korangi Industrial Area, Karachi.
	Brand Name + Dosage Form + Strength	Atasart **32mg** Tablet
	Diary No. Date of R & I & fee	Diary No:15751 ,20/09/2017, Rs: 20,000/-
	Composition	Each tablet contains: Candesartan cilexetil …**16mg**
	Pharmacological Group	Angiotensin II antagonists, plain
	Type of Form	Form-5
	Finished Product Specification	JP
	Pack Size & Demanded Price	10's, 14's, 20's, 28's, 30's / As per SRO
	Approval Status of Product in Reference Regulatory Authorities.	Amias 16 mg Tablets by M/s Takeda UK Limited (MHRA Approved)
	Me-too Status	Cansar 32mg Tablets by M/s Pharmatec (Reg#035902)
	GMP Status	Last GMP inspection conducted on 19-07-2017 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator.	
	Decision: Approved.	

Registration letter could not be issued due to disparity in strengths mentioned in composition and alongside the brand name.

In this context original dossier could not be retrieved from available record, however, the firm has submitted copies of DRAP's acknowledged receipts & fee challans of both strengths i.e., 32mg and 16mg. Furthermore, the firm has also submitted copy of registration letter of 16mg strength of above-mentioned formulation (R#091208).

Accordingly, the case has been placed for correction in strength/label claim of above-mentioned product which appears to be due to typographical (cut-paste) error.

Decision: Registration Board decided as under:

i. Approved correction in strength/ label claim of product at S.No.1 as per following detail:

Co-Mesart 40mg+5mg Tablet
Each film-coated tablet contains:
Olmesartan Medoxomil …….40mg
Amlodipine as Besilate ……..5mg
(USP Specifications)

ii. Approved correction in strength/ label claim of product at S.No.2 as per following detail:

Atasart 32mg Tablet
Each tablet contains:
Candesartan Cilexetil ……32mg
(JP Specifications)

iii. Furthermore, for product at S.No.1, the applicant shall submit fee of Rs. 7500/- in the light of notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 for pre-registration correction in finished product specifications.

Case No.14. Correction in Label Claim/ Strength of Approved Products of M/s Lisko Pakistan (Pvt) Ltd., L-10-D Block-21, Shaheed Rashid Minhas Road, Federal B Industrial Area Karachi (DML No. 000110)**.**

Registration Board in its 273rd meeting held on 28th -29th August, 2017 approved the following product of M/s Lisko Pakistan (Pvt) Ltd., L-10-D Block-21, Shaheed Rashid Minhas Road, Federal B Industrial Area Karachi (DML No. 000110) as per below mentioned details:

Name and address of manufacturer / Applicant	M/s. Lisko Pakistan (PVT.) LTD.L-10-D, BlockNo.21, Shaheed Rashid Minhas Road, Federal-B, Industrial Area, Karachi
Brand Name +Dosage Form+ Strength	Claricure Dry Suspension **250 mg/5ml**
Diary No. Date of R& I & fee	Dy. No. 255, 21-08-2015 , Rs.20,000/- (20-08-2015)
Composition	Each **5 ml** contains: Clarithromycin… **125mg**
Pharmacological Group	Macrolide Antibiotic
Type of Form	Form 5
Finished Product Specification	USP
Pack Size & Demanded Price	70ml: Glass Bottle: Rs. 408.00/-
Approval Status of Product in Reference Regulatory Authorities	Biaxin by M/s. Abbott Laboratories, USFDA
Me-too Status	Clarivin by M/s. Wnsfeld Pharmaceuticals, Hattar (R No. 069709)
GMP Status	Last inspection conducted on 23-01-2017—Good compliance.
Remarks of the Evaluator.	
Decision: Approved.	

Registration letter could not be issued due to disparity in strengths mentioned in composition and alongside the brand name.

In this context original dossier could not be retrieved from available record, however, the firm has submitted copies of DRAP's acknowledged receipts & fee challans of both strengths i.e., 250mg/5ml and 125mg/5ml. Furthermore, the firm has also submitted copy of registration letter of 125mg/5ml strength of above-mentioned formulation (R#085681) and copy of form-5 of 250mg/5ml strength stating correct label claim.

Accordingly, the case has been placed for correction in strength/label claim of above-mentioned product which appears to be due to typographical (cut-paste) error.

Decision: Registration Board approved correction in strength/ label claim of above-mentioned product as per following detail:
Claricure Dry Suspension 250 mg/5ml
Each 5ml contains:
Clarithromycin……. 250mg
(USP Specifications)

Case No.15. Correction in Composition of Approved Products of M/s Platinum Pharmaceuticals (Pvt) Ld, A-20, North western Industrial Zone, Bin Qasim Karachi (DML No. 000415).

Registration Board in its 295th meeting held on 8th-11th June 2020 approved the following product of M/s Platinum Pharmaceuticals (Pvt) Ld, A-20, North western Industrial Zone, Bin Qasim Karachi (DML No. 000415) as per below mentioned details:

Name and address of manufacturer / Applicant	"M/s Platinum Pharmaceuticals Pvt Ltd A-20, North western Industrial Zone, Bin Qasim Karachi"
Brand Name +Dosage Form + Strength	Bislol 10mg Tablet
Composition	"Each Film Coated Tablet Contains:

	Bisoprolol as fumarate….10mg
Diary No. Date of R& I & fee	Dy.No 8135 dated 25-02-2019 Rs.20,000/- Dated 15-02-2019
Pharmacological Group	Beta Blocking Agents
Type of Form	Form-5
Finished product Specification	USP
Pack size & Demanded Price	10's,20's,30's,50's,100's, As per sro.
Approval status of product in Reference Regulatory Authorities.	MHRA Approved.
Me-too status	077051 "Bisfat Tablets 10mg "M/s. Dyson Research Laboratories (Pvt) Ltd,28Km, Ferozepur Road, Lahore."
GMP status	
Remarks of the Evaluator (V)	Latest GMP inspection report (which should have been conducted within the period of last three years).
Decision: Approved.	

Registration letter could not be issued as reference/ standard formulation approved by RRA contains "**Bisoprolol fumarate**….**10mg**" instead of **"Bisoprolol as fumarate…10mg"**. However, when the firm was advised to submit correct formulation in line with that approved by RRAs, the firm submitted copies of form-5 and fee challan stating correct composition/ label claim. In this regard, original dossier could not be retrieved for confirmation of firm's claim.

Decision: **Registration Board approved correction in composition/ label claim of above-mentioned product as per following detail:**
Bislol 10mg Tablet
Each film coated tablet contains:
Bisoprolol Fumarate….10mg
(USP Specifications)

Case No.16. **Correction in Minutes of M-295th of Approved Products of** M/s Getz Pharma (Pvt.) Ltd., 29-30, Sector 27, Korangi Industrial Area, Karachi (DML No.000284)

Registration Board in its 295rd meeting held on 8th-11th June 2020 approved the following product of M/s Getz Pharma (Pvt.) Ltd., 29-30, Sector 27, Korangi Industrial Area, Karachi (DML No.000284) as per below mentioned details:

Name and address of manufacturer / Applicant	M/s Getz Pharma Private Limited. 29-30/27, Korangi Industrial area, Karachi
Brand Name +Dosage Form + Strength	Rival Oral Solution 1mg/ml
Composition	Each ml contains: Risperidone…….1mg
Diary No. Date of R& I & fee	Dy.No. 42007 dated 07-12-2018 Rs.20,000/- 07-12-2018
Pharmacological Group	Antipsychotic
Type of Form	Form-5
Finished Product Specification	BP
Pack size & Demanded Price	15ml ; Rs:270/- 30ml ; Rs:540/- 60ml ; Rs:1080/- 120ml ; Rs:2160/-
Approval status of product in Reference Regulatory Authorities.	Risperidone oral solution by Sandoz Ltd. (MHRA approved)
Me-too status	Rislet 1mg/ml Oral Solution of M/s High-Q Pharmaceuticals

GMP status	Last GMP inspection conducted on 16-12-2019, and the report concludes that the firm is considered to be operating at an acceptable level of compliance of GMP requirements.
Remarks of the Evaluator[IV]	
Decision: Approved with innovator's specification.	

Accordingly, the firm was issued registration of "Risperiget Oral Solution 1mg/ml" (R#104292). The firm has now requested for issuance of corrigendum stating that the product was applied through contract manufacturing at M/s. Herbion Pakistan (Pvt) Ltd. Industrial Triangle Kahuta Road, Humak, Islamabad, however, registration letter has been issued for self-manufacturing. In this regard, the firm has provided copy of DRAP acknowledged receipt, copy of fee challan (#0785792) of Rs.50000/- and Form-5, all stating/indicating particulars of contract manufacturing.

Decision: **Registration Board approved correction in manufacturer of Risperiget Oral Solution as per following detail:**

Reg. No.	Product Name & Composition	Registration Holder	Contract Manufacturer
104292	**Risperiget Oral Solution 1mg/ml Each ml contains: Risperidone…….1mg (USP Specifications)**	M/s Getz Pharma (Pvt.) Ltd., 29-30, Sector 27, Korangi Industrial Area, Karachi (DML No.000284)	**M/s. Herbion Pakistan (Pvt) Ltd. Industrial Triangle Kahuta Road, Humak, Islamabad** (DML No.000795)

Case No.17. Request for Change in Registration Status of Products from M/s OBS Pakistan Pvt. Ltd., (New Title: M/s Searle Pakistan Limited) C/14, Manghopir Road, S.I.T.E Karachi (DML No. 000012) to M/s AGP Limited B-23-C, S.I.T.E. Karachi (DML No. 000348)

M/s AGP Limited B-23-C, S.I.T.E. Karachi (DML No. 000348) has requested for change in registration status of following products from M/s OBS Pakistan Pvt. Ltd. (New Title: M/s Searle Pakistan Limited) C/14, Manghopir Road, S.I.T.E Karachi (DML No. 000012) to their name by way of contract manufacturing at M/s. Geofman Pharmaceuticals, 20/23, Korangi Industrial Area, Karachi (000090).

Administrative Documents Submitted in the light of SOP approved by the Registration Board in its 283rd meeting
i. Copy of GMP certificate of M/s Geofman on the basis of inspection conducted on 05-012021.
ii. Copy of DML of M/s AGP B-23-C, S.I.T.E. Karachi renewed w.e.f. 06-02-2020.
iii. Copy of approval letter dated 07-10-2021 issued by Licensing Division confirming "Injectable (Steroid Hormone) (SVP) Ampoule Section" of M/s Geofman.
iv. NOC from M/s Searle Pakistan Limited (Previous Title: M/s OBS Pakistan Pvt. Ltd.) C/14, Manghopir Road, S.I.T.E Karachi dated 12-08-2021.
v. NOC from M/s Aspin Pharma (Pvt) Ltd. Plot No.10 & 25 Sector 20 Korangi Industrial Area Karachi dated 15-08-2021 as below mentioned products were approved in 289th meeting of RB for change in registration status to M/s Aspin, Karachi, however, registration letter was not issued.
vi. Relevant undertakings & commitments.

I	II	III	IV	V
S.No.	**Reg. No.**	**Registered Product Name &**	**Registration Trail**	**Dy. No./ Fee/**

		Composition		**Date** Remarks
1.	002446	Sustanon Injection 250mg/ml Testosterone Propionate……30mg Testosterone Phenylpropionate…….60mg Testosterone Isocaproate…….60mg Testosterone Decanoate……..100mg	Initial Registration in the name of M/s Hormone Laboratories Pakistan Ltd, Karachi: 18-02-1977 Transfer to M/s. Organon: 27-02-1990 Transfer to M/s MSD: 13-12-2008 Transfer to OBS: 09-07-2009 Last Renewal Submission Date: 20-09-2019 <u>Remarks of RRR Section:</u> Renewal applications for above products for year 2014 were submitted on 17-06-14 and for year 2019 on 20-05-2019 i.e., within time w.r.t. PRV approval dated 09-07-2009	Dy.No.2428/R&I 25-01-2022
2.	002442	Deca-Durabolin Injection 25mg/ml Nandrolone Decanoate……..25mg		Dy.No.2429/R&I 25-01-2022
3.	002443	Deca-Durabolin Injection 50mg/ml Nandrolone Decanoate……..50mg		Dy.No.2427/R&I 25-01-2022
4.	002444	Deca-Durabolin Injection 100mg/ml Nandrolone Decanoate……..100mg		Dy.No.2430/R&I 25-01-2022

The cases were referred to Pharmaceutical Evaluation Cell/ QMS for scrutinization/evaluation. Detail of submitted documents remarks of evaluators have been mentioned as under:

1.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s Geofman Pharmaceuticals 20/23, Korangi Industrial Area, Karachi.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of contract manufacturing agreement between Geofman Pharma and AGP dated 25-09-2019).
	GMP status of the firm	Firm has submitted copy of GMP certificate of manufacturer dated 01-01-2020 issued on the basis of inspection dated 30-12-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 7th October 2021

		specifyng Injectable (steroid hormone) (SVP) Ampoule section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Details of fee submitted	PKR 30,000/: 03-01-2020
	The proposed proprietary name / brand name	**Sustanon 250mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml ampoule contains: Testosterone propionate…..30mg Testosterone phenylpropionate….60mg Testosterone isocaproate….60mg Testerone decanoate…..100mg
	Pharmaceutical form of applied drug	Clear yellow oily solution
	Pharmacotherapeutic Group of (API)	Sex hormones and modulators of the genital system (G03BA03)
	Reference to Finished product specifications	In house specification
	Proposed Pack size	1ml x 1's
	Proposed unit price	Already registered
	The status in reference regulatory authorities	Sustanon 250 mg/ml, solution for injection (**Netherland** Approved)
	For generic drugs (me-too status)	Sestonil injection by Hansel Pharma (Reg # 074304)
	Name and address of API manufacturer.	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Testosterone propionate:** Firm has submitted stability study data of 4 batches of drug substance only at real time conditions. The real time stability data is conducted at 25°C ± 2°C / 605% ± 5% RH for 60 months for 3 batches and 48 months for 1 batch. **Testosterone phenylpropionate:** Firm has submitted stability study data of 4 batches of drug substance. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 12 months for only 1 batch. The real time stability data is conducted at 25°C ± 2°C / 605% ± 5% RH for 60 months for 3 batches and 24 months for 1 batch. **Testosterone isocaproate:** Firm has submitted stability study data of 4 batches of drug substance only at real time conditions. The real time stability data is conducted at 25°C ± 2°C / 605% ± 5% RH for 60 months for 2 batches and 48 months for 2 batches. **Testerone decanoate:** Firm has submitted real time stability study data of 2 batches of drug substance The real time stability data is conducted at 2 – 8°C for 5 years for 1 batch and for 4 years of the second batch.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted that their product is an innovator product.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.
API Lot No.	**Testosterone propionate:** TEP01A020 **Testosterone phenylpropionate:** TPPZ01A018 **Testosterone isocaproate:** TEIC01A024 **Testerone decanoate:** TEDC01A018
Description of Pack (Container closure system)	Clear glass ampoule

Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	1401	1402	1403
Batch Size	(2 Liters)	(2 Liters)	(2 Liters)
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	03-2021	03-2021	03-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 2018/828) dated 08-08-2018 issued by Directorate of Drugs Control Health & Family Welfare Department. **The certificate was valid till 24-10-2019.**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying all drug substances from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted raw data sheets and HPLC chromatograms for 3rd month and 6month testing.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

Firm has submitted 6-month stability study data of three batches of drug product. Firm has initially submitted stability data of three batches Trial 001, Trial 002 and Trial 003. Later on in the response has submitted revised data of three different batches ***with submission of 75,000 fee (dated 27-06-2022).*** **The submitted stability study data are of 3 batches having batch size 2L each.**

Shortcomings communicated	**Response by the firm**
Valid GMP certificate of API manufacturer since the submitted GMP certificate was valid till 2019.	Firm has submitted copy Letter (No. 3785) dated 29-01-2021 issued by Directorate of Drugs Control Health & Family Welfare Department wherein it has been certified that License no. DL-1576-M & DL-802-MB

		issued in the name of ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, is valid till 24-10-2024.
	Verification studies of analytical method of drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies.
	Accelerated stability study data of 3 batches of all drug substance is not provided.	Accelerated stability studies data for three batches has been submitted.
	Validation / verification studies of the analytical method of drug product is not provided.	Analytical method verification report has been submitted.
	Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted copy of commercial invoice specifying purchase of all drug substances from ASG Biochem. The invoice was cleared by AD (I&E) on 08-02-2019.
	Submit stability study data including raw data sheets and chromatograms of initial testing of all batches.	Firm has submitted raw data sheet for initial analysis
	Justify why only 3 standard injections were used for HPLC analysis of the drug product instead of using 5 injections of standard solution.	The Firm submitted that the testing was done as per previous procedure provided by our principal; However, 5 injection practice will be implemented after the validation of testing method on new HPLC for the testing of commercial batches.
	Submit Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The Firm submitted that stability testing was done on old HPLCs, However Firm has purchase new HPLC which is 21CFR compliant and all testing of commercial batches will be done on new HPLC after the validation of testing method.
	Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted data logger record of accelerated & long term stability studies chamber.
2.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s Geofman Pharmaceuticals 20/23, Korangi Industrial Area, Karachi.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of contract manufacturing agreement between Geofman Pharma and AGP dated 25-09-2019).
	GMP status of the firm	Firm has submitted copy of GMP certificate of manufacturer dated 01-01-2020 issued on the basis of inspection dated 30-12-2019. The GMP certificate does not specify any section where steroid injection can be manufactured since the applied drug is an anabolic steroid.

	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of Drug Manufacturing License of M/s Geofman Pharmaceuticals dated 20-09-2012 specifying liquid injectable (SVP) hormone. The letter do not specify any section where steroid injection can be manufactured since the applied drug is an anabolic steroid.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Details of fee submitted	PKR 30,000/: 03-01-2020
	The proposed proprietary name / brand name	**Deca Durabolin 25mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml ampoule contains: Nandrolone decanoate…..25mg
	Pharmaceutical form of applied drug	Clear light yellow oily solution
	Pharmacotherapeutic Group of (API)	Anabolic Steroids (A14AB01)
	Reference to Finished product specifications	BP
	Proposed Pack size	1ml x 1's
	Proposed unit price	Already registered
	The status in reference regulatory authorities	Deca-Durabolin 25 mg/ml solution for injection (**Austria** Approved)
	For generic drugs (me-too status)	Deka-duralin injection by Hansel Pharma (Reg # 071401)
	Name and address of API manufacturer.	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis

		and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted real time stability study data of 3 batches of drug substance The real time stability data is conducted at 2 – 8°C.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted that their product is an innovator product.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.		
API Lot No.	NADC01A030		
Description of Pack (Container closure system)	Clear glass ampoule		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	1101	1102	1103
Batch Size	1818 ampoules (2 Liters)	1818 ampoules (2 Liters)	1818 ampoules (2 Liters)
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	03-2021	03-2021	03-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 2018/828) dated 08-08-2018 issued by Directorate of Drugs Control Health &

		Family Welfare Department. The certificate was valid till 24-10-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying 2.1 Kg Nandolone Dacanoate from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted raw data sheets and results of UV absorption values since product testing has been conducted at UV as per BP monograph.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable since product testing has been conducted at UV as per BP monograph.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for accelerated conditions from 01-03-2021 till 30-09-2021

Evaluation by PEC:

Firm has submitted 6-month stability study data of three batches of drug product. Firm has initially submitted stability data of three batches Trial 001, Trial 002 and Trial 003. Later on in the response has submitted revised data of three different batches with submission of fee of Rs. 75,000/- vide deposit slip# 9320496659. The submitted stability study data are of 3 batches having batch size 2L (1818 ampoules) each.

Shortcomings communicated	**Response by the firm**
The applied product is an anabolic steroid while as per the submitted letter of renewal of DML and GMP certificate, the manufacturing firm does not have any section where steroids can be manufactured. The firm has liquid injectable SVP (Hormone) section.	Firm has submitted copy of letter of grant of additional section dated 7th October 2021 specifying **Injectable (steroid hormone) (SVP) Ampoule section.**
Submit GMP certificate of API manufacturer	Firm has submitted copy Letter (No. 3785) dated 29-01-2021 issued by Directorate of Drugs Control Health & Family Welfare Department wherein it has been certified that License no. DL-1576-M & DL-802-MB issued in the name of ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), West Bengal, is valid till 24-10-2024.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Analytical method verification studies have been submitted.
Accelerated stability study data of drug substance is not provided.	Accelerated stability studies of three batches shave been submitted.
Validation / verification studies of the analytical method of drug product is not provided.	Analytical method verification studies have been submitted for the drug product.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted copy of commercial invoice specifying 2.1 Kg Nandolone Dacanoate from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.

Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).		Firm has submitted record of data logger for accelerated & long term conditions.
3.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s Geofman Pharmaceuticals 20/23, Korangi Industrial Area, Karachi.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of contract manufacturing agreement between Geofman Pharma and AGP dated 25-09-2019).
	GMP status of the firm	Firm has submitted copy of GMP certificate of manufacturer dated 01-01-2020 issued on the basis of inspection dated 30-12-2019. The GMP certificate does not specify any section where steroid injection can be manufactured since the applied drug is an anabolic steroid.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of Drug Manufacturing License of M/s Geofman Pharmaceuticals dated 20-09-2012 specifying liquid injectable (SVP) hormone. The letter do not specify any section where steroid injection can be manufactured since the applied drug is an anabolic steroid.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Details of fee submitted	PKR 30,000/-: 03-01-2020
	The proposed proprietary name / brand name	**Deca Durabolin 50mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml ampoule contains: Nandrolone decanoate…..50mg
	Pharmaceutical form of applied drug	Clear light yellow oily solution
	Pharmacotherapeutic Group of (API)	Anabolic Steroids (A14AB01)
	Reference to Finished product specifications	BP
	Proposed Pack size	1ml x 1's
	Proposed unit price	Already registered
	The status in reference regulatory authorities	Deca-Durabolin 50 mg/ml solution for injection (**Austria** Approved)
	For generic drugs (me-too status)	Deka-duralin injection by Hansel Pharma (Reg # 074302)

	Name and address of API manufacturer.	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted real time stability study data of 3 batches of drug substance. Real time stability data is conducted at 2 – 8°C.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted that their product is an innovator product.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.
API Lot No.	NADC01A030
Description of Pack (Container closure system)	Clear glass ampoule
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	1201	1202	1203
Batch Size	1818 ampoules (2 Liters)	1818 ampoules (2 Liters)	1818 ampoules (2 Liters)
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	03-2021	03-2021	03-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 2018/828) dated 08-08-2018 issued by Directorate of Drugs Control Health & Family Welfare Department. **The certificate was valid till 24-10-2019.**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying 2.1 Kg Nandolone Dacanoate from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted raw data sheets and results of UV ansorption values since product testing has been conducted at UV as per BP monograph.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable since product testing has been conducted at UV as per BP monograph.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for accelerated conditions from 01-03-2021 till 30-09-2021

Evaluation by PEC:

Firm has submitted 6 month stability study data of three batches of drug product. Firm has initially submitted stability data of three batches Trial 001, Trial 002 and Trial 003. Later on in the response has submitted revised data of three different batches with submission of fee of Rs. 75,000/- vide deposit slip# 15282525908. The submitted stability study data are of 3 batches having batch size 2L (1818 ampoules) each.

Shortcomings communicated	**Response by the firm**
The applied product is an anabolic steroid while as per the submitted letter of renewal of DML and GMP certificate, the manufacturing firm does not have any section where steroids can be manufactured. The firm has liquid injectable SVP (Hormone) section.	Firm has submitted copy of letter of grant of additional section dated 7th October 2021 specifying **Injectable (steroid hormone) (SVP) Ampoule section.**

Submit GMP certificate of API manufacturer	Firm has submitted copy Letter (No. 3785) dated 29-01-2021 issued by Directorate of Drugs Control Health & Family Welfare Department wherein it has been certified that License no. DL-1576-M & DL-802-MB issued in the name of ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), West Bengal, is valid till 24-10-2024.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Analytical method verification studies have been submitted.
Accelerated stability study data of drug substance is not provided.	Accelerated stability studies of three batches shave been submitted.
Validation / verification studies of the analytical method of drug product is not provided.	Analytical method verification studies have been submitted for the drug product.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted copy of commercial invoice specifying 2.1 Kg Nandolone Dacanoate from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of data logger for accelerated & long term conditions.

4.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s Geofman Pharmaceuticals 20/23, Korangi Industrial Area, Karachi.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of contract manufacturing agreement between Geofman Pharma and AGP dated 25-09-2019).
	GMP status of the firm	Firm has submitted copy of GMP certificate of manufacturer dated 01-01-2020 issued on the basis of inspection dated 30-12-2019. The GMP certificate does not specify any section where steroid injection can be manufactured since the applied drug is an anabolic steroid.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of Drug Manufacturing License of M/s Geofman Pharmaceuticals dated 20-09-2012 specifying liquid injectable (SVP) hormone. The letter do not specify any section where steroid injection can be manufactured since the applied drug is an anabolic steroid.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Details of fee submitted	PKR 30,000/-: 03-01-2020
	The proposed proprietary name / brand name	**Deca Durabolin 100mg Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml ampoule contains: Nandrolone decanoate…..100mg
	Pharmaceutical form of applied drug	Clear light yellow oily solution
	Pharmacotherapeutic Group of (API)	Anabolic Steroids (A14AB01)
	Reference to Finished product specifications	BP
	Proposed Pack size	1ml x 1's
	Proposed unit price	Already registered
	The status in reference regulatory authorities	**Discontinued in USFDA and could not be confirmed from any other RRA**
	For generic drugs (me-too status)	Deka-duralin injection by Hansel Pharma (Reg # 074187)
	Name and address of API manufacturer.	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted real time stability study data of 3 batches of drug substance. Real time stability data is conducted at 2 – 8^{o}C.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control,

		process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted that their product is an innovator product.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), Wesat Bengal, PIN-700132, West Bengal India.		
API Lot No.	NADC01A030		
Description of Pack (Container closure system)	Clear glass ampoule		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	1301	1302	1303
Batch Size	1818 ampoules (2 Liters)	1818 ampoules (2 Liters)	1818 ampoules (2 Liters)
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	03-2021	03-2021	03-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. 2018/828) dated 08-08-2018 issued by Directorate of Drugs Control Health & Family Welfare Department. **The certificate was valid till 24-10-2019.**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice specifying 2.1 Kg Nandrolone Dacanoate from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted raw data sheets and results of UV absorption values since product testing has been conducted at UV as per BP monograph.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable since product testing has been conducted at UV as per BP monograph.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for accelerated conditions from 01-03-2021 till 30-09-2021

Evaluation by PEC:

Firm has submitted 6-month stability study data of three batches of drug product. Firm has initially submitted stability data of three batches Trial 001, Trial 002 and Trial 003. Later on, in the response has submitted revised data of three different batches with submission of fee of Rs. 75,000/- vide deposit slip# 812475565471. The submitted stability study data are of 3 batches having batch size 2L (1818 ampoules) each.

Shortcomings communicated	**Response by the firm**
Evidence of approval of applied formulation in reference regulatory authorities is required.	• Firm has referred to the list published on TGA website for "Designated orphan drugs prior to 1 July 2017", wherein **"Nandrolone decanoate (DECA-DURABOLIN 100)"** has been designated as orphan drug dated 30-12-99, verifiable from following weblink: https://www.tga.gov.au/orphan-drugs#summary-n • Further firm has referred to the US Federal Register wherein determination has been made for Deca-Durabolin 200mg/ml FDA has reviewed its records and, under § 314.161, has determined that Deca-Durabolin (nandrolone decanoate) Injection, 200 mg/mL, 1 mL, was not withdrawn from sale for reasons of safety or effectiveness. https://www.federalregister.gov/documents/2010/08/10/2010-19698/determination-that-deca-durabolin-nandrolone-decanoate-injection-200-milligramsmilliliter-1 • Firm has referred to the Deca-Durabolin injection 100mg from US FDA Approved Drug database, wherein the status has been declared as Discontinued. • Firm has also referred to following text from section 314.161 (Determination of reasons for voluntary withdrawal of a listed drug) of Chapter I of Title 21 of US Code of Federal Regulations: "*A drug that the agency determines is withdrawn for safety or effectiveness reasons will be removed from the list, under § 314.162.* The drug may be relisted if the agency has evidence that marketing of the drug has resumed or that the withdrawal is not for safety or effectiveness reasons. A determination that the drug is not withdrawn for safety or effectiveness reasons may be made at any time after its removal from the list, upon the agency's initiative, or upon the submission of a petition under §§ 10.25(a) and 10.30 of this chapter. If the agency determines that the drug is not withdrawn for safety or effectiveness reasons, the agency shall publish a notice of this determination in the Federal Register. The notice will also announce that the drug is relisted, under § 314.162(c). The notice will also serve to reinstate approval of all suspended

	abbreviated new drug applications that referred to the listed drug."
The applied product is an anabolic steroid while as per the submitted letter of renewal of DML and GMP certificate, the manufacturing firm does not have any section where steroids can be manufactured. The firm has liquid injectable SVP (Hormone) section.	Firm has submitted copy of letter of grant of additional section dated 7th October 2021 specifying **Injectable (steroid hormone) (SVP) Ampoule section.**
Submit GMP certificate of API manufacturer	Firm has submitted copy Letter (No. 3785) dated 29-01-2021 issued by Directorate of Drugs Control Health & Family Welfare Department wherein it has been certified that License no. DL-1576-M & DL-802-MB issued in the name of ASG Biochem Pvt. Ltd. Ganganagar 24 PGS (N), West Bengal, is valid till 24-10-2024.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Analytical method verification studies have been submitted.
Accelerated stability study data of drug substance is not provided.	Accelerated stability studies of three batches shave been submitted.
Validation / verification studies of the analytical method of drug product is not provided.	Analytical method verification studies have been submitted for the drug product.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted copy of commercial invoice specifying 2.1 Kg Nandolone Dacanoate from ASG Biochem. The invoice was cleared by AD (I&E) on 09-08-2019.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of data logger for accelerated & long-term conditions.

Proceeding of M-320:

i. It was informed that above-mentioned products were previously manufactured by M/s Pharmatec Pakistan (Pvt.) Ltd., Karachi on contract basis.

ii. CLB in its 251st meeting held on 6th December 2017 considered and deliberated the case of M/s Pharmatec Pakistan (Pvt) Ltd., D-86/A, S.I.T.E, Karachi under DML No. 000024 by way of formulation and decided to allow grant of renewal section for 'Sterile Liquid Ampoule Section' with the direction that Registration Board be informed about approval of sterile Liquid ampoule section only.

iii. Accordingly, M/s OBS Pakistan (Pvt.) Ltd., Karachi was issued show cause notice in the light of decision taken by the Registration Board in its 275th meeting (held on 25th-27th Oct, 2017) as to why the registration of above mentioned products manufactured in hormone facility of M/s. Pharmatec Pakistan (Pvt.) Ltd., Karachi on contract basis may not be cancelled with immediate effect.

iv. Later on, the case was approved in 289th meeting of Registration Board (held on 14th-16th May, 2019) for change in registration status of above-mentioned products from M/s OBS Pakistan (Pvt.) Ltd., Karachi to M/s Aspin Pharma (Pvt.) Ltd, Plot No.10 & 25 Sector 20 Korangi Industrial Area Karachi (DML No. 000045) through contract manufacturing at M/s. Geofman Pharmaceuticals, 20/23 Main Korangi Industrial Area, Karachi.

v. However, while the cancellation & registration letters (w.r.t. point iv) were under-process, the application was submitted (dated 19-09-2019 with fee of Rs.20000/each) by M/s AGP Limited B-23-C S.I.T.E., Karachi for change in registration status from M/s Aspin Pharma (Pvt.) Ltd, Plot No.10 & 25 Sector 20 Korangi Industrial Area Karachi to M/s M/s AGP Limited B-23-C S.I.T.E., Karachi through contract manufacturing at M/s. Geofman Pharmaceuticals, 20/23 Main Korangi Industrial Area, Karachi .

Decision: Registration Board decided as under:

i. Cancelled registration of following products from the name of M/s OBS Pakistan (Pvt.) Ltd. (New Title: M/s Searle Pakistan Limited) C-14, Manghopir Road, S.I.T.E Karachi (DML # 000012)

S. No.	Reg. No.	Product Name & Composition
1.	002446	Sustanon Injection 250mg/ml Testosterone Propionate……30mg Testosterone Phenylpropionate…….60mg Testosterone Isocaproate…….60mg Testosterone Decanoate……..100mg
2.	002442	Deca-Durabolin Injection 25mg/ml Nandrolone Decanoate……..25mg
3.	002443	Deca-Durabolin Injection 50mg/ml Nandrolone Decanoate……..50mg
4.	002444	Deca-Durabolin Injection 100mg/ml Nandrolone Decanoate……..100mg

ii. Approved registration of following products in the name of M/s AGP Limited B-23-C, S.I.T.E. Karachi (DML No. 000348) by way of contract manufacturing at M/s. Geofman Pharmaceuticals, 20/23, Korangi Industrial Area, Karachi (DML No.000090).

a) Manufacturer will place first three production batches of both products on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

b) Manufacturer will perform process validation of first three batches of both products as per the commitment submitted in the registration application.

S. No.	Product Name & Composition
1.	Sustanon 250mg Injection Each ml ampoule contains: Testosterone Propionate……..30mg Testosterone Phenylpropionate……..….60mg Testosterone Isocaproate…….60mg Testerone Decanoate……....100mg

	(In House Specifications)
2.	**Deca Durabolin 25mg Injection** **Each ml ampoule contains:** **Nandrolone Decanoate……...25mg** **(BP Specifications)**
3.	**Deca Durabolin 50mg Injection** **Each ml ampoule contains:** **Nandrolone Decanoate……..50mg** **(BP Specifications)**
4.	**Deca Durabolin 100mg Injection** **Each ml ampoule contains:** **Nandrolone Decanoate……....100mg** **(BP Specifications)**

iii. **Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).**

iv. **Registration letter will be issued after submission of following fee/ information/ documents:**

a) **Differential fee of Rs.45000/each for change in registration status from one manufacturer to another manufacturer by way of contract manufacturing.**

b) **Report of Pharmaceutical Equivalence study performed against the innovator's product.**

Case No.18. Request for Change in Registration Status of Products from M/s Novartis Pharma (Pakistan) Limited, 15-West Wharf, Dockyard Road, Karachi (DML No.000193) to M/s AGP Limited B-23-C, S.I.T.E. Karachi (DML No. 000348)

M/s AGP Limited B-23-C, S.I.T.E. Karachi (DML No. 000348) has requested for change in registration status of following products from M/s Novartis Pharma (Pakistan) Limited, 15- West Wharf, Dockyard Road, Karachi (DML # 000193) to their name. **The products are currently registered by way of contract manufacturing at M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore and permission is valid till 30-06-2025.** Manufacturing site will remain same.

Administrative Documents Submitted in the light of SOP approved by the Registration Board in its 283rd meeting
i. Copy of GMP certificate of M/s CSH, Lahore on the basis of inspection conducted on **22-07-2019**
ii. Copy of DML of M/s AGP B-23-C, S.I.T.E. Karachi renewed w.e.f. 06-02-2020.
iii. Copy of approval letter issued dated 01-08-2012 by Licensing Division confirming "Tablet (Penicillin) Section & Dry Powder for Suspension (Penicillin) Section"
iv. NOC from M/s. Novartis Pharma (Pakistan) Limited, 15- West Wharf, Dockyard Road, Karachi dated 23-06-2022.
v. Relevant undertakings & commitments.

I	**II**	**III**	**IV**
S.No.	**Reg. No.**	**Registered Product Name & Composition**	**Dy. No./ Fee/ Date** Remarks
1.	007688	Ospamox 125mg/5ml Dry Suspension Each 5ml contains: Amoxicillin (as trihydrate)…125mg	Dy.No.10670/R&I Dated 26-04-2022
2.	007689	Ospamox 250mg/5ml Dry Suspension	Dy.No.10671/R&I

		Each 5ml contains: Amoxicillin (as trihydrate)…250mg	Dated 26-04-2022
3.	007684	Ospamox 500mg Tablet Each film coated tablet contains: Amoxicillin (as trihydrate)…500mg	Dy.No.10672/R&I Dated 26-04-2022
4.	007686	Ospamox 1000mg tablet Each film coated tablet contains: Amoxicillin (as trihydrate)…1000mg	Dy.No.10673/R&I Dated 26-04-2022
5.	031358	Amoxi-Clav 156.25mg Dry Suspension Each 5ml contains: Amoxicillin (as trihydrate)….125mg Clavulanic acid (as potassium)…31.25mg	Dy.No.8953/R&I Dated 07-04-2022
6.	031359	Amoxi-Clav 312.5mg Dry Suspension Each 5ml contains: Amoxicillin (as trihydrate)….250mg Clavulanic acid (as potassium)…62.5mg	Dy.No.8954/R&I Dated 07-04-2022
7.	031335	Amoxi-Clav 375mg Tablets Each film coated tablet contains: Amoxicillin (as trihydrate)….250mg Clavulanic acid (as potassium)…125mg	Dy.No.8955/R&I Dated 07-04-2022
8.	031356	Amoxi-Clav 625mg Tablets Each film coated tablet contains: Amoxicillin (as trihydrate)….500mg Clavulanic acid (as potassium)…125mg	Dy.No.8956/R&I Dated 07-04-2022
9.	031357	Amoxi-Clav 1gm Tablets Each film coated tablet contains: Amoxicillin (as trihydrate)….875mg Clavulanic acid (as potassium)…125mg	Dy.No.8957/R&I Dated 07-04-2022

The cases were referred to Pharmaceutical Evaluation Cell/ QMS for scrutinization/evaluation. Detail of submitted documents remarks of evaluators have been mentioned as under:

1.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin),

		Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10670: 26-04-2022
	Details of fee submitted	PKR 75,000/-: 14-04-2022
	The proposed proprietary name / brand name	**OSPAMOX 125mg Granules for suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Amoxicillin (as trihydrate)…….125mg
	Pharmaceutical form of applied drug	White to yellowish granules
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	60ml & 90ml
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Amoxil suspension **(USFDA** Approved)
	For generic drugs (me-too status)	Oximox suspension by CSH
	Name and address of API manufacturer.	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities,

		physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 60 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted report of pharmaceutical equivalence study of their product against Amoxil Suspension.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers - Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain		
API Lot No.	B393297		
Description of Pack (Container closure system)	Amber color glass bottle		
Stability Storage Condition	Real time: $30^{\circ}C \pm 2^{\circ}C$ / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17SC030	18SC054	19SC026
Batch Size	10,813 Packs	11,111 Packs	11,111 Packs
Manufacturing Date	05-2017	10-2018	09-2019
Date of Initiation	26-05-2017	29-10-2018	06-12-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	N/A

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Valid GMP certificate of API manufacturer since the submitted GMP certificate was valid till 2019.	Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for amoxicillin trihydrate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has submitted referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence study is not provided.	Firm has submitted report of pharmaceutical equivalence study of their product against Amoxil Suspension.
Submit COA of working standard / reference standard used in the analysis of drug substance and drug product.	Firm has submitted COA of working standard.
Batch 19SC026 is manufactured in 09-2019 while stability is initiated on 06-12-2019. Justification is required in this regard.	The batch no. 19SC026 was manufactured in 09-2019 whereas it was decided by the principal in Dec-2019 to place this batch on stability on random basis.

Justify why accelerated stability study of drug product is not conducted.	Firm has now submitted accelerated stability study data sheets for 3 different batches i.e. 15SC01, 15SC02 and 15SC03.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch.
Submit stability study data including raw data sheets and chromatograms of initial testing of all batches.	Firm has submitted stability study record for accelerated (6 months) and long term stability studies (24 months) as per Zone IV a conditions for three batches.
Submit Compliance Record of HPLC software 21CFR & audit trail reports on product testing	As the stability studies were conducted in 2015, 2017, 2018 and 2019 the audit trail is not available. However, all HPLCs are 21CFR compliant
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger of real time and accelerated stability study chamber.

2.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10671: 26-04-2022
	Details of fee submitted	PKR 75,000/-: 14-04-2022

	The proposed proprietary name / brand name	**OSPAMOX 250mg Granules for suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Amoxicillin (as trihydrate)…….250mg
	Pharmaceutical form of applied drug	White to yellowish granules
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	60ml & 90ml
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Amoxil suspension **(USFDA** Approved)
	For generic drugs (me-too status)	Oximox suspension by CSH
	Name and address of API manufacturer.	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 60 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture,

		manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence studies have been submitted against Amoxil forte 250mg suspension of M/s GSK.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers - Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain		
API Lot No.	B393297		
Description of Pack (Container closure system)	Amber color glass bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17SD035	18SD104	19SD080
Batch Size	8,512 Packs	8,333 Packs	5,200 Packs
Manufacturing Date	05-2017	12-2018	05-2019
Date of Initiation	01-06-2017	28-12-2018	23-05-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Amoxicillin Trihydrate:** Firm has submitted copy of GMP certificate (No. NCF-II/1823/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Department of Health General Directorate of Proessional Health Planning and Regulation, Government of Catalonia dated 03-07-2018 based on inspection conducted dated 22 May 2018. As per the certificate it is valid for 3 years.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Valid GMP certificate of API manufacturer since the submitted GMP certificate was valid till 2019.	Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for amoxicillin trihydrate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence study is not provided.	Firm has submitted report of pharmaceutical equivalence study of their product against Amoxil Suspension.
Submit COA of working standard / reference standard used in the analysis of drug substance and drug product.	Firm has submitted COA of working standard.
Batch 17SD035 is manufactured in 05-2017 while stability is initiated on 06-2017. Justification is required in this regard.	The batch no. 17SD035 was manufactured in 05-2017 whereas it was decided by the principal in 06-2017 to place this batch on stability.
Justify why accelerated stability study of drug product is not conducted.	Firm has now submitted accelerated stability study data sheets for 3 different batches i.e. 15SD03, 15SD04 and 15SD05.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch.
Submit stability study data including raw data sheets and chromatograms of initial testing of all batches.	Firm has submitted stability study record for accelerated (6 months) and long-term stability studies (24 months) as per Zone IV a conditions for three batches.

Submit Compliance Record of HPLC software 21CFR & audit trail reports on product testing	As the stability studies were conducted in 2015, 2017, 2018 and 2019 the audit trail is not available. However, all HPLCs are 21CFR compliant
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger of real time and accelerated stability study chamber.

3.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10672: 26-04-2022
	Details of fee submitted	PKR 75,000/-: 14-04-2022
	The proposed proprietary name / brand name	**OSPAMOX 500mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablet contains: Amoxicillin (as trihydrate)…….500mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	12’s, 20’s, & 100’s

	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Amoxicillin Tablets **(USFDA** Approved)
	For generic drugs (me-too status)	Oximox Tablet by CSH
	Name and address of API manufacturer.	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 60 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted.

		CDP is performed but the name of the reference product is not mentioned against which CDP is performed.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers - Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain		
API Lot No.	B393297		
Description of Pack (Container closure system)	Alu-PVC blister		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17TD025	18TD043	19TD001
Batch Size	24,396 Packs	300,000 Tablets	300,000 Tablets
Manufacturing Date	06-2017	10-2018	04-2019
Date of Initiation	06-07-2017	29-10-2018	16-07-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. NCF-11/1823/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Department of Health General Directorate of Proessional Health Planning and Regulation, Government of Catalonia dated 03-07-2018 based on inspection conducted dated 22, 23, 24 and 25th May 2018. As per the certificate it is valid for 4 years.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

Shortcomings communicated	Response by the firm
Valid GMP certificate of API manufacturer since the submitted GMP certificate was valid till 2019.	Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for amoxicillin trihydrate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence study is not provided.	Firm has submitted pharmaceutical equivalence studies & CDP report in three dissolution medias with acceptable value of f2 factor, against the Amoxistad 500mg tablets of M/s Stada Arzneimittel, Austria.
Provide details of the reference product against which CDP studies are conducted.	Firm has submitted pharmaceutical equivalence studies & CDP report in three dissolution medias with acceptable value of f2 factor, against the Amoxistad 500mg tablets of M/s Stada Arzneimittel, Austria.
Submit COA of working standard / reference standard used in the analysis of drug substance and drug product.	Firm has submitted COA of working standard.
Justify why accelerated stability study of drug product is not conducted.	Firm has now submitted accelerated stability study data sheets for 3 different batches.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate.
Submit stability study data including raw data sheets and chromatograms of initial testing of all batches.	Firm has submitted stability study record for accelerated (6 months) and long-term stability studies (24 months) as per Zone IV a conditions for three batches.
Submit Compliance Record of HPLC software 21CFR & audit trail reports on product testing	As the stability studies were conducted in 2015, 2017, 2018 and 2019 the audit trail is not available. However, all HPLCs are 21CFR compliant
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger of real time and accelerated stability study chamber.

4.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10673: 26-04-2022
	Details of fee submitted	PKR 75,000/-: 14-04-2022
	The proposed proprietary name / brand name	**OSPAMOX 1000mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablet contains: Amoxicillin (as trihydrate)…….1000mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	10’s, 12’s, & 100’s
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	**Could not be confirmed from any RRA**
	For generic drugs (me-too status)	Oximox Tablet by CSH
	Name and address of API manufacturer.	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -

		08520 Les Franqueses Del Valles, Barcelona, Spain
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 60 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted. CDP is performed but the name of the reference product is not mentioned against which CDP is performed.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.
STABILITY STUDY DATA		
Manufacturer of API	SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers - Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain	

API Lot No.	B393297		
Description of Pack (Container closure system)	Alu-PVC blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17TE009	18TE017	19TE007
Batch Size	12,359 Packs	150,000 Tablets	12,500 Tablets
Manufacturing Date	06-2017	11-2018	04-2019
Date of Initiation	15-06-2017	15-11-2018	02-05-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Evidence of approval of applied formulation in RRA is required.	Firm has referred to the "Amoxilane tablet 1000g of M/s GL Pharma GmbH, approved by AGES of Austria, verified from following web link: Register of proprietary medicinal products (basg.gv.at)

Valid GMP certificate of API manufacturer since the submitted GMP certificate was valid till 2019.	Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E - 08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.
Verification studies of analytical method of drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for amoxicillin trihydrate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence study is not provided.	Firm has submitted pharmaceutical equivalence studies & CDP report in three dissolution medias with acceptable value of f2 factor, against the Amoxilan 1000mg tablets of M/s GL pharma Austria
Provide details of the reference product against which CDP studies are conducted.	Firm has submitted pharmaceutical equivalence studies & CDP report in three dissolution medias with acceptable value of f2 factor, against the Amoxilan 1000mg tablets of M/s GL pharma Austria
Submit COA of working standard / reference standard used in the analysis of drug substance and drug product.	Firm has submitted COA of working standard.
Justify why accelerated stability study of drug product is not conducted.	Firm has now submitted accelerated stability study data sheets for 3 different batches.
Submit evidence of procurement of relevant batch of drug substances used in the manufacturing of batches of drug product whose stability data is submitted.	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch.
Submit stability study data including raw data sheets and chromatograms of initial testing of all batches.	As the Accelerated stability performed in 2015, raw data of initial month testing is not available. However, available raw data of Accelerated 03rd and 06th month and For Long Term Initial, 3rd, 06th, 09th, 12th, 18th and 24th month data has been provided. Firm has submitted the commitment as: "*We have submitted the stability data (commercial batches) of Ospamox 125mg Granules for oral Suspension at 40°C + 2°C/ 75% + 5% RH, 25°C + 2°C/ 60% + 5% RH & 30°C + 2°C/ 65% + 5% RH*. We *hereby commit that after the transfer of registration of product we will again conduct the stability studies of first three commercial batches and submit the complete testing."* *Stability data sheets and commitment are attached* **Firm has not provided raw data and chromatograms for stability study.**

Submit Compliance Record of HPLC software 21CFR & audit trail reports on product testing	As the stability studies were conducted in 2015, 2017, 2018 and 2019 the audit trail is not available. However, all HPLCs are 21CFR compliant
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger of real time and accelerated stability study chamber.

5.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8953: 07-04-2022
	Details of fee submitted	PKR 75,000/-: 02-03-2022
	The proposed proprietary name / brand name	**Amoxi-clav 156.25mg granules for oral suspension**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Amoxicillin trihydrate eq to Amoxicillin…….125mg Potassium clavulanate eq to Clavulanic acid……31.25mg
	Pharmaceutical form of applied drug	White to yellowish white crystalline powder
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP

	Proposed Pack size	60ml, 90ml & 100ml
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Augmentin suspension **(USFDA** Approved)
	For generic drugs (me-too status)	Amclav suspension by Getz Pharma
	Name and address of API manufacturer.	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Amoxicillin Trihydrate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 60 months. **Potassium Clavulanate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 24 months

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted. CDP is not applicable as per the firm.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia		
API Lot No.	**Amoxicillin Trihydrate:** B393297 **Potassium Clavulanate:** B418839AA, B449299AA, B485491AA		
Description of Pack (Container closure system)	Amber color glass bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17SA031	18SA026	19SA010
Batch Size	19,260 Packs	19,736 Packs	19,736 Packs
Manufacturing Date	07-2017	10-2018	05-2019
Date of Initiation	21-07-2017	06-11-2018	16-05-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Amoxicillin Trihydrate:** Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023.

		Potassium Clavulanate: Firm has submitted copy of GMP certificate (401-3/2022-5) of M/s Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia dated 24-06-2022 issued by Agency for medicinal products and medical devices of the Republic of Slovenia based on the inspection dated 18-03-2022 valid till 17-03-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The APIs were procured in 2016 for commercial batches. All APIs ware cleared from customs and DRAP as per applicable procedure.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that as the stability studies were conducted in 2017 and 2018 the audit trail is not available. However, all HPLCs are 21CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger from 01-01-2018 till 09-06-2021.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Revise label claim as per the reference product along with submission of fee. (firm has applied for clavulanic acid…125mg instead of potassium clavulanate eq to clavulanic acid 125mg).	The firm has submitted the response. The label claim is as per Innovator's/ Reference Product Each 5ml contains: Amoxicillin Trihydrate corresponding to 125mg Amoxicillin Potassium clavulinate corresponding to 31.25mg Clavulanic Acid
Verification studies of analytical method of both drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for amoxicillin trihydrate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence is not submitted.	Firm has submitted the pharmaceutical equivalence studies against reference product of Augmentin.
Submit compatibility studies of the drug product with recommended diluent / solvent.	Submitted.
Provide exact COA of RS used in stability testing. Further justify how RS of clavulanate lithium is used from Shandong New Time Pharmaceutical. Submitted COA are of 2019 and 2020 while stability batches were of 2017, 2018 and 2019.	Firm has submitted COA of USP reference standard for Clavulanate lithium (Lot#K0J130)

Submit analytical record for long term stability studies	Frim has submitted analytical record along with chromatograms.
BMR of three stability batches are not provided.	As per manufacturers procedure the BMR was destroyed after 1 year of the expiry of product However, few documents related to batch manufacturing like batch release certificate, dispensing order sheet etc are attached
Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch. Firm has submitted Air way bill dated 20-06-2017 for import of 600Kg of Potassium Clavulanate along with COA of relevant batch.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger of real time & accelerated stability study chamber.

6.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8954: 07-04-2022
	Details of fee submitted	PKR 75,000/-: 02-03-2022
	The proposed proprietary name / brand name	**Amoxi-clav 312.5mg granules for oral suspension**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Amoxicillin trihydrate eq to Amoxicillin…….250mg Potassium clavulanate eq to Clavulanic acid……62.50mg
	Pharmaceutical form of applied drug	White to yellowish white crystalline powder
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	60ml, 90ml & 100ml
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Augmentin suspension **(USFDA** Approved)
	For generic drugs (me-too status)	Amclav suspension by Getz Pharma
	Name and address of API manufacturer.	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Amoxicillin Trihydrate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data

		is conducted at 30°C ± 2°C / 65% ± 5% RH for 60 months. **Potassium Clavulanate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75% ± 5% RH for 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted. CDP is not applicable as per the firm.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia		
API Lot No.	**Amoxicillin Trihydrate:** B396480, B396486, B448004 **Potassium Clavulanate:** B400346AA, B438707AA		
Description of Pack (Container closure system)	Amber color glass bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17SB024	18SB005	19SB011
Batch Size	19,200 Packs	19,736 Packs	16,298 Packs
Manufacturing Date	06-2017	06-2018	04-2019
Date of Initiation	19-06-2017	05-07-2018	23-04-2019
No. of Batches	03		
DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Amoxicillin Trihydrate:** Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023. **Potassium Clavulanate:** Firm has submitted copy of GMP certificate (401-3/2022-5) of M/s Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia dated 24-06-2022 issued by Agency for medicinal products and medical devices of the Republic of Slovenia based on the inspection dated 18-03-2022 valid till 17-03-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The APIs were procured in 2016 for commercial batches. All APIs ware cleared from customs and DRAP as per applicable procedure.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that as the stability studies were conducted in 2017 and 2018 the audit trail is not available. However, all HPLCs are 21CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for accelerated and long term stability studies.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Revise label claim as per the reference product along with submission of fee. (firm has applied for clavulanic acid…125mg instead of potassium clavulanate eq to clavulanic acid 125mg).	The firm has submitted the response. The label claim is as per Innovator's/ Reference Product Each 5ml contains: Amoxicillin Trihydrate corresponding to 250mg Amoxicillin Potassium clavulanate corresponding to 62.50mg Clavulanic Acid.
Verification studies of analytical method of both drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for both Amoxicillin & Potassium clavulanate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.

Pharmaceutical equivalence is not submitted.	Firm has submitted the pharmaceutical equivalence studies against reference product of Augmentin.
Submit compatibility studies of the drug product with recommended diluent / solvent.	Submitted
Provide exact COA of RS used in stability testing. Further justify how RS of clavulanate lithium is used from Shandong New Time Pharmaceutical. Submitted COA are of 2019 and 2020 while stability batches were os 2017, 2018 and 2019.	Firm has submitted COA of USP reference standard for Clavulanate lithium (Lot#K0J130)
Justify long term stability studies of product at 25 degree.	Firm has submitted accelerated and long-term stability record as per Zone IV a condition for three batches.
BMR of three stability batches are not provided.	As per manufacturers procedure the BMR was destroyed after 1 year of the expiry of product However, few documents related to batch manufacturing like batch release certificate, dispensing order sheet etc are attached
Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch. Firm has submitted Air way bill dated 20-06-2017 for import of 600Kg of Potassium Clavulanate along with COA of relevant batch.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for accelerated and long term stability studies.

7.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule

		(Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8955: 07-04-2022
	Details of fee submitted	PKR 75,000/-: 02-03-2022
	The proposed proprietary name / brand name	**Amoxi-clav 375mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablet contains: Amoxicillin trihydrate eq to Amoxicillin…….250mg Potassium clavulanate eq to Clavulanic acid……125mg
	Pharmaceutical form of applied drug	White to almost white oblong film coated tablet with bevelled edges and score on both sides.
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	2 x 3's
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Augmentin 375mg Tablets **(MHRA** Approved)
	For generic drugs (me-too status)	Amclav Tablet by Getz Pharma
	Name and address of API manufacturer.	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature,

		structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Amoxicillin Trihydrate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 60 months. **Potassium Clavulanate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75% ± 5% RH for 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted. CDP is performed against Augmentin Tablet.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia
API Lot No.	**Amoxicillin Trihydrate:** B396478, B396473, B440845 **Potassium Clavulanate:** B403093AA, B461888AA
Description of Pack (Container closure system)	Alu-alu strip
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH
Time Period	Real time: 24 months

Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17TA005	18TA006	19TA001
Batch Size	400,000 Tablets	400,000 Tablets	400,000 Tablets
Manufacturing Date	06-2017	05-2018	07-2019
Date of Initiation	07-06-2017	14-05-2018	16-07-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Amoxicillin Trihydrate:** Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023. **Potassium Clavulanate:** Firm has submitted copy of GMP certificate (401-3/2022-5) of M/s Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia dated 24-06-2022 issued by Agency for medicinal products and medical devices of the Republic of Slovenia based on the inspection dated 18-03-2022 valid till 17-03-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The APIs were procured in 2016 for commercial batches. All APIs ware cleared from customs and DRAP as per applicable procedure.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that as the stability studies were conducted in 2017 and 2018 the audit trail is not available. However, all HPLCs are 21CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger from 01-01-2018 till 09-06-2021. The data logger was set at 25°C and 60% RH.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Revise label claim as per the reference product along with submission of fee. (firm	The firm has submitted corrected formulation as per reference product.

has applied for clavulanic acid…125mg instead of potassium clavulanate eq to clavulanic acid 125mg).	**Amoxi-Clav 375mg Film Coated Tablets** Each Film coated tablet contains: Amoxicillin Trihydrate equivalent to 250mg amoxicillin and Potassium clavulanate equivalent to 125mg of Clavulanic acid. Firm has submitted fee of R/s.7,500/-
Verification studies of analytical method of both drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for both Amoxicillin & Potassium clavulanate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product of similar qualitative composition.
Pharmaceutical equivalence is not submitted.	Firm has submitted the pharmaceutical equivalence studies against reference product of Augmentin tablet.
How CDP results decrease with time i.e. from 81.6% to 93%, 88.1% and 81.8% in 4.5 pH acetate buffer and 88.29 to 95.17%, 90.8% and 87.1% in 6.8 pH buffer.	Due to un-stability/degradation behavior with passing time in these medium, CDP results decreased. This observation is similar in both test product & reference product.
CDP time points are significantly different from that specified in FDA dissolution database.	Both test are different. FDA dissolution data base is for development of product dissolution with defined parameters, while CDP is part of therapeutic equivalence, performed in at least three media covering the physiological range, including pH 1.2 hydrochloric acid, pH 4.5 buffer and pH 6.8 buffer. As per WHO (Technical Report Series, No. 1003, 2017) minimum of three time points (zero excluded) should be included, the time points for both reference (comparator) and test product being the same.
Significant difference in peak areas of system suitability / stanard solution in AMV and in stability studies.	Difference of peak areas has no impact for calculation of results. As peak areas are depends on brand, life, sensitivity of system & column while results calculation depends on current peak areas of standard and sample solution which eluted in same system environment.
Provide exact COA of RS used in stability testing. Further justify how RS of clavulanate lithium is used from Shandong New Time Pharmaceutical. Submitted COA are of 2019 and 2020 while stability batches were as 2017, 2018 and 2019.	Firm has submitted COA of USP reference standard for Clavulanate lithium (Lot#K0J130)
Justify long term stability studies of product at 25 degree.	Firm has submitted accelerated and long-term stability record as per Zone IV a condition for three batches.
BMR of three stability batches are not provided.	As per manufacturers procedure the BMR was destroyed after 1 year of the expiry of product However, few documents related to batch manufacturing like batch release certificate, dispensing order sheet etc are attached
Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch.

	Firm has submitted Air way bill dated 20-06-2017 for import of 600Kg of Potassium Clavulanate along with COA of relevant batch.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for accelerated and long term stability studies.

8.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**
	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8956: 07-04-2022
	Details of fee submitted	PKR 75,000/-: 02-03-2022
	The proposed proprietary name / brand name	**Amoxi-clav 625mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablet contains: Amoxicillin trihydrate eq to Amoxicillin…….500mg Potassium clavulanate eq to Clavulanic acid……125mg
	Pharmaceutical form of applied drug	White to almost white oblong film coated tablet with bevelled edges and score on both sides.
	Pharmacotherapeutic Group of (API)	Penicillin

	Reference to Finished product specifications	USP
	Proposed Pack size	2 x 3's
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Augmentin 625mg Tablets **(MHRA** Approved)
	For generic drugs (me-too status)	Amclav Tablet by Getz Pharma
	Name and address of API manufacturer.	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Amoxicillin Trihydrate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 60 months. **Potassium Clavulanate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data

		is conducted at 30ºC ± 2ºC / 75% ± 5% RH for 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted. CDP is performed against Augmentin Tablet.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia		
API Lot No.	**Amoxicillin Trihydrate:** B396478, B441618 **Potassium Clavulanate:** B403093AA, B462465AA		
Description of Pack (Container closure system)	Alu-alu strip		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17TB023	18TB028	19TB008
Batch Size	44329 Packs	270,000 Tablets	45,000 Packs
Manufacturing Date	05-2017	05-2018	05-2019
Date of Initiation	06-06-2017	01-06-2018	21-05-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Amoxicillin Trihydrate:** Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines &

		Health Products dated 13-05-2022 valid till 22/05/2023. **Potassium Clavulanate:** Firm has submitted copy of GMP certificate (401-3/2022-5) of M/s Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia dated 24-06-2022 issued by Agency for medicinal products and medical devices of the Republic of Slovenia based on the inspection dated 18-03-2022 valid till 17-03-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The APIs were procured in 2016 for commercial batches. All APIs ware cleared from customs and DRAP as per applicable procedure.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that as the stability studies were conducted in 2017 and 2018 the audit trail is not available. However, all HPLCs are 21CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger from 01-01-2018 till 09-06-2021. The data logger was set at 25°C and 60% RH.

Evaluation by PEC:

Firm has submitted real time stability sudy data of 3 batches till 24 months where firm has performed stability studies at 25°C ± 2°C / 60% ± 5%RH as well as at 30°C ± 2°C / 65% ± 5%RH. However accelerated stability study data is not provided.

Shortcomings communicated	**Response by the firm**
Revise label claim as per the reference product along with submission of fee. (firm has applied for clavulanic acid…125mg instead of potassium clavulanate eq to clavulanic acid 125mg).	The firm has submitted corrected formulation as per reference product. **Amoxi-Clav 625mg Film Coated Tablets** Each Film coated tablet contains: Amoxicillin Trihydrate equivalent to 500mg amoxicillin and Potassium clavulanate equivalent to 125mg of Clavulanic acid. Firm has submitted fee of Rs. 7,500/- vide deposit slip# 48092838.
Verification studies of analytical method of both drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for both Amoxicillin & Potassium clavulanate.
Justify why the qualitative composition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence is not submitted.	Firm has submitted that the pharmaceutical equivalence studies against Augmentin tablet.
How CDP results decrease with time i.e. from 81.6% to 93%, 88.1% and 81.8% in 4.5 pH	Due to un-stability/degradation behavior with passing time in these medium, CDP results

acetate buffer and 88.29 to 95.17%, 90.8% and 87.1% in 6.8 pH buffer.	decreased. This observation is similar in both test product & reference product.
CDP time points are significantly different from that specified in FDA dissolution database.	Both test are different. FDA dissolution data base is for development of product dissolution with defined parameters, while CDP is part of therapeutic equivalence, performed in at least three media covering the physiological range, including pH 1.2 hydrochloric acid, pH 4.5 buffer and pH 6.8 buffer. As per WHO (Technical Report Series, No. 1003, 2017) minimum of three time points (zero excluded) should be included, the time points for both reference (comparator) and test product being the same.
Significant difference in peak areas of system suitability / stanard solution in AMV and in stability studies.	Difference of peak areas has no impact for calculation of results. As peak areas are depending on brand, life, sensitivity of system & column while results calculation depends on current peak areas of standard and sample solution which eluted in same system environment.
Provide exact COA of RS used in stability testing. Further justify how RS of clavulanate lithium is used from Shandong New Time Pharmaceutical. Submitted COA are of 2019 and 2020 while stability batches were os 2017, 2018 and 2019.	Firm has submitted COA of USP reference standard for Clavulanate lithium (Lot#K0J130)
Justify long term stability studies of product at 25 degree.	Firm has submitted accelerated and long-term stability record as per Zone IV a condition for three batches.
Stability data summary sheets do not specify the exact lot of API used in the manufacturing of each batch.	The stability studies of Finished product were performed in 2017, 2018 & 2019, at that time, it was not mandatory to mentioned API lot number on data sheets. However, the lot of API used in stability studies of Finished product is attached
BMR of three stability batches are not provided.	As per manufacturers procedure the BMR was destroyed after 1 year of the expiry of product However, few documents related to batch manufacturing like batch release certificate, dispensing order sheet etc are attached
Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch. Firm has submitted Air way bill dated 20-06-2017 for import of 600Kg of Potassium Clavulanate along with COA of relevant batch.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for accelerated and long term stability studies.

9.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan**

	Name, address of Manufacturing site.	M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) (Firm has submitted copy of novation agreement between Novartis Pharma, CSH Pharma and AGP dated 17-03-2021).
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 26-08-2019 issued on the basis of inspection dated 22-07-2019. The GMP certificate specifies Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manufacturing License of M/s CSH Pharmaceuticals dated 01-08-2012 specifying Tablet (Penicillin), Capsule (Penicillin) and Dry Powder for suspension (Penicillin) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8957: 07-04-2022
	Details of fee submitted	PKR 75,000/-: 02-03-2022
	The proposed proprietary name / brand name	**Amoxi-clav 1g Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablet contains: Amoxicillin trihydrate eq to Amoxicillin…….875mg Potassium clavulanate eq to Clavulanic acid……125mg
	Pharmaceutical form of applied drug	White to almost white oblong film coated tablet with bevelled edges and score on both sides.
	Pharmacotherapeutic Group of (API)	Penicillin
	Reference to Finished product specifications	USP
	Proposed Pack size	2 x 3's
	Proposed unit price	As per DRAP approved MRP at the time of issuance of letter
	The status in reference regulatory authorities	Augmentin 875 Tablets **(USFDA** Approved)
	For generic drugs (me-too status)	Amclav Tablet by Getz Pharma

	Name and address of API manufacturer.	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Amoxicillin Trihydrate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 60 months. **Potassium Clavulanate:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications,

		reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is not submitted. CDP is performed against Augmentin Tablet.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Amoxicillin Trihydrate:** SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain **Potassium Clavulanate:** Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia		
API Lot No.	**Amoxicillin Trihydrate:** B394377, B441626 **Potassium Clavulanate:** B403911AA, B403093AA, B462469AA		
Description of Pack (Container closure system)	Alu-alu strip		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Real time: 24 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17TC005	18TC007	19TC003
Batch Size	200,000 Tablets	32,718 Packs	45,000 Packs
Manufacturing Date	05-2017	04-2018	07-2019
Date of Initiation	26-05-2017	20-04-2018	06-07-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No previous product specific inspection of the manufacturer firm has been conducted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Amoxicillin Trihydrate:** Firm has submitted copy of GMP certificate (No. NCF-II/2222/001/CAT) of M/s SANDOZ INDUSTRIAL PRODUCTS, SA Ctra. Granollers -Cardedeu C-251, Km 4 E -08520 Les Franqueses Del Valles, Barcelona, Spain issued by Spanish Agency for Medicines & Health Products dated 13-05-2022 valid till 22/05/2023. **Potassium Clavulanate:** Firm has submitted copy of GMP certificate (401-3/2022-5) of M/s Lek Pharmaceuticals d.d. Verovskova 57, 1526 Ljubljana Slovenia dated 24-06-2022 issued by Agency for medicinal products and medical devices of the Republic of Slovenia based on the inspection dated 18-03-2022 valid till 17-03-2025.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	The APIs were procured in 2016 for commercial batches. All APIs ware cleared from customs and DRAP as per applicable procedure.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted analytical record and raw data sheets, HPLC chromatograms and
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted that as the stability studies were conducted in 2017 and 2018 the audit trail is not available. However, all HPLCs are 21CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger from 01-01-2018 till 09-06-2021. The data logger was set at 25°C and 60% RH.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
Revise label claim as per the reference product along with submission of fee. (firm has applied for clavulanic acid…125mg instead of potassium clavulanate eq to clavulanic acid 125mg).	The firm has submitted corrected formulation as per reference product. **Amoxi-Clav 1g Film Coated Tablets** Each Film coated tablet contains: Amoxicillin Trihydrate equivalent to 875mg amoxicillin and Potassium clavulanate equivalent to 125mg of Clavulanic acid. Firm has submitted fee of Rs. 7,500/- vide deposit slip# 68190325699
Verification studies of analytical method of both drug substances from drug product manufacturer is required.	Firm has submitted analytical method verification studies for both Amoxicillin & Potassium clavulanate.
Justify why the qualitative compositition of your formulation is different from that of the reference product.	Firm has referred to the reference product having similar qualitative composition as applied.
Pharmaceutical equivalence is not submitted.	Firm has submitted pharmaceutical equivalence studies against Augmentin tablet
How CDP results decrease with time i.e. from 81.6% to 93%, 88.1% and 81.8% in 4.5 pH acetate buffer and 88.29 to 95.17%, 90.8% and 87.1% in 6.8 pH buffer.	Due to un-stability/degradation behavior with passing time in these medium, CDP results decreased. This observation is similar in both test product & reference product.
CDP time points are significantly different from that specified in FDA dissolution database.	Both test are different. FDA dissolution data base is for development of product dissolution with defined parameters, while CDP is part of therapeutic equivalence, performed in at least three media covering the physiological range, including pH 1.2 hydrochloric acid, pH 4.5 buffer and pH 6.8 buffer. As per WHO (Technical Report Series, No. 1003, 2017) minimum of three time points (zero excluded) should be included, the time points for both

	reference (comparator) and test product being the same.
Significant difference in peak areas of system suitability / stanard solution in AMV and in stability studies.	Difference of peak areas has no impact for calculation of results. As peak areas are depends on brand, life, sensitivity of system & column while results calculation depends on current peak areas of standard and sample solution which eluted in same system environment.
Provide exact COA of RS used in stability testing. Further justify how RS of clavulanate lithium is used from Shandong New Time Pharmaceutical. Submitted COA are of 2019 and 2020 while stability batches were os 2017, 2018 and 2019.	Firm has submitted COA of USP reference standard for Clavulanate lithium (Lot#K0J130)
Justify long term stability studies of product at 25 degree.	Firm has submitted accelerated and long-term stability record as per Zone IV a condition for three batches.
BMR of three stability batches are not provided.	As per manufacturers procedure the BMR was destroyed after 1 year of the expiry of product However, few documents related to batch manufacturing like batch release certificate, dispensing order sheet etc are attached
Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted Air way bill dated 29-11-2016 for import of 1230Kg of Amoxicillin trihydrate along with COA of relevant batch. Firm has submitted Air way bill dated 20-06-2017 for import of 600Kg of Potassium Clavulanate along with COA of relevant batch.
Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of digital data logger for accelerated and long term stability studies.

Decision: Registration Board decided as under:

i. Cancelled registration of following products from the name of M/s Novartis Pharma (Pakistan) Limited, 15- West Wharf, Dockyard Road, Karachi (DML No. 000193).

S. No.	Reg. No.	Product Name & Composition
1.	**007688**	**Ospamox 125mg/5ml Dry Suspension** **Each 5ml contains:** **Amoxicillin (as Trihydrate)…125mg**
2.	**007689**	**Ospamox 250mg/5ml Dry Suspension** **Each 5ml contains:** **Amoxicillin (as Trihydrate)…250mg**
3.	**007684**	**Ospamox 500mg Tablet** **Each film coated tablet contains:** **Amoxicillin (as Trihydrate)…500mg**
4.	**007686**	**Ospamox 1000mg tablet** **Each film coated tablet contains:** **Amoxicillin (as Trihydrate)…1000mg**
5.	**031358**	**Amoxi-Clav 156.25mg Dry Suspension** **Each 5ml contains:**

		Amoxicillin (as Trihydrate)….125mg **Clavulanic Acid (as Potassium)…31.25mg**
6.	**031359**	**Amoxi-Clav 312.5mg Dry Suspension** **Each 5ml contains:** **Amoxicillin (as Trihydrate)….250mg** **Clavulanic Acid (as Potassium)…62.5mg**
7.	**031335**	**Amoxi-Clav 375mg Tablets** **Each film coated tablet contains:** **Amoxicillin (as Trihydrate)….250mg** **Clavulanic Acid (as Potassium)…125mg**
8.	**031356**	**Amoxi-Clav 625mg Tablets** **Each film coated tablet contains:** **Amoxicillin (as Trihydrate)….500mg** **Clavulanic acid (as Potassium)…125mg**
9.	**031357**	**Amoxi-Clav 1gm Tablets** **Each film coated tablet contains:** **Amoxicillin (as Trihydrate)….875mg** **Clavulanic Acid (as Potassium)…125mg**

ii. Approved registration of following products in the name of M/s AGP Limited B-23-C, S.I.T.E. Karachi (DML No. 000348) by way of contract manufacturing at M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore (DML No. 000737).

a) Manufacturer will place first three production batches of both products on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

b) Manufacturer will perform process validation of first three batches of both products as per the commitment submitted in the registration application.

S. No.	Product Name & Composition
1.	**Ospamox 125mg Granules for suspension** **Each 5ml contains:** **Amoxicillin (as Trihydrate)…….125mg** **(USP Specifications)**
2.	**Ospamox 250mg Granules for suspension** **Each 5ml contains:** **Amoxicillin (as Trihydrate)…….250mg** **(USP Specifications)**
3.	**Ospamox 500mg Tablet** **Each film coated tablet contains:** **Amoxicillin (as Trihydrate)…….500mg** **(USP Specifications)**
4.	**Ospamox 1000mg Tablet** **Each Film coated tablet contains:** **Amoxicillin (as Trihydrate)…….1000mg** **(USP Specifications)**
5.	**Amoxi-clav 156.25mg Granules for Oral Suspension** **Each 5ml contains:** **Amoxicillin Trihydrate Eq. to Amoxicillin…….125mg** **Potassium Clavulanate Eq. to Clavulanic Acid……31.25mg** **(USP Specifications)**

6.	**Amoxi-clav 312.5mg Granules for Oral Suspension** **Each 5ml contains:** **Amoxicillin Trihydrate Eq. to Amoxicillin…….250mg** **Potassium Clavulanate Eq. to Clavulanic Acid……62.50mg** **(USP Specifications)**
7.	**Amoxi-clav 375mg Tablet** **Each film coated tablet contains:** **Amoxicillin Trihydrate Eq. to Amoxicillin…….250mg** **Potassium Clavulanate Eq. to Clavulanic Acid……125mg** **(USP Specifications)**
8.	**Amoxi-clav 625mg Tablet** **Each film coated tablet contains:** **Amoxicillin Trihydrate Eq. to Amoxicillin…….500mg** **Potassium Clavulanate Eq. to Clavulanic Acid……125mg** **(USP Specifications)**
9.	**Amoxi-clav 1g Tablet** **Each film coated tablet contains:** **Amoxicillin Trihydrate Eq. to Amoxicillin…….875mg** **Potassium Clavulanate Eq. to Clavulanic Acid……125mg** **(USP Specifications)**

iii. **Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).**

iv. **Updated GMP status/ inspection report of M/s CSH Pharmaceuticals (Pvt) Ltd. 32-Km Ferozepur Road Lahore (DML No. 000737) will be submitted before issuance of registration letter.**

Case No. 01 Registration Status of Formulations (Diclofenac Potassium 75mg & 100mg and Famotidine 10mg/5ml) not approved by Reference Regulatory Authorities & Previous Decisions Taken by the Registration Board in its 250th & 258th Meeting.

1. Registration Board, in its various meetings considered the case regarding *"Registration Status of Formulations (Diclofenac Potassium 75mg & 100mg and Famotidine 10mg/5ml) not approved by Reference Regulatory Authorities & Previous Decisions Taken by the Registration Board in its 250th & 258th Meeting".*

2. With respect to "Diclofenac Potassium", complete record including proceedings & decisions of Registration Board and relevant decisions of DRAP's Authority have been reproduced as under:

Sr. No.	Formulation	Ref. Meeting No. of RB	Decision/Remarks
1.	Diclofenac Potassium 75mg & 100mg	M-258 *(held on 25th-26th April, 2016)*	**Decision:** Diclofenac Potassium is not registered in any reference country in dose more than 50mg, thus Registration Board decided to issue show cause notices to manufacturers of Diclofenac Potassium (75 and 100mg) for de-registration of these products.

3. With respect to Famotidine Suspension, complete record including proceedings & decisions of Registration Board and relevant decisions of DRAP's Authority have been reproduced as under:

Sr. No.	Formulation	Ref. Meeting No. of RB	Decision/Remarks
1.	Famotidine 10mg/5ml Suspension	M-250 *(held on 09th 10th July, 2015)*	***Remarks:*** ***Not approved by reference drug regulatory agencies. Internationally available formulation is dry powder for suspension in the strength of 40 mg/ 5 ml.*** ***(Ref: US FDA)*** **Decision:** i. Applicants shall revise their formulation as per innovator (new registration application with complete fee) within six months if manufacturing facility is approved by CLB. ii. For already registered drugs, same procedure as mentioned above (at Sr. No. i) shall be adopted. Otherwise show cause notice shall be issued for de-registration of registered drugs in this formulation. iii. All such application shall be processed on priority basis.

4. ***Decision taken by DRAP's Authority in its 70th meeting held on 05th Sep, 2019:***

For formulations containing "drugs" which were previously registered by the Registration Board and have proof of availability and prescription of last 10 years but are not available in the Reference Regulatory Authorities shall continue to be considered/ registered as drugs until and unless withdrawn on Safety, Efficacy and Quality reasons.

5. ***Decision of M-296 held on 08th-10th Sep, 2020:***

Registration Board deliberated the case in the light of above stated facts / opinions and decided as under:

i. *Since, all such formulations which are not approved by the Reference Regulatory Authorities; the safety and efficacy profile cannot be established in the absence of a well-established system for reporting of adverse events, so a reference shall be forwarded to DRAP's Authority with the request to review the decision taken in its 70th meeting held on 05-09-2019. In this regard, PE&R Division shall prepare a comprehensive document/agenda for consideration of Authority, keeping in view the practices adopted by RRA for all such formulations;*

ii. *For all those formulations which are registered/ applied in strengths, different from those approved by reference regulatory authorities, the registration holders/ applicants shall standardize their formulations (by submitting registration application with requisite fee, provided that the firm did not have same registration) in line with those approved by reference regulatory authorities. In this regard, recommendation shall be forwarded to DRAP's Authority to exempt all such cases/applications for standardization of formulation to be submitted on Form-5F/CTD format as notified vide SRO 713(I)/2018 dated 09-06-2018.*

iii. *Drug products withdrawn from RRA due to any commercial reason shall be considered for registration by Registration Board.*

iv. *Vitamin-mineral formulations will be considered as per vitamin policy approved by Policy Board and further adopted by Registration Board in its 295th meeting.*

Keeping in view the point (i) and in order to proceed further for effective implementation/ execution of point (ii) to (iv) of the above-mentioned decision, the Authority was requested to review the decision taken vide its 70th meeting held on 05-09-2019.

6. <u>Proceedings of M-313:</u>

i. The concept of reliance on the decisions of reference regulatory authorities adopted by the Registration Board in its 275th meeting was reiterated as deliberated during proceedings of 296th meeting with respect to instant case.

ii. Furthermore, Registration Board was apprised that a policy of reliance on reference regulatory authorities has also been approved by the Authority in its 73rd meeting held on 06-11-2019.

iii. Registration Board was also informed regarding court case (CP No.1545/2017) filed by M/s Cibex (Pvt.) Ltd., Karachi vs DRAP & others i.e, sub-judiced before the hon'ble Sindh High Court and written statement/updated registration status of such formulations on behalf of DRAP is required to be furnished.

iv. It was further deliberated that relevant registration holders/ manufacturers shall be provided with an opportunity to submit their response regarding (a) evidence for approval status of such formulation in reference regulatory authorities (b) product development data and relevant studies with respect to quality, safety and efficacy of these formulations.

7. <u>Decision of M-313 held on 16th-18th Nov, 2021:</u>

Keeping in view the detailed deliberations during proceedings of its 296th and 313th meeting, Registration Board decided as under:

i. ***To issue show cause notices to all registration holders/ manufacturers (including those listed in above tables) of below mentioned formulations under Section 7 (11)(d) of the Drug Act, 1976 that why the registration of their products may not be cancelled in the public interest. In this regard, the Board advised relevant registration sections to review the above-mentioned lists for correctness and issue notices accordingly. Moreover,***

any registration holder not included in above lists shall also be issued show cause notice after approval of Chairman Registration Board.

ii. ***Furthermore, management of these firms shall also be given the opportunity of personal hearing in the forthcoming meeting of the Board under section 42 of the Drugs Act, 1976.***

S. No.	***Formulations***
1.	*Diclofenac Potassium Tablets/ Capsules in strengths greater than 50mg*
2.	*Famotidine Suspension in strength/dosage form other than 40mg/5ml Powder for Oral Suspension.*

iii. *The Board also advised to share the updated status with hon'ble Sindh High Court if required.*

8. **Decision of 128th meeting of Authority held on 14th Dec, 2021:**

I. The Authority endorsed the recommendations of Registration Board and made following decisions:-

A. Partially reviewed its earlier decision taken in its 70th meeting held on 05-09-2019, consolidated amended decision is reproduced as under:

1. For molecules falling in the grey areas or overlapping between PE&R and H&OTC division:

a. Formulations/molecules already registered as "drugs" by Registration Board shall continue to be considered / registered as drugs irrespective of their status in Reference Regulatory Authorities until and unless withdrawn on Safety, Efficacy and Quality reasons.

b. If any such formulation was also enlisted by H&OTC Division, it will be un-enlisted. The applicants shall be advised to approach PE&R Division for processing of application for registration. For such un-enlisted applications, a separate queue shall be prepared by the PE&R Division in order to avoid discomfort to the applicants and assurance of availability of such formulations for patients.

c. This decision shall not apply to those formulations / molecules covered under Vitamin-Policy as approved by the Policy Board.

2. New formulations/molecules other than those which were already registered by Registration Board will be considered on the basis of their status in Reference Regulatory Authorities. If in the RRA, these are considered as drugs, these will be dealt by the PE&R Division while otherwise will be dealt by Health & OTC Division.

3. Endorsed the Reference Regulatory Authorities as adopted by the Registration Board from time to time and the criteria being opted to adopt RRAs. Registration Board was advised to issue a notification of adopted RRAs and comprehensive selection criteria for information and easy understanding of all relevant stakeholders.

4. Drug formulations/strengths which were previously registered by the Registration Board but are not available in any Reference Regulatory Authorities, shall be reviewed and disposed off keeping in view of safety and efficacy evidence / data in the Reference Regulatory Authorities.

B. Registration Board may decide and dispose off such formulations as and when identified/reported.

II. *The Authority further advised Registration Board to review existing RRAs for veterinary drugs and submit its recommendations to the Authority for its consideration.*

9. In line with the decision taken by the Board in its 313th meeting, show-cause/personal hearing notices were issued to **162** registration holders.

10. Accordingly, Registration Board in its 317th meeting decided as under;

For Diclofenac Potassium:

In light of the foregoing discussions, risk-benefit analysis and public health impact of Diclofenac Potassium 75mg and 100mg, the Board made following decisions:

i. Suspended all drug registrations of Diclofenac Potassium 75mg and 100mg under Section 7 (11) (d) read with Section 42 of the Drugs Act, 1976 in the larger public interest, with immediate effect as these are neither approved by any Reference Regulatory Authority nor any safety and efficacy data regarding them is available with any registration holder. Period of suspension will be for one (01) year or till demonstration of its safety and efficacy by conducting indigenous clinical trials in accordance with the Bio Study Rules, 2017 or its approval by the Reference Regulatory Authorities, whichever is earlier. After provision of aforementioned data, cases of such pharmaceutical firms shall be considered on merit by Registration Board.

ii. Suspended manufacturing and import of these drug products immediately and directed to withdraw available stocks from the market in the larger public interest. QA&LT Division, DRAP will monitor and implement the decision in coordination with the respective provincial governments.

iii. Recommended Licensing Division, DRAP for approval of Qualified person for Pharmacovigilance (QPPV) / Local Safety Officer (LSO) whichever is applicable in licensed pharmaceutical units and advised PE&R and BE&R Divisions for implementing similar action for importers of finished drug products as required under Pharmacovigilance Rules, 2022.

iv. Final decision regarding pharmaceutical firms who have obtained interim relief from the Hon'ble Lahore High Court, Lahore shall be announced after decision and direction by the Hon'ble Court. Legal Affairs Division is requested to place the instant decision before the Hon'ble Court and seek expeditious disposal of the matter in the larger public interest.

v. Recommended DRAP Authority for out of queue consideration of registration applications of Diclofenac Potassium 50mg, 25mg and 12.5mg Tablet and 50mg Sachet in order to facilitate the registration holders affected by the instant decision.

For Famotidine Suspension:

In light of the foregoing discussions, risk-benefit analysis and public health impact of Famotidine 10mg/5ml and 40mg/5ml, the Board made following decisions:

i. Suspended all drug registrations of Famotidine 10mg/5ml and 40mg/5ml Liquid Suspension under Section 7(11)(d) read with Section 42 of the Drugs Act, 1976 in the larger public interest, with immediate effect as neither approved by any Reference Regulatory Authorities nor efficacy data is available with any registration holder. Period of suspension will be for one (01) year or till demonstration of efficacy by conducting indigenous clinical trials in accordance with Bio Study Rules, 2017 or approval by Reference Regulatory Authorities whichever is earlier. After provision of aforementioned data, cases of such pharmaceutical firms shall be considered on merit by the Registration Board

ii. Suspended manufacturing and import of these drug products immediately and directed to withdraw available stocks from the market in the larger public interest. QA&LT Division, DRAP will monitor and implement the decision in coordination with the respective provincial governments.

iii. Final decision regarding pharmaceutical concerns who have obtained interim relief from the Hon'ble Lahore High Court, Lahore shall be announced after decision and direction by the Hon'ble Court. Legal Affairs Division is requested to place the instant decision before the Hon'ble Court and seek expeditious disposal of the matter in the larger public interest.

iv. Recommended DRAP Authority for out of queue consideration of registration applications of Famotidine 40mg/5ml Dry Suspension in order to facilitate the registration holders affected by the instant decision.

11. Accordingly, suspension letters have been issued to all the firms. However, inadvertently following registration holders of Famotidine Suspension 10mg/5ml and Diclofenac Potassium 75mg & 100mg Tablet could not be included in the list previously presented before the Board. Detail is as under;

Famotidine Suspension 10mg/5ml			
Sr. No.	**Reg. No.**	**Brand Name & composition**	**Registration Holder**
1.	025157	Gimed Suspension Each 5ml contains:- Famotidine 10mg	M/s. Albro Pharmaceutical (Pvt) Ltd. 340-S Industrial Area, Lahore.
2.	027948	Famron Suspension Each 5ml contains:- Famotidine 10mg	M/s. PDH Pharmaceuticals Pvt Ltd, 19-km, Ferozpur Road, Lahore
3.	059498	Fedcid Suspension Each 5ml contains:- Famotidine USP……..10mg	Fedro Pharmaceutical Labs (Pvt) Ltd. 149-Industrial Estate Jamrud Road Peshawar.
Diclofenac Potassium 75mg Tablet			

1.	022485	Ostefen 75mg Tablet Each tablet contains:- Diclofenac Potassium….75mg	Saydon Pharmaceutical Industries (Pvt) Ltd. 77/A Hayatabad Industrial Estate Peshawar
2.	021599	Moven Tablet Each tablet contains:- Diclofenac Potassium….75mg	Fedro Pharmaceutical Labs (Pvt) Ltd. 149-Industrial Estate Jamrud Road Peshawar.
3.	036815	Dic-P 75mg Tablets Each tablet contains:- Diclofenac Potassium….75mg	M/s. Shaheen Pharmaceuticals 3 K.M Murghzar Road Saidu Sharif Swat
4.	058262	Velflex 75mg Tablet Each film coated tablet contains:- Diclofenac Potassium...75mg	Kaizen Pharmaceuticals (Pvt) Ltd. Plot No. E-127 E-128 & E-129 North Western Industrial Zone Port Qasim Authority Karachi
5.	058263	Velflex 100mg Tablet Each film coated tablet contains:- Diclofenac Potassium...100mg	Kaizen Pharmaceuticals (Pvt) Ltd. Plot No. E-127 E-128 & E-129 North Western Industrial Zone Port Qasim Authority Karachi

Decision: Registration Board deferred the case for decision of Drugs Appellate Board.

Case No. 02 M/s. Health Care Pharmaceuticals 40-Km, Lahore Road Multan.

Registration Board in its 293rd meeting approved following product of M/. Health Care Pharmaceuticals 40-Km, Lahore Road Multan. Detail is as under;

Sr. No.	**Name of Drug(s) with composition**	**Decision of 293rd meeting of Registration Board**
1.	COUGHGO SYRUP Each 5ml contains Sodium citrate……..58mg Chlorpheniramine maleate……...2mg Ammonium Chloride …100mg Manufacture specs	**Approved with change of brand name**

Later on, during review of products it was transpired that above stated formulation is not approved in any reference regulatory authority.

Decision: Registration Board deferred the case for further deliberation.

Case No. 03 M/s. Saffron Pharmaceuticals (Pvt.) Ltd; 19 Km, Sheikhupura Road, Faisalabad

M/s. Saffron Pharmaceuticals (Pvt.) Ltd; 19 Km, Sheikhupura Road, Faisalabad were granted registration of following products with MRP demanded by the firm as mentioned in the minutes. However, the firm has submitted a request that these MRPs are not viable for manufacturing and they unable to manage the cost. Same case was placed in 2nd meeting of C&P Division & PE&R Division and it was decided in said meeting that "The MRPs were granted to firm as per their demand, hence the request of the firm cannot be acceded for revision in MRP, firm may approach C&P Division". The detail is given below:-

S. No.	Reg. No. & Date	Name of Drug(s) with composition	Existing MRP & Pack size
1.	057446 29-04-2009	Dystrone Tablet Each tablet contains:- Dydrogesterone …… 10mg (BP Specifications)	Rs.25/20's
2.	081383 27-07-2016	Episaf 250mg Tablet Each film coated tablet contains:- Levetiracetam …… 250mg (USP Specifications)	Rs.40/1x10's

Later on, firm has submitted fresh applications for product Episaf 250mg Tablet in 293rd meeting and registration letter has also been issued with following details

S. No.	Reg. No. & Date	Name of Drug(s) with composition	Existing MRP & Pack size
1.	102374 29-04-2020	Episaf 250mg Tablet Each film coated tablet contains:- Levetiracetam …… 250mg (USP Specifications)	Rs.787.00 / 30s

For product Dystrone 10mg Tablet, firm has also submitted fresh application which was approved in 313th meeting but registration letter was not yet issued as it was revealed during scrutiny of record that firm has already been granted registration of said product as mentioned above.

Now firm has applied for correction in MRP of Dystrone 10mg Tablet (Reg. No. 057446) as per of C&P Division's letter No. F. 11-12/2021-DD (P) dated 25-06-2021 regarding "Clarification with respect to issuance of revised MRP where the applicant/ pharmaceutical concern had demanded lower MRPs at the time of submission of application for registration" clarified as under;

> The matter was placed before Drug Pricing Committee (DPC) in its 48th meeting held on 03-06-2021 and DPC after considering statutory construction of law, provisions of Drug Pricing Policy-2018 and facts, decided as under;
>
> ***"MRPs of generics are fixed with prospective effect on uniform basis under Drug Pricing Policy- 2018 without regard to a particular brand or applicant. Therefore, all applicants whose registration letters are issued under sub-rule (4) of rule 29 of the Drugs (Licensing, Registration and Advertising) Rules, 1976 after notification of MRPs are entitled for notified MRPs. If a lower MRP is issued to any applicant on the basis of an initial demanded MRP, it will create anomalies against provision of paragraph 12(5) of the Drug Pricing Policy-2018. Therefore, applicants be issued with SRO notified MRPs instead of initial demanded prices. Moreover, corrigendum be issued to applicant companies if initial demanded MRP was notified in registration letter instead of SRO notified MRP under section 12 of the Drugs Act,1976 after approval by the Federal Government.".***

Decision: Registration Board decided to issue show cause notice under section 42 of the Drugs Act, 1976 read with Rule 7 (11) of The Drug (L, R & A) Rules, 1978 to M/s. Saffron Pharmaceuticals (Pvt.) Ltd., Faisalabad for cancellation of Episaf 250mg Tablet (Reg. No. 102374). The Board further decided that registration letter shall not be issued to the firm for product Dystrone 10mg Tablet approved in 313th meeting, as the firm already holds registration of same product.

Case No. 04 M/s. Shrooq Pharmaceuticals (Pvt) Ltd 21-Km Ferozepur Road, Lahore

Registration Board in its 226th meeting considered the following application of M/s. Shrooq Pharmaceuticals (Pvt) Ltd 21-Km Ferozepur Road, Lahore. Detail is as under:-

Sr. No.	Name of Drug(s)	Demanded Pack Size/Price	Decision	Remarks
1.	Tdol Capsule Each capsule contains:- Tramadol Hydrochloride …….. 50mg	10's/ As Per SRO	Deferred for confirmation of separate section by licensing section.	MHRA Approved. Product is available in BP.

Firm has submitted following documents;

i. Form 5
ii. Photocopy of fee challan of Rs.8000/- and fresh submission of Rs.12,000/- dated 24-08-2022.
iii. Section approval of Capsule (General).
iv. Firm has submitted copy of GMP Certificate issued based upon evaluation conducted dated 29-10-2021.

Decision: Registration Board approved registration of above product in the name of M/s. Shrooq Pharmaceuticals (Pvt) Ltd 21-Km Ferozepur Road, Lahore. Registration letter shall be issued after verification of fee of Rs.8000/- as per decision of 285th meeting and submission of fee of Rs.7500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

Case No.05 Correction in Minutes of Registration Board Meetings.

i. M/s Briell Pharmaceuticals Pvt. LTD. 538-C, Sundar Industrial Estate, Lahore.

Registration Board in its 295th meeting approved following product of M/s Briell Pharmaceuticals Pvt. LTD. 538-C, Sundar Industrial Estate, Lahore. Registration letter was not issued as there is some typo error while drafting decision of Registration Board. Details are as under;

Sr. No.	Name of Approved Drug(s) & Composition	Decision of 307th Meeting of RB	Remarks
1.	Cvox Dry Powder Suspension 250mg Each 5ml contains: Ciprofloxacin as HCl…250mg Innovator Source M/s. Vision	**Approved with USP specifications and with following composition / label claim:** **Each 5ml of reconstituted suspension contains:** **Ciprofloxacin……125mg**	Registration letter not yet issued

Firm had submitted receiving of registration application which reveals that applied strength is 250mg instead of 125mg and firm has also applied for registration of 125mg for which registration letter has also been issued.

Decision: Registration Board decided to approved the correction in decision of above product with following details.
"Approved with USP specifications and with following composition / label claim:
Each 5ml of reconstituted suspension contains:
Ciprofloxacin……250mg"
Details of diluent shall be added as per decision of 290th meeting.

Case No.06 Registration of M/s. Medipak Ltd. Plot No 132 Industrial Estate Kot Lakhpat, Lahore.

The Registration Board has deferred following products of M/s Medipak, Lahore in 286th meetings for confirmation of approval status in RRA. Detail is as under;

S. No.	Name of Drug(s) with formulation	Demanded MRP/Pack size	Previous Remarks	Current Remarks
1.	Voluven Infusion Solution. Each 1000ml Contains:- Poly(O-2-Hydroxyethyl) starch (Hydroxyethyl starch 130/0.4)……60.0gm Sodium Chloride……..9.0gm	Rs.521.70 /500ml	Approval status in SRA not confirmed	Approved in TGA Australia as under; Poly (O-2-Hydroxyethyl) starch (Hydroxyethyl starch 130/0.4)……60.0gm/L **Excipient;** Sodium Chloride…9.0gm

Registration Board in its 297th meeting deferred the product for confirmation of formulation of Innovator Product.

Now firm has submitted fee of Rs.5000/- dated 18-03-2021 for correction of formulation as per reference as in TGA Sodium Chloride is mentioned as an excipient.

Decision: Registration Board decided as under;

a. **Approved registration of above product in the name of M/s. Medipak Ltd. Plot No 132 Industrial Estate Kot Lakhpat, Lahore with following label claim.**
   Each 1000ml Contains:-
   Poly(O-2-Hydroxyethyl) starch
   (Hydroxyethyl starch 130/0.4)……60.0gm
   Excipient;
   Sodium Chloride……..9.0gm

b. **Registration letter shall be issued after verification of fee as per decision of 285th meeting and submission of fee of Rs.7500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

Case No.07 Registration of Drug M/s. Synchro Pharmaceuticals 77-Industrial Estate Kot Lakhpat Lahore

Registration Board in its 228th meeting approved the following products of M/s. Synchro Pharmaceuticals 77-Industrial Estate Kot Lakhpat Lahore and the firm has informed that they have not yet got registration letter:-

Sr. No.	Name of Drug(s)	Demanded Pack Size/Price	Remarks
1.	Teraxone Injection IM Each vial contains:- Ceftriaxone(as sodium)…..500mg (USP Specifications)	Rs.240.00 Per Vial	Product is approved in MHRA
2.	Teraxone Injection IM Each vial contains:- Ceftriaxone (as sodium)…..250mg (USP Specifications)	Rs.140.00 Per Vial	Product is approved in MHRA.

Firm has submitted following documents;

i. Form 5
ii. Fresh submission of Rs.30,000/- dated 25-03-2022.
iii. Section approval of Dry Powder Injection (Cephalosporin).
iv. Firm has submitted copy of GMP Certificate issued based upon evaluation conducted dated 22-01-2021.

Decision: Registration Board approved registration of above product in the name of M/s. Synchro Pharmaceuticals 77-Industrial Estate Kot Lakhpat Lahore.

Case No.08 Registration of Drug M/s. Medisearch Pharmacal (Pvt) Ltd. 5 Km Raiwind Manga Road, Lahore.

Registration Board in its 237th meeting considered following products of M/s. Medisearch Pharmacal (Pvt) Ltd. 5 Km Raiwind Manga Road, Lahore. As per minutes of 237th meeting of Registration Board, firm has previously applied for registration of above stated products by way of contract manufacturing from M/s. Dyson and M/s. Mcolson and then requested to register these products at their own facility as firm has established their own facility to manufacture these products. Detail is as under;

Sr. No.	Name of Drug(s)	Demanded Pack Size/Price	Decision M-237	Remarks
1.	Medipram Tablets 10mg Each Film Coated Tablet contains:- Escitalopram (as Oxalate) ... 10mg (Manufacturer Specifications)	Rs.600.00 14's	Deferred. The firm has not submitted differential fee	MHRA Approved Product is available in USP
2.	L-Pride 50mg Tablets Each tablet contains:- Levosulpiride…….50mg (Manufacturer Specifications)	Rs.360.00 20's	Deferred. The firm has not submitted differential fee	Approved in Italy. Product is not available in any Pharmacopoeia.

Firm has submitted following documents;

i. Form 5
ii. Photocopy of fee challan of Rs.8,000/- and 12000/-.
iii. Firm has submitted GMP Certificated issued based upon evaluation conducted on 22-02-2021.

Decision: Registration Board approved registration of above product in the name of M/s. Medisearch Pharmacal (Pvt) Ltd. 5 Km Raiwind Manga Road, Lahore. Registration letter shall be issued after verification of fee as per decision of 285th meeting and submission of fee of Rs.7500/- for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

Case No.09 Transfer of Registration from M/s. Horizon Healthcare (Pvt) Ltd. 35-A, Punjab Small Industrial Estate, Taxila to M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate, Lahore.

1.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Evidence of availability of manufacturing facility	Firm has submitted copy of GMP certificate issued on basis of inspection conducted on 18-06-2020 wherein availability of tablet general section is confirmed.
	Dy. No. and date of submission	Dy. No 12558 R&I dated 23-05-2022
	Details of fee submitted	Rs.30,000/- dated 23-05-2022
	The proposed proprietary name / brand name	**Doxelo Capsule 30mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Enteric coated pellets of Duloxetine Hydrochloride equivalent to Duloxetine …… 30mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Antidepressants
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	As Per SRO
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved by USFDA
	For generic drugs (me-too status)	Lyta capsule of M/s Getz Pharma
	GMP status of the Finished product manufacturer	Firm has submitted copy of GMP certificate issued on basis of inspection conducted on 18-06-2020.
	Name and address of API manufacturer.	SURGE LABORATORIES (PVT) LTD. 10th KM, Faisalabad Road Bikhi, District Sheikhupura –Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance from M/s Surge Labs Limited and drug product from the M/s Horizon Healthcare. Batch manufacturing records have also been submitted for all three stability batches.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures, method validation from M/s Horizon, batch analysis and justification of specification, reference standard COA form USP,

		container closure system and stability studies of from M/s Surge Labs.
	Stability studies of drug substance	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability studies.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence & CDP studies in three dissolution mediums against the reference product "Lyta capsules" of M/s Getz Pharma, has been submitted with acceptable results of similarity factor.
	Analytical method validation/verification of product	Firm has submitted analytical method verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Name: M/s Symed Labs Limited** **Address:** UNIT-III, Plot No. 19 & 20, Phase-I, IDA, Jeedimetla, Hyderabad, Telangana, India.		
API Lot No.	3TI0020420		
Description of Pack (Container closure system)	Alu PVC Blisters.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T1/20	T2/20	T3/20
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	08-2020	08-2020	08-2020
No. of Batches	03		

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above mentioned product from the name of M/s. Horizon Healthcare (Pvt) Ltd. 35-A, Punjab Small Industrial Estate, Taxila.**
b. **Approved registration of above mentioned product in the name of M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate, Lahore subject to submission of CDP with Innovator's Product.**
c. **Reference will be sent to Cost and Pricing Division for confirmation of maximum retail price (MRP).**

2.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate,Lahore**
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate,Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Evidence of availability of manufacturing facility	Firm has submitted copy of GMP certificate issued on basis of inspection conducted on 18-06-2020 wherein availability of Capsule general section is confirmed.
	Dy. No. and date of submission	Dy. No 12559 R&I dated 23-05-2022
	Details of fee submitted	Rs.30,000/- dated 23-05-2022
	The proposed proprietary name / brand name	**Doxelo Capsule 60mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Enteric coated pellets of Duloxetine Hydrochloride equivalent to Duloxetine …… 60mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Antidepressants
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	As Per SRO
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved by USFDA
	For generic drugs (me-too status)	Lyta capsule of M/s Getz Pharma
	GMP status of the Finished product manufacturer	Firm has submitted copy of GMP certificate issued on basis of inspection conducted on 18-06-2020.
	Name and address of API manufacturer.	SURGE LABORATORIES (PVT) LTD. 10th KM, Faisalabad Road Bikhi, District Sheikhupura –Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance from M/s Surge Labs Limited and drug product from the M/s Horizon Healthcare. Batch manufacturing records have also been submitted for all three stability batches.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures, method validation from M/s Horizon, batch analysis and justification of specification, reference standard COA form USP, container closure system and stability studies of from M/s Surge Labs.
	Stability studies of drug substance	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability studies.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence & CDP studies in three dissolution mediums against the reference product "Lyta capsules" of M/s Getz Pharma, has been submitted with acceptable results of similarity factor.
	Analytical method validation/verification of product	Firm has submitted analytical method verification studies of the drug substance and the drug product.

STABILITY STUDY DATA

Manufacturer of API	SURGE LABORATORIES (PVT) LTD. 10th KM, Faisalabad Road Bikhi, District Sheikhupura –Pakistan.		
API Lot No.	DXP-20-003		
Description of Pack (Container closure system)	Alu Alu Blisters.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	DTH-001	DTH-002	--
Batch Size	5000 capsules	5000 capsules	--
Manufacturing Date	09-2021	09-2021	--

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product Empazon Tablet 10mg & 25mg which was conducted on 01-06-2021 and was presented in 307th meeting of Registration Board held on 08-10th June, 2021. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued to M/s Surge Labs, by DRAP on basis of inspection conducted n 03-07-2019
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted of commercial invoice form M/s Surge Labs dated 28-04-2021 for purchase of 5Kg Duloxetine pellets.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product Empazon Tablet 10mg & 25mg which was conducted on 01-06-2021 and was presented in 307th meeting of Registration Board held on 08-10th June, 2021. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted valid DML/GMP Certificate of Symed Labs Limited Unit-III, Plot No. 19 & 20, Phase-I, IDA, Jeedimetla, Hyderabad, Telangana, India, issued by DCA Telangana valid up to 29/09/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	--
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator[II]:

Sr.#	Section#	Observation	Firm's response
1.	**3.2.S.4.1**	Submitted drug substance specifications shall declare the %age w/w of the drug substance in pellets.	Firm has submitted revised specifications declaring the percentage content as 20%w/w for Duloxetine HCl pellets as per supplier's COA.
2.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical Equivalence & CDP studies against the innovator product	Doxelo me too status is available in market so CDP studies have been performed with local brand.
3.	**3.2.P.5.2**	Justify variation in the standard concentration applied in the dissolution test form that recommended by USP monograph.	Firm has submitted that we adjusted the concentration of standard as per sample concentration.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above mentioned product from the name of M/s. Horizon Healthcare (Pvt) Ltd. 35-A, Punjab Small Industrial Estate, Taxila.**
b. **Approved registration of above mentioned product in the name of M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate, Lahore subject to submission of CDP with Innovator's Product.**
c. **Reference will be sent to Cost and Pricing Division for confirmation of maximum retail price (MRP).**

3.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Horizon Healthcare (Pvt.) Ltd. Plot No. 33 Sundar Industrial Estate Lahore.**
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd. Plot No. 33 Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐ Domestic and Export sales

Dy. No. and date of submission	Dy.No 16908 dated 24-12-2021
Details of fee submitted	Rs.30,000/- dated 24-12-2021
The proposed proprietary name / brand name	Fanaze 150mg Capsule
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Fluconazole …….. 150mg
Pharmaceutical form of applied drug	White to off white colored fine powder filled in hard gelatin capsule size 1 with blue cap and ivory body pack in alu alu blister in unit carton.
Pharmacotherapeutic Group of (API)	Fluconazole: Antimycotics for systemic use, triazole derivatives.
Reference to Finished product specifications	As per BP Specifications
Proposed Pack size	As per SRO
Proposed unit price	As per SRO
The status in reference regulatory authorities	UK-MHRA (Fluconazole 150mg capsules)
For generic drugs (me-too status)	Diflucan PFIZER LABORATORIES LTD.
GMP status of the Finished product manufacturer	Last inspection report dated 18.06.2020 concluded good level of cGMP compliance.
Name and address of API manufacturer.	Fluconazole: M/s Symed labsLimited. (Unit II) Plot 25/B-Phase-Ill, I.D.A., Jeedimetla, Hyderabad-Distic-500055, Telangana, India
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
Module III (Drug Substance)	The firm as submitted detail of General information, General properties, Manufacturers, description of manufacturing process and process controls, Characterization, Impurities, Control of drug substance, Reference standard or materials container closure system and stability studies of drug substance.
Stability studies	Fluconazole: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
Module-III (Drug Product):	The firm has submitted detail of Drug Products including Description and composition of drug product, Pharmaceutical Development, Manufacturing process development, Microbiological attribution, Manufacturer, Master formulations, Description of Manufacturing Process and

		Process Controls, Control of Critical Steps and Intermediates, Process Validation and/ or Evaluation, Control of Excipients with specification and Analytical methods, Control of Drug Products including Finished product specifications and test methods, validation of Analytical methods, Batch analysis, Characterization of impurities, reference standard or impurities, Container closure and stabilities studies.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Diflucan PFIZER LABORATORIES LTD. By performing quality tests (Identification, Assay, Dissolution) CDP has been performed against the same brand that is Diflucan PFIZER LABORATORIES LTD in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)
	Analytical method validation/verification of product	Method verification studies have submitted including Introduction, Verification of assay method, Specificity, Accuracy, Precision, Linearity concentration and peak range.

STABILITY STUDY DATA		
Manufacturer of API	Fluconazole: M/s Symed labsLimited. (Unit II)Plot 25/B-Phase-Ill, I.D.A., Jeedimetla, Hyderabad-Distic-500 055, Telangana, India	
API Lot No.	Fluconazole: 2FLZ0030220	
Description of Pack (Container closure system)	Alu alu blister 1x1's packed in unit carton.	
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH	
Time Period	Real time: 6 months Accelerated: 6 months	
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 8, 12, 16, 20, 24(Months)	
Batch No.	FC-001	FC-002
Batch Size	5000 Capsules	5000 Capsules
Manufacturing Date	09-2021	09-2021
Date of Initiation	09-2021	09-2021
No. of Batches	02	
Documents submitted along with stability data		

<table>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td>Firm has referred to onsite inspection report of their product:

EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) which was conducted on 1st June, 2021 and was presented in 307th meeting of Registration Board held on 08-10th June , 2021.
Registration Board decided to approve registration of

EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) by M/s. Horizon Healthcare (Pvt) Ltd. Lahore.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.
Following two observations were reported in the report: i. The HPLC software is 21 CFR compliant.
iv. Audit trail on the testing reports of EMPAZON 10mg and 25mg Tablets, Dayzol 30mg and 60mg Capsules is available.
v. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Fluconazole:
Firm had provided valid GMP and DML Certificate of M/s Symed labs Limited. (Unit II) Plot 25/B-Phase-Ill, I.D.A., Jeedimetla, Hyderabad-Distic-500 055, Telangana, India.
GMP Valid upto:29-09-2022
DML Valid upto: 09-03-2025</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted.
Fluconazole:
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>2FLZ0030220</td><td>1373</td><td>1.8KGS</td><td>06-05-2021</td></tr>
</table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Audit trail reports have been submitted.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers.</td></tr>
<tr><td colspan="3">Remarks of Evaluator:</td></tr>
<tr><td colspan="3">Decision: Registration Board decided as follows:
a. Cancellation of registration of above mentioned product from the name of M/s. Horizon Healthcare (Pvt) Ltd. 35-A, Punjab Small Industrial Estate, Taxila.
b. Approved registration of above mentioned product in the name of M/s Horizon Healthcare (Pvt.) Ltd., 33- Sundar Industrial Estate, Lahore.</td></tr>
</table>

c. Reference will be sent to Cost and Pricing Division for confirmation of maximum retail price (MRP).

Case No. 10 Complaint from Pakistan Citizen's Portal Regarding Manufacturing of Same Product with Two Different Brand Names.

A complaint has been received from Prime Minister's Performance Delivery Unit (PMDU), Pakistan Citizen's Portal that M/s. Pacific Pharmaceuticals 30Km Multan Road, Lahore is manufacturing a product by two names and the firm also marketing the products with two different MRPs i.e Rs.355.56 for Plasenzyme & Rs.227.13 for Plasil witth Enzyme. The details are given as under:-

Sr.#	Reg. No.	Product Name and Composition
1.	021646	Plasenzym Tablet Each tablet contains: - Metoclopramide HCl ……..…… 6mg Sodium dehydrochlolate ……... 20mg Bromelain Proteolytic unit …….. 35,000 Pancreatin FIP Proteolytic unit …… 210 Simethicon …… 50mg
2.	012130	Plasil with Enzyme Tablet Each tablet contains: - Metoclopramide HCl ……..…… 6mg Sodium dehydrochlolate ……... 20mg Bromelain Proteolytic unit …….. 35,000 Pancreatin FIP Proteolytic unit …… 210 Simethicon …… 50mg

M/s. Pacific Pharmaceutical Lahore has submitted following documents:-

i. Copy of registration letter of **Plasil with Enzyme Tablet** (Reg.No.012130) dated 02-01-1991 registered in the name of M/s. Pacific Pharmaceuticals Ltd; 29th Km Multan Road, Lahore. Previously this drug was registered in the name of M/s. Mars Pharma, Lahore in finished import under the brand name **Plasil Enzymatico (Reg.No.002659)** manufactured by M/s. Lepitit Millan Italy and transferred to M/s. Isman Drug House, 26 Commercial Building Shahra-e-Quaid-e-Azam Road, Lahore **dated 18th November, 1978**

ii. Copy of registration letter of **Plasenzym Tablet (Reg.No.021646) dated 20-05-1998** registered in the name of M/s. Pacific Pharmaceuticals Ltd; 29th Km Multan Road, Lahore.

It is submitted that the firm has not provided any evidence regarding change of registration status from M/s. Isman Drug House Lahore to M/s. Pacific Pharmaceutical, Lahore. Now firm contains two registrations of same formulation with two different brand names in local manufacturing and marketing with two different MRPs as complained stated above.

Registration Board in 297th meeting decided to issue show cause to M/s. Pacific Pharmaceutical, Lahore.

Accordingly show cause notice has been issued to the firm and firm has submitted a reply which is as under;

1. This is in regards to the Show Cause Notice received by Pacific Pharmaceuticals (Private) Limited's (the "Company") dated 21st October 2021 in regards to the registration of two different brand names for the same product.
2. That the Plasil with Enzyme bearing Registration No. 012130 was a registered product of Isman Drug House, a parent company of the Company, whereby the same was being imported by the Isman Drug House at that time, which was later on transferred to the Company for manufacturing locally. Furthermore, the Plasenzym bearing Registration No. 021646 is a product registered by the Company itself, since, one of the old products was

transferred to our Company, we started using both names to avoid disrupting the market. That both products are owned and are being manufactured by the Company not to defraud the public but in order to help them carry on with the product name they are comfortable with and have been using for decades.

3. It is pertinent to mention here that; several other companies are following the same market practice in order to cater to different segments or regions of the market. Please see below the similar products of only one company, Global Pharmaceutical, marketing its medicines under several brand names.

Sr. No.	Product Name	Generic	Registration Holder
1.	Norbac injection 250mg IV	Ceftrixone	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
2.	Norbac injection 500mg IV	Ceftrixone	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
3.	Aczon I.M Injection 500mg	Ceftrixone	M/s. Vision Pharmaceuticals (Pvt) Ltd., Plot No. 22-23 Industrial Triangle Kahuta Road Islamabad
4.	Amizone 250mg Injection	Ceftrixone	M/s. Aims Pharmaceuticals, Industrial triangle Kahuta Road, Islamabad **Contract Manufactured By:** M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
5.	Nafcin 500mg Tablet	Ciprofloxacin HCl eq. to Ciprofloxacin…....500mg	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
6.	Artinil-K 50mg Tablet	Diclofenac Potassium	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
7.	Ostinac 50mg Tablet	Diclofenac Sodium	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
8.	Ostinac 75mg Tablet	Diclofenac Sodium	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
9.	Zoycin 2.25gm Injection	Piperacillin (as Piperacillin Sodium): 2gm Tazobactam (as Tazobactam Sodium): 0.25gm	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
10.	Zoycin 4.5gm Injection	Piperacillin (as Piperacillin Sodium): 4gm Tazobactam (as Tazobactam Sodium): 0.50gm	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
11.	Tazpin 2.25gm Injection	Piperacillin (as Piperacillin Sodium): 2gm Tazobactam (as Tazobactam Sodium): 0.25gm	M/s. Vision Pharmaceuticals (Pvt) Ltd., Plot No. 22-23 Industrial Triangle Kahuta Road Islamabad **Contract Manufactured By:**

			M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
12.	Tazpin 4.5gm Injection	Piperacillin (as Piperacillin Sodium): 4gm Tazobactam (as Tazobactam Sodium): 0.50gm	M/s. Vision Pharmaceuticals (Pvt) Ltd., Plot No. 22-23 Industrial Triangle Kahuta Road Islamabad **Contract Manufactured By:** M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
13.	Bestoxil 500Mg Capsules	Cefadroxil	M/s. Vision Pharmaceuticals (Pvt) Ltd., Plot No. 22-23 Industrial Triangle Kahuta Road Islamabad
14.	Ceroxil Cap 500 mg	Cefadroxil	M/s. Global Pharmaceuticals (Pvt) Ltd., Plot No 204-205 Kahuta Triangle Industrial Area Islamabad

4. Furthermore, the above-mentioned products belong to one single company who is marketing several of its products under different brand names having similar salts. There are several other companies involved in the same practice in order to cater different demands and regions.
5. This practice does not constitute to any sort of violation; hence, it is respectfully prayed that the Authority may kindly suspend the working of its Show Cause Notice dated 21st October 2021.

As per above reply of the firm, stance of the firm is not justified as all above stated products are not registered products of M/s. Global.

Decision of 316th meeting of registration Board:

Registration Board decided to call M/s. Pacific Pharmaceuticals Limited, Lahore for personal hearing for cancellation of one of above-mentioned products registered in their name.

Accordingly, firm has been called for personal hearing at 12.30 P.M.

Proceedings of 317th Meeting:

Mr. Gazi Mustansar Riaz appeared on behalf of firm and requested to re-schedule the hearing as their technical head is on medical leave.

Decision of 317th Meeting

Registration Board considered the request of the firm and decided to postpone the personal hearing till forthcoming meeting of the Board.

Accordingly, firm has been called for personal hearing at 12.30 P.M

Proceeding of 320th Meeting:

Registration Board was informed that firm has applied for cancellation of registration of product at Sr. No. 1 of para-1 Plasenzym Tablet (Reg. No. 021646) in the name of M/s. Pacific Pharmaceuticals 30Km Multan Road, Lahore and registration of same in the name of M/s. Pacific Pharmaceuticals Ltd Ravi Lane, Plot No. 384, Sundar Industrial Estate, Raiwind Road, Lahore by way of contract manufacturing from M/s. Pacific Pharmaceuticals 30Km Multan Road, Lahore. Hence, personal hearing is not required, as firm has already applied for cancellation of registration of one of the product Plasenzym Tablet (Reg. No. 021646).

Decision: Registration Board decided to withdraw the show cause notice issued in the name of M/s. Pacific Pharmaceuticals 30Km Multan Road, Lahore and advised PE&R Division to place the case before the Board after its evaluation.

Referred case of 80th PRVC

Case No. 01: Application of M/s Martin Dow Marker Ltd. Quetta for extension of shelf life..

Product name: **Neurobion injection (Reg No. 001485)**
(Vitamin B1, Vitamin B6 and Vitamin B12)

Current shelf life: **12 months**

Proposed shelf life: **24 months**

Sr.#	Documents required (as per SOP M-283)	Information provided
1.	Application with required fee as per relevant SRO.	Date of application:25.10.2021 DRAP (R&I) 26.10.2021 PR-1(PE&R). Reply dated: 08.02.2022 DRAP (R&I) Rs 7500/- deposited dated 15.09.2021 Rs 2500/- deposited dated 24.01.2022
2.	Copy of registration letter and last renewal status	Reg No. **001485** dated 15th August,1976 Last renewal submitted on 21st Feb 2018
3.	Proposed shelf-life, justification & data of long-term stability testing (as per conditions of zone IV-A) including chromatograms for a minimum of 3 commercial scale batches or development scale batches as set by Registration Board in 276th meeting up to the proposed shelf-life.	**Long term studies** (Temp 30◦C±2◦C /RH 65%±5%) **Interval**: 0,3,6,9,12,18,24 and 36 months **Testing parameters**: Appearance, pH, identification and Assay **Batch size**: 275 Liter **Batch no**: Q7498, Q7499, Q7500. **Type of container: Amber color glass ampoule (USP type I)**
4.	An undertaking that: • No change to the primary packaging type that is in direct contact with the FPP and recommended conditions of storage • No change in formulation and specification either of finished product, API and excipients etc. • In case both the above conditions are involved then manufacturer will submit complete requisite information as per procedure • In case of any quality complaint/ OOS result observed by the marketing authorization holder as a result of this change, the same shall be reported to registration board and all the stock shall be recalled from the market immediately.	Provided

Firm has submitted documents as follows:

S.No	Document submitted	Remarks
1.	Analytical validation studies	Firm has submitted analytical method along with validation studies such as Linearity, specificity, accuracy, precision, range, robustness
	Stability protocol	Information provided about: stability study requirement, batch size, batch information, storage condition and testing interval, sampling plan, testing parameter and acceptance criteria,
2.	Stability data	Firm has submitted summary data sheet and certificate of analysis for each time interval along with chromatograms
3.	Digital data logger	Firm has submitted digital data logger for entire study period i.e.year 2017 to 2018

Decision 80th PRVC:

The committee considered the case and referred to Registration Board.

Decision: Registration Board considered the case and deferred the request of the firm for following:

a) **Confirmation of shelf life of innovator's product of principal manufacturer in country of origin.**
b) **Confirmation of shelf life of same/similar formulation available in RRA countries.**
c) **Confirmation of shelf life of same/similar formulation available in countries of Zone IV-A/IV -B**

EXPORT FACILITATION DESK

Case No.01: Registration of Drug (s) of M/s Genome Pharmaceuticals (Pvt.) Ltd, 16/1, Phase-Iv, Industrial Estate, Hattar Haripur, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from letter No. F 3-7/95-Lic dated 07-07/2021
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 02-04-2021
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	II	III	IV
1.	Montogen 5mg Tablet Each film coated tablet contains: Montelukast (as Sodium).....5mg	Purchase order from Viet Nam	Dy. No. 7794 (28.05.2022) Rs.30,000/- (13.05.2022) Rs.45,000/- (24.05.2022) Remarks Chewable form is available in RRA

Decision: Registration Board approved above mentioned product of M/s Genome Pharmaceuticals (Pvt.) Ltd, 16/1, Phase-Iv, Industrial Estate, Hattar Haripur, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.

Case No.02: Registration of Drug (s) of M/s Star Laboratories (Pvt.) Ltd, 23-Km, Multan Road Chung Lahore, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;

Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from Inspection report renewal of DML dated 14-12/2015
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 24-01-2020
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	Oxytab 250 Tablets Each film coated tablet contains: Oxytetracycline HCl.....250mg	Purchase order from Uzbekistan	Dy. No. 7821 (04.06.2022) Rs.75,000/- (23.05.2022) Available in MHRA in sugar coated form
2.	Oxytab 500Tablets Each film coated tablet contains: Oxytetracycline HCl.....500mg	Purchase order from Uzbekistan	Dy. No. 7822 (04.06.2022) Rs.75,000/- (23.05.2022) Available in MHRA in sugar coated form with 250mg strength
3.	Oxytab 100 Tablets Each film coated tablet contains: Oxytetracycline HCl.....100mg	Purchase order from Uzbekistan	Dy. No. 7823 (04.06.2022) Rs.75,000/- (23.05.2022) Available in MHRA in sugar coated form with 250mg strength
4.	Caropain 75 chewable tablets Each chewable tablet contains: Carprofen.....75mg (non-narcotic non-steroidal anti-inflammatory drug)	Purchase order from Uzbekistan	Dy. No. 7960 (05.07.2022) Rs.75,000/- (27.06.2022) Available in 25mg and 100mg strengths in USFDA and HPRA
5.	Flotosin Injection 100ml Each ml contains: Florfenicol.....200mg Tylosin Tartrate.....57.50mg (Antibiotics)	Purchase order from Uzbekistan	Dy. No. 7961 (05.07.2022) Rs.75,000/- (27.06.2022) available as single ingredient florfenicol 300mg/ml injection in USFDA
6.	Flotosin Injection 50ml Each ml contains: Florfenicol.....200mg Tylosin Tartrate.....57.50mg (Antibiotics)	Purchase order from Uzbekistan	Dy. No. 7962 (05.07.2022) Rs.75,000/- (27.06.2022) available as single ingredient florfenicol 300mg/ml injection in USFDA

7.	Milpraz chewable tablets Each chewable tablet contains: Milbemycin Oxime.....12.5mg Praziquantel.....12mg (antihelmintic)	Purchase order from Uzbekistan	Dy. No. 7963 (05.07.2022) Rs.75,000/- (28.06.2022) available as single ingredient milbemycin oxime n USFDA
8.	Emprastar 30/150 chewable tablets Each chewable table contains: Emodepside.....30mg Praziquantel.....150mg (antihelmintic)	Purchase order from Uzbekistan	Dy. No. 7964 (05.07.2022) Rs.75,000/- (28.06.2022) available as single ingredient Praziquantel in USFDA in 600mg film coated form
9.	Emprastar 10/50 chewable tablets Each chewable table contains: Emodepside.....10mg Praziquantel.....50mg (antihelmintic)	Purchase order from Uzbekistan	Dy. No. 7965 (05.07.2022) Rs.75,000/- (28.06.2022) available as single ingredient Praziquantel in USFDA in 600mg film coated form
10.	Emprastar 3/15 chewable tablets Each chewable table contains: Emodepside.....3mg Praziquantel.....15mg (antihelmintic)	Purchase order from Uzbekistan	Dy. No. 7966 (05.07.2022) Rs.75,000/- (28.06.2022) available as single ingredient Praziquantel in USFDA in 600mg film coated form
11.	Pyrostar Oral solution Each ml contains: Pyrantel (as Pyrantel Pamoate).....50mg (antihelmintic)	Purchase order from Uzbekistan	Dy. No. 8083 (27.07.2022) Rs.75,000/- (19.07.2022) available as 180mg tablet in USFDA
12.	Fiprosta Spray Each ml contains: Fipronil.....0.25% w/v (insecticide)	Purchase order from Uzbekistan	Dy. No. 8084 (27.07.2022) Rs.75,000/- (21.07.2022)
13.	Parapyzol Chewable tablet Each chewable tablet contains: Praziquantel.....50mg Pyrantel Embonate.....144mg Fenbendazole.....200mg	Purchase order from Uzbekistan	Dy. No. 8094 (29.07.2022) Rs.75,000/- (25.07.2022) available as 180mg tablet of pyrantel embonate in USFDA and 50mg/ml suspension of pyrantel embonate in HPRA
14.	Clindavet Tablet Each tablet contains: Clindamycin HCl eq to Clindamycin.....150mg	Purchase order from Uzbekistan	Dy. No. 8105 (10.08.2022) Rs.75,000/- (04.08.2022)

			Clindamycin 150mg capsule is available in MHRA
15.	Star Petcal forte syrup Each 50ml contains: Vitamin A.....45000IU Vitamin D3.....8000IU Calcium.....1628mg Phosphorus.....838.50mg Vitamin B12.....100mcg	Purchase order from Uzbekistan	Dy. No. 8106 (10.08.2022) Rs.75,000/- (25.07.2022)
16.	Marbocin 25mg tablet Each tablet contains: Marbofloxacin.....25mg	Purchase order from Uzbekistan	Dy. No. 8124 (17.08.2022) Rs.75,000/- (01.08.2022) Marbofloxacin 20mg tablet is available in HPRA
17.	Zanmatema Plus (60ml, 90ml, 120ml, 240ml) Each 5ml contains: Artemether.....20mg Lumefantrine.....120mg	Purchase order from Uzbekistan	Dy. No. 8165 (19.08.2022) Rs.75,000/- (12.08.2022) Artemether/Lumefantrine 150/90, 15/90. 180/1080, 360/2160 are approved in WHO.

Decision: Registration Board approved above mentioned products of M/s Star Laboratories (Pvt.) Ltd, 23-Km, Multan Road Chung Lahore, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.

Case No.03: Registration of Drug (s) of M/s Pharma Lord (Pvt.) Ltd, 12-Km, Lahore Road, Layyah, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from letter No. F 1-8/2011-Lic dated 21-02/2013
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 03-05-2019
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	Rahol250mg Tablet Each film coated tablet contains:	Purchase order from Africa	Dy. No. 7832 (07.06.2022) Rs.75,000/- (03.06.2022)

	Tapentadol as Hydrochloride.....250mg		200mg table in extended release form in MHRA

Decision: Registration Board approved above mentioned product of M/s Pharma Lord (Pvt.) Ltd, 12-Km, Lahore Road, Layyah, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product. Moreover, following conditions will be mentioned on export registration letter.

a. ***Registration of Tapentadol containing product(s) of exporter in importing country.***
b. ***Legal status of Tapentadol in importing country, whether controlled under INCB convention or otherwise.***

Case No.04: Registration of Drug (s) of M/s Fedro Pharmaceutical Labs (Pvt.) Ltd, 149 Industrial Estate, Hayatabad, Peshawar, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from letter No. F 3-6/85-Lic dated 29-04/2022
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 03-02-2022
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	II	III	IV
1.	Fegar-V Syrup Each 5ml contains: Pizotifen (as hydrogen malate) 0.363eq to..... 0.25mg Thiamin HCl.....0.875mg Riboflavin 5 Phosphate eq to riboflavin..1.31mg Pyridoxine HCl.....0.77mg Nicotinamide.....5.25mg	Purchase order from Afghanistan	Dy. No. 7874 (20.06.2022) Rs.75,000/- (18.05.2022)

Decision: Registration Board approved above mentioned product of M/s Fedro Pharmaceutical Labs (Pvt.) Ltd, 149 Industrial Estate, Hayatabad, Peshawar for export purpose only.. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting)

hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.

Case No.05: Registration of Drug (s) of M/s Hilton Pharma (Pvt.) Ltd, Plot No. 13-14 & 43, Sector-15, Korangi Industrial Area, Karachi¸ for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from letter No. F 2-14/85-Lic dated 30-06/2020
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 19-01-2021
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	HIBU-P Injection 100ml Each ml contains: **Ibuprofen Sodium dihydrate equivalent to Ibuprofen,.....3mg** **Paracetamol…….10mg**	Purchase order from Afghanistan	Dy. No. 7952 (04.07.2022) Rs.75,000/- (07.06.2022) 400mg/ml ibuprofen inj is available in MHRA
2.	HIBU-P 125mg/250mg tablet Each film coated tablet contains: Ibuprofen,.....125mg Paracetamol.....250mg	Purchase order from Afghanistan	Dy. No. 7953 (04.07.2022) Rs.75,000/- (16.05.2022) 200mg/500mg strengths are available in MHRA
3.	HIBU-P 150mg/500mg tablet Each film coated tablet contains: Ibuprofen.....150mg Paracetamol.....500mg	Purchase order from Afghanistan	Dy. No. 7954 (04.07.2022) Rs.75,000/- (07.06.2022) 200mg/500mg strengths are available in MHRA

Decision: Registration Board considered the case and decided as follows:

a) **Deferred the product at Sr No 01 for approval status of applied formulation internationally as well as in importing country.**

b) **Approved products at Sr No 2-3 for export purpose only. Since applied formulations is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.**

Case No.06: Registration of Drug (s) of M/s Nabi Qasim Industries (Pvt.) Ltd, 17/24, Korangi Industrial Area, Karachi, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents

Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from letter No. F 2-20/85-Lic dated 27-04/2020
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 05-08-2019
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	Myzovag Plus Vaginal Tablet Each vaginal tablet contains: Metronidazole.....100mg Miconazole Nitrate.....100mg	Purchase order from Ugenda	Dy. No. 7957 (04.07.2022) Rs.75,000/- (09.06.2022) Miconazole in gel form is available in RRA
2.	Myzovag Plus Vaginal Gel Each 30g contains: Miconazole Nitrate .....20mg (2% w/w) Metronidazole .....10mg (1% w/w	Purchase order from Ugenda	Dy. No. 7975 (18.07.2022) Rs.75,000/- (09.06.2022) Miconazole as single ingredient in gel form is available in RRA
3.	Gloza 900mg Lyophilized Injection Each vial contains: Glutathione.....900mg	Purchase order from Uganda	Dy. No. 7976 (18.07.2022) Rs.75,000/- (29.06.2022) Glutathione 600mg is available in AIFA

Decision: Registration Board considered the case and decided as follows:

a) **Approved products at Sr No 1-2 for export purpose only. Since applied formulations is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product**

b) **Deferred the product at Sr No 03 for approval / regulatory status of applied formulation in importing country.**

Case No.07: Registration of Drug (s) of M/s Pacific Pharmaceuticals Ltd, 30-Km, Multan Road, Lahore, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified from Inspection report renewal of DML dated 13-04/2017

GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 14-09-2021
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	Parafic 1000mg tablet Each tablet contains: Paracetamol.....1000mg	Purchase order from Iraq	Dy. No. 8035 (25.07.2022) Rs.30,000/- (20.05.2022) Rs.45,000/- (18.07.2022) Paracetamol 500mg tablet is available in RRA
2.	Mefafic 500mg Capsule Each capsule contains: Mefenamic acid.....500mg	Purchase order from Iraq	Dy. No. 8103 (10.08.2022) Rs.75,000/- (28.07.2022) mefenamic acid 250mg capsule is available in rra
3.	Citicoline Infusion 10mg/ml (250ml) Each ml contains: Citicoline.....10mg	Purchase order from Tajikistan	Dy. No. 8169 (22.08.2022) Rs.30,000/- (02.06.2022) Rs.45,000/- (22.08.2022)

Decision: Registration Board approved above mentioned products of M/s Pacific Pharmaceuticals Ltd, 30-Km, Multan Road, Lahore, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.

Case No.08: Registration of Drug (s) of M/s Medisure Laboratories Pakistan (Pvt.) Ltd, A-115, S.I.T.E. Super Highway Karachi, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified letter No. F 2-2/2001-Lic dated 12-04/2018
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 07-09-2021
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	II	III	IV
1.	Garasef 1.5gm Injection Each vial contains: Cefoperazone Sodium equivalent to Cefoperazone.....1000mg Sulbactam Sodium equivalent to Sulbactam.....500mg	Purchase order from Myanmar	Dy. No. 8099 (02.08.2022) Rs.75,000/- (18.07.2022) 1gm and 2gm strengths are available in RRA

Decision: Registration Board approved above mentioned product of M/s Medisure Laboratories Pakistan (Pvt.) Ltd, A-115, S.I.T.E. Super Highway Karachi, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.

Case No.09: Registration of Drug (s) of M/s Davis Pharmaceuticals, Plot No. 121, Industrial Triangle Kahuta Road, Islamabad, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified letter No. F 1-22/95-Lic dated 20-11/2015
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 02-02-2022
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	II	III	IV
1.	Klobal Cold Tablet Each uncoated tablet contains: Paracetamol.....500mg Bromhexine hydrochloride.....8mg Guaifenesin.....100mg Phenylephrine Hydrochloride.....10mg Chlorphrniramine Maleate.....4mg	Purchase order from Colombo	Dy. No. 8109 (12.08.2022) Rs.75,000/- (01.08.2022)
2.	Davigas Suspension Each 5ml contains: Aluminium Hydroxide.....200mg Magnesium Hydroxide.....200mg Simethicone.....50mg Domperidone Ph. Eur.....5mg	Purchase order from Colombo	Dy. No. 8110 (12.08.2022) Rs.75,000/- (01.08.2022)

Decision: Registration Board approved above mentioned products of M/s Davis Pharmaceuticals, Plot No. 121, Industrial Triangle Kahuta Road, Islamabad, for

export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product.

Case No.10: Registration of Drug (s) of M/s Fahmir Pharma (Pvt.) Ltd, Main Mandiwala Stop, 26-Km, Lahore Jaranwala Road, Tehsil Sharaqpur, distt, Shaikhupura, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5;
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided Approval of relevant section verified letter No. F 1-5/2012-Lic dated 11-04/2018
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 27-05-2021
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	Tramakin-SR 100mg Capsule Each **sustained release** capsule contains: Tramadol HCl.....100mg	Purchase order from Nigeria	Dy. No. 8161 (18.08.2022) Rs.30,000/- (27.06.2022) Rs.45,000/- (16.08.2022)
2.	Panabro-CF Tablet Each tablet contains: Ibuprofen.....200mg Paracetamol.....325mg Caffeine.....30mg	Purchase order from Burundi	Dy. No. 8170 (22.08.2022) Rs.30,000/- (21.04.2022) Rs.45,000/- (23.06.2022)

Decision: Registration Board approved above mentioned products of M/s Fahmir Pharma (Pvt.) Ltd, Main Mandiwala Stop, 26-Km, Lahore Jaranwala Road, Tehsil Sharaqpur, distt, Shaikhupura, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product. Moreover, following conditions will be mentioned on export registration letter.

*a. **Registration of Tapentadol containing product(s) of exporter in importing country.***
*b. **Legal status of Tapentadol in importing country, whether controlled under INCB convention or otherwise.***

Referred case of 84th PRVC

Case No.09: Registration of Drug (s) of M/s Medisure Laboratories Pakistan (Pvt.) Ltd, A-115, S.I.T.E. Super Highway Karachi, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents

Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5; (Pages.278-305 & 459-470/C)
Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided (Page-283/C). Approval of relevant section verified from letter No. F Nil dated 18-09-2014 (Page 285/C).
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 07-09-2021 (Page 284/C).
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided (Pages. 286-306 &468-471 /C)

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	**II**	**III**	**IV**
1.	Bisomedi 5mg/5mg tablet Each film coated tablet contains: Bisoprolol fumarate.....5mg Amlodipine Besylate eq to amlodipine.....5mg	RRA reference not found	Dy. No. 8064/22 (27.07.2022) Rs.75,000/- (20.07.2022) Applied combination is not available in RRA
2.	Tamral 250mg tablet Each tablet contains: Tramadol HCl.....250mg	RRA reference not found moreover not approved by RB yet	Dy. No. 8065/22 (27.07.2022) Rs.30,000/- (21.07.2022) Rs.45,000/- (22.07.2022) 200mg table in extended release form in MHRA

Decision: Registration Board approved above mentioned products of M/s Medisure Laboratories Pakistan (Pvt.) Ltd, A-115, S.I.T.E. Super Highway Karachi, for export purpose only. Since applied formulation is neither registered for local use nor approved by any RRA (as adopted by Registration Board in 275th meeting) hence manufacturer and importing country shall be responsible for safety, efficacy and quality of drug product. Moreover, following conditions will be mentioned on export registration letter.

a. Registration of Tapentadol containing product(s) of exporter in importing country.

b. Legal status of Tapentadol in importing country, whether controlled under INCB convention or otherwise.

<u>Referred case of 84th PRVC</u>

Case No.16: Registration of Drug (s) of M/s Indus Pharma (Pvt.) Ltd, Plot No. 26-27, 63-67, Sector-27, Korangi Industrial Area Karachi, for export purposes only.

Firm has applied for registration of drug(s) only for export purpose as per following details:

Requirements As Per SOP	Submitted Documents
Application on Form-5/ Form 5-D with required fee as per relevant SRO.	Form5; (Pages.554-585/C)

Copy of DML (Renewal status) along with approval of relevant sections verified by licensing Division or inspection report for renewal of DML before 2005.	Copy of DML provided (Page-561/C). Approval of relevant section verified from letter No. F 2-13-/85-Lic dated 21-07-2020 (Page 562/C).
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 17-12-2021 (Page 563/C).
Undertakings that the applied product is exclusively for export purpose and the proposed names/ label/ colour do not resemble with already registered brands in importing country.	Provided

Detail of the products is given below:

Sr.#	Name of Drug(s) with composition	Generic/RRA Status	Dy.No.(EFD)/Fee with date
I	II	III	IV
1.	Bromoz-Q (Bromazepam) 3mg tablet Each tablet contains: Bromazepam.....3mg	Sambro 3mg tablet by M/s Sami	Dy. No. 7945/22 (29.06.2022) Rs.30,000/- (09.06.2022) **Tablet (Psychotropic) section to be confirmed**

Decision 84th PRVC: ***The Committee considered the case and referred the product to Registration Board after confirmation of Tablet (Psychotropic) section.***

Update Status

The firm has provided evidence of approval of Tablet (Psychotropic) Section by the Licensing Division vide letter No F.2-13/85-Lic(Vol-V) dated 31/06/2022.

Decision: Registration Board approved above mentioned product of M/s Indus Pharma (Pvt.) Ltd, Plot No. 26-27, 63-67, Sector-27, Korangi Industrial Area Karachi for export purpose only. The firm shall comply with all rules and regulations specified for export of controlled drugs.

Case No.01: Change of Specifications / Standardization

Sr. No.	Reg. No.	Name of Product with existing composition, Specifications	Name of Product with proposed Change in Specifications	Initial Date of Registration Renewal Application	Remarks
I	II	III	IV	V	VI
iii. M/s. Synchro Pharmaceuticals, Lahore					
1.	044749	Matilda –D Syrup Each 5ml contains:- Calcium Phosphate (tribasic)……210mg Vitamin D3…350Units	Matilda –D **Suspension** Each 5ml contains:- Calcium Phosphate (tribasic)……210mg Vitamin D3……350Units	18-01-2007 17-01-2017 12-01-2017 Renewal is ok	Fee Rs. 10,000/- deposited for each product dated 21-06-2021 Dy. No. 25297 R&I dated 10-09-2021 Dy. No. 1370PR-II dated 13-09-2021

Remarks:-

- Both the ingredients used in formulation are below RDA level, accordingly does not fall under the category of drug as per current vitamin policy.
- The firm has provided the evidence of generic status as follows:-

Name of product	Calcium –P suspension
Registration no.	005761
Composition of generic status	Each 5ml contains:- Calcium Phosphate (tribasic) …210mg Vitamin **D3**……350 IU
Unit carton of available formulation	Not provided

Decision 68th PRVC	The Committee considered and deferred the request as both the ingredients used in formulation are below RDA level, accordingly does not fall under the category of drug as per decision of 295th meeting of Registration Board.

Fresh / Reply by the firm

The committee has deferred the request as both ingredients used in formulation are below RDA Level. In the view of above-mentioned decision, the firm has again resubmitted the application as their formulation is previous registered in their name and they also submit the evidence of same formulation registered with Suspension Specification of different firms. In the above scenario the firm has requested to allow print Matilda-D Suspension instead of Syrup as their products is supply to different government hospital etc.

Decision 74th PRVC	The Committee considered and deferred the request for submission of reference of innovator's product/similar formulation approved in RRA. Moreover, reference regarding formulation of generic versions available (in suspension form) to be provided by the firm.

Updated status: Firm has submitted unit carton as evidence of availability of proposed formulation in local market as follows: **Calcium-P suspension** **Reg No 005761** **M/s PDH Pharmaceutical Pvt Ltd**	
Decision 76th PRVC	The committee considered the case and referred it to Registration Board.
Decision 316th meeting: ***Registration Board considered the case and deferred the request of firm for submission of Batch Manufacturing Record to clarify whether firm has been manufacturing Matilda –D Syrup (Reg No 044749) in suspension form or syrup form.***	

Updated Status:

Now the firm has submitted Batch Manufacturing Record confirming firm has been manufacturing above mentioned product in suspension form, moreover firm has further clarified that Calcium Phosphate (tribasic)is poorly soluble in water hence its formulation is oral liquid suspension.

Decision: Registration Board considered the case and acceded to request of firm for standardization/correction of nomenclature of dosage form of Matilda –D Syrup (Reg No 044749) as suspension from syrup.

Case No 2 Application for Change of Formulation of Already Registered Drug Rifapin-H Plus Powder Suspension

M/s Schazoo Zaka (Pvt) Ltd have applied for change of formulation for their already registered product "**Rifapin H Plus Powder Suspension (Reg No. 071498)**" dated 30.06.2020. The initial registration of the said product was granted to the firm on 04.09.2012. The details of the already registered formulation and proposed revised formulation of the firm along with its approval status in reference regulatory authorities is provided in the table below:

Already registered formulation of the firm	**Newly applied formulation by the firm**	**RRA approved formulation**
Each 5ml contains: Rifampicin……150mg Isoniazid……75mg	Each 5ml of reconstituted suspension contains: Rifampicin……150mg Isoniazid……100mg	Each **dispersible tablet** contains: Rifampicin…. 75 mg Isoniazid…… 50 mg Each **film coated tablet** contains Rifampicin……..150 mg Isoniazid……..75 mg

According to firm they have applied to change formulation in line with the revised dosing published in the 2014 WHO Guidance on childhood TB. Firm has further submitted that Dry Powder Suspension form is mother and child friendly. It is the conventional and convenient method of consuming medicine. Mostly mothers can easily administer reconstituted suspension as compared to sachet or dispersible tablet. WHO prefers dispersible tablet just to avoid the heavy freight cost for Dry Powder Suspension (include weight of bottle and cap). The reason is not due to any quality, safety or efficacy.

As per the summary of product characteristics of Isoniazid/rifampicin 50mg/75mg dispersible tablets of Macleods Pharmaceuticals Ltd, Reference Number: TB302 a WHO Prequalified Medicinal Products the dose of isoniazid/rifampicin for prevention or treatment of tuberculosis (TB) in children weighing less than 25 kg is as follows:

Patient's weight	Dose (isoniazid/rifampicin)	Number of [TB302 trade name] tablets
4-7 kg	50mg / 75mg	1
8-11 kg	100mg / 150mg	2
12-15 kg	150mg / 225mg	3
16-24 kg	200mg / 300mg	4
> 25 kg	--*	--*

*For these patients, formulations containing more isoniazid/rifampicin should be used.

(Accessed on 04.07.2022 at https://extranet.who.int/pqweb/sites/default/files/TB302part4v2_0.pdf).

It is evident that the newly applied formulation is not approved by any reference regulatory authority nor is part of WHO essential model list / WHO prequalified medicinal product list and not recommended as a single dose / dosage form by any clinical guidelines. The newly applied formulation is different from the reference product both in terms of strength as well as dosage form.

Decision: **Registration Board considered the case and deferred the request of firm for rationale of proposed change. Since applied formulation is neither approved by any reference regulatory authority nor is part of WHO essential model list / WHO prequalified medicinal product list. Moreover, applied formulation is different from the reference product both in terms of strength as well as dosage form.**

Case No. 3: Change in status of Product Registration Holder from Drug Manufacturing License (000234) to Drug Sale License without change in manufacturing site.

M/s Bayer Pakistan (Pvt) Limited has applied for change of registration status of already registered products as follows:

DML Site (current)	DSL Site (Proposed)	
DML No. 000243 Bayer Pakistan Pvt Ltd Plot No. 108, Quaid-e-Azam Industrial Esate, Kot Lakhpat, Lahore Pakistan	**DSL No. 01. Bayer Pakistan Pvt Ltd. Plot No. 23 Sector No. 22, Korangi Industrial Area, Karachi 74900, Pakistan**	**Manufacturing site shall remain same i.e M/s Novartis pharma, C-21, S.I.T.E Karachi**

Following are the products applied by the firm for proposed change:

S. No.	Products Details	Reg. No.	Fee Paid
1	Canesten 1, Vaginal Cream with applicator	107229	Fee of Rs. 30,000/- (Deposit Slip No. 3620099532)
2.	Canesten Clotrimazole Cream	107227	Fee of Rs. 30,000/- (Deposit Slip No. 60106706910)
3.	Canesten 1 Vaginal Tablet 0.5g	107224	Fee of Rs. 30,000/- (Deposit Slip No. 7993597883)
4.	Baycuten N Cream	012639	Fee of Rs. 30,000/- (Deposit Slip No. 635276035343)
5.	Canesten 6 Vaginal Tablet of 0.1g	107226	Fee of Rs. 30,000/- (Deposit Slip No. 60106706910)
6.	Canesten Extra Bifonazole Cream	107226	Fee of Rs. 30,000/- (Deposit Slip No. 017332495525)

7.	Baydal Tablet	109734	Fee of Rs. 30,000/- (Deposit Slip No. 540447322218)

According to firm proposed change is with reference to rule 20A 1 (c) of SRO 1347(I)/2021 dated 15th October,2021.

"*a foreign pharmaceutical company (manufacturer or marketing authorization holder) having drug sale licence in Pakistan for their research, innovator, originator drug products or drug products already registered for sale by any of reference regulatory authorities adopted by the Registration Board;"*

Decision: Registration Board after deliberation deferred the request and advised the firm to explain relevant rule for consideration of the proposed change.

VETERINARY CASES

Case.No.01:- Request of M/s. Nawal Pharmaceuticals, Taxila Registration of Drugs.

M/s. Nawal Pharmaceuticals, Taxila has requested for registration of following veterinary products for local manufacture in their name and cancellation of same from the name of M/s. Breeze Pharma (Pvt.) Ltd., Islamabad.

S. No.	Reg. No.	Name of Drug(s)/ Composition	Already Approved Pack Size(s)	Initial Date of Registration	Date of Application Receiving in R&I-DRAP
1.	059179	Pro VADE Injection Each ml contains:- Vitamin A……..80,000IU Vitamin D3……40,000IU Vitamin E……....20mg	10ml 20ml 50ml 100ml	18-08-2009 31-07-2019	17-03-2021
2.	059133	HIT-CRD Injection Each ml contains:- Tylosin Tartrate……...50mg Colistin Sulphate…….10mg Streptomycin…….100mg	10ml 20ml 50ml 100ml	01-08-2009 30-07-2019	17-03-2021
3.	059108	Tylogent Injection Each ml contains:- Gentamycin (as Sulphate)…..50mg Tylosin (as Tartrate)…….100mg	50ml 100ml	01-08-2009 30-07-2019	17-03-2021
4.	059120	Spectral Injection Each ml contains:- Lincomycin (as HCI)……50mg Spectinomycin (as HCI)…..100mg	50ml 100ml	01-08-2009 30-07-2019	17-03-2021

M/s. Nawal Pharmaceuticals, Taxila has deposited the required fee Rs.20,000 x 4 = Rs.80,000/- and submitted following supporting documents:-

(i) Original NOC dated 26-01-2021 & 15-03-2021 from M/s. Breeze Pharma (Pvt.) Ltd., Islamabad.
(ii) Copy of initial registration letters and renewal status.
(iii) Copy of Drug Manufacturing License.
(iv) GMP inspection report conducted on 29-10-2018 DML No.000735 (Formulation).
(v) Copy of approved sections.
(vi) Applications on Form 5.
(vii) Undertaking.

Registration Board in its 307th meeting defer the case for seeking opinion from Legal Division as the Central Licensing Board in its 280th meeting held On 26th & 27th April, 2021 cancelled the Drug Manufacturing License No.000659 (Formulation) of M/s. Breeze Pharma (Pvt.) Ltd., Islamabad.

Accordingly letter issued to Legal Division for seeking opinion from Legal Division. In response the Legal Division has informed that as per available facts/record of the case, M/s. Breeze Pharma, Islamabad issued various NOC's to different firms for transfer of registration of products from its name to other manufacturer. Central Licensing Board cancelled the Drug Manufacturing License of the said firm in its 280th meeting held on 26th & 27th April, 2021. Hence, this Division is opined that those from who got NOC's from M/s. Breeze Pharma, Islamabad and applied well within time for transfer of registration to PE&R Division before

cancellation of Drug Manufacturing License, their cases for transfer of registration may be processed by the Division in accordance with law.

Registration Board in its 312th meeting decided as follow;

(a) Deferred products for NOC clarification.

The NOC of above mentioned products have also been issued to M/s. Nawal Pharmaceuticals, Taxila by M/s. Breeze Pharma, Islamabad. I/we on behalf of M/s. Eterna Pharma (Pvt) Ltd., Mirpur, AJK hereby request you to transfer the registration alongwith brand name of the following products to M/s. Nawal Pharmaceuticals, Taxila, so that M/s. Nawal Pharmaceuticals, Taxila should be able to manufacture these products in their own name. We have no objection regarding the transfer of the registrations alongwith brand name of the above products.

Decision:- Registration Board decided as follow;

(a) Approved cancellation of registration of above mentioned products from the name of M/s. Breeze Pharma, Islamabad.

(b) Approved the registration of above mentioned products in the name of M/s Nawal Pharmaceuticals, Plot No.11-A Punjab Small Industrial Estate, Taxila-Rawalpindi.

Case No. 02:- Request of M/s. Selmore Pharmaceuticals (Pvt) Ltd., Lahore for Grant of Additional Packs for their already Registered Veterinary Drug.

M/s. Selmore Pharmaceuticals (Pvt) Ltd., Lahore has applied for grant of additional packs of their following registered veterinary drug as per details mentioned against each:-

S. No.	Regn. No.	Name of Drug(s)/ Composition	Already Pack Size Granted	Demanded Additional Pack	Initial registration/ renewal status	Remarks/Justification Diary No.
1.	049629	Supertone Solution Each ml contains:- Vitamin E……200mg Sorbitol…….50mg Choline Chloride…..50mg Selenium……..2.3mg Zinc…….4mg	100ml 250ml 500ml 1000ml	2 Litre 5 Litre	14-10-2008 Registration Board in its 292nd granted the renewal w.e.f. 14-10-2018 to 13-10-2023	Dy.No.6379-(R&I) DRAP dated 25th February, 2021. Just to fulfill the requirements of market and Veterinary Doctor's

M/s. Selmore Pharmaceuticals (Pvt) Ltd., Lahore has deposited the required fee of Rs.5,000 x 2 = Rs.10,000/- and submitted following supporting documents:-

(i) Copy of initial registration letters/ renewal.
(ii) Copy for change of composition for product for at Sr.No.3.
(iii) Details of previously granted pack size.
(iv) GMP inspection conducted by DRAP on 17-08-2018.
(v) Undertaking that the provided information/documents are true/correct.

The demanded pack size is not given to other firms.

Registration Board in its 307th meeting defer the case for further deliberation.

The firm has provided details machinery and equipment. The details are as under:-

List of machinery/equipment

Sr. No.	Machine Code	Machinery/Equipment	Origin	Capacity	Document Number
1.	MV - 004	St. Steel Manufacturing Vessel With Silver Son Mixer	Local	500L - 2000 L	SPL/IMS/PD/SOP/ME/025
2.	JV - 005	St. Steel double Jacketed Manufacturing Vessel With Mixer	Local	100L - 500 Ltr	SPL/IMS/PD/SOP/ME/024
3.	MV – 006	St. Steel Manufacturing Vessel	Local	100L -400 Ltr	SPL/IMS/PD/SOP/ME/025
4.	SV – 005	St. Steel Storage Vessel With Slow Speed Mixer	Local	200L - 2000 Ltr	SPL/IMS/PD/SOP/ME/026
5.	SV – 006	St. Steel Storage Vessel	Local	100L - 400 Ltr	SPL/IMS/PD/SOP/ME/026
6.	SS – 003	St. Steel Silver Son Mixer With Stand	Local	1800RPM	SPL/IMS/PD/SOP/ME/027
7.	TP – 003	Transfer Pump	Local	13-40Ltr/Min	SPL/IMS/PD/SOP/ME/030
8.	FL – 001	Automatic Bottle Filling Line 8 Nozzles 50 – 200ml	China	4000/Hour	SPL/IMS/PD/SOP/ME/011
9.	FL – 002	Liquid Filling Line 4 Nozzles(500 –1000ml)	Local	1200/Hour	SPL/IMS/PD/SOP/ME/012
10.	FL – 003	Liquid Filling Line 4 Nozzles(1000 –5000ml)	Local	800/Hour	SPL/IMS/PD/SOP/ME/012-A
11.	AS – 001	Aluminum Seals Sealing Machine	Local	1500/Hour	SPL/IMS/PD/SOP/ME/003
12.	CS – 001	PP Cap Sealing Machine	Local	2500/Hour	SPL/IMS/PD/SOP/ME/002
13.	BB - 001	Bottle Blowing Machine	Local	700-2000/Hour	SPL/IMS/PD/SOP/ME/010
14.	AS – 002	Aluminum Seals Sealing Machine(Induction Sealing)	China	10-50Bottles/Min	SPL/IMS/PD/SOP/ME/070
15.	FE - 001	Fluid Equipment WT600F-2A	China	6-60Bottles/Min	SPL/IMS/PD/SOP/ME/071
16.	FE - 002	Fluid Equipment WT600F-2A	China	6-60Bottles/Min	SPL/IMS/PD/SOP/ME/071

Decision:- Keeping in view available manufacturing facility, Registration Board approved grant of additional packs as per following details.-

S. No.	Regn. No.	Name of Drug(s)/ Composition	Already Pack Size Granted	New Approved Additional Pack Size(s)
1.	049629	Supertone Solution	100ml 250ml 500ml 1000ml	2 Litre 5 Litre

Case No. 03:- Registration of Drugs under the Drugs Act, 1976.

Registration Board in its 308th meeting approved following imported veterinary drugs of M/s.Vety-Care (Pvt) Ltd., Rawalpindi as per decision mentioned alongside.

S. No.	Name of Importer/ Manufacturer	Name of Drug(s) & Composition	Approved Packs Size/ Shelf Life	Decision & Remarks
1.	M/s. Vety Care (Pvt) Ltd. 4-A, Block A Satelite Town Rawalpindi. / Manufacturer: M/s. Intervet GesmbH, Siemensstrasse 107, 1210, Vienna, Austria. Marketing Authorization Holder: M/s. Intervet International B.V., Wim de Korverstraat 35, 5831 An Boxmeer, the Netherlands.	Bravecto 1000mg Chewable Tablets for Dogs Each chewable table contains:- Fluralaner…..1000mg	1's 2's 4's 24 months	Approved with innovator's specifications as per import policy for inspection of Manufacturer abroad. The Board further decided that the panel should verify the authenticity of submitted stability data.
2.	-do-	Bravecto 112.5mg Chewable Tablets for Dogs Each chewable table contains:- Fluralaner…112.5mg	1's 2's 4's 24 months	Approved with innovator's specifications as per import policy for inspection of Manufacturer abroad. The Board further decided that the panel should verify the authenticity of submitted stability data.
3.	-do-	Bravecto 250mg Chewable Tablets for Dogs Each Chewable table contains:- Fluralaner…..250mg	1's 2's 4's 24 months	Approved with innovator's specifications as per import policy for inspection of Manufacturer abroad. The Board further decided that the panel should verify the authenticity of submitted stability data.

4.	-do-	Bravecto 500mg Chewable Tablets for Dogs Each chewable table contains:- Fluralaner……500mg	1's 2's 4's 24 months	Approved with innovator's specifications as per import policy for inspection of Manufacturer abroad. The Board further decided that the panel should verify the authenticity of submitted stability data.

Decision of Registration Board shows that panel should verify authenticity of submitted stability data, but subject products are EMA approved and exempted from inspection abroad. It is informed that products are being manufactured in Netherlands which is RRA, and thus inspection was not conducted. Accordingly registration letter issued to the firm.

Decision: Registration Board noted the information.

Case No. 04:- Request of M/s. Mallard Pharmaceuticals (Pvt) Ltd., Multan for Grant of Additional Packs for their already Registered Veterinary Drugs.

M/s. Mallard Pharmaceuticals (Pvt) Ltd., Multan has applied for grant of additional packs of their following registered veterinary drugs as per details mentioned against each:-

S. No.	Regn. No.	Name of Drug(s)/ Composition	Already Pack Size Granted	Demanded Additional Pack	Initial registration/ renewal status	Remarks/ Justification Diary No.
1.	078361	ARTD FOARD Liquid Each 100ml contains:- Doxycycline HCL BP……20g Tylosin Tartrate BP……10g Colistin Sulphate BP…40MIU Bromhexine BP…….....0.3g	100ml 250ml 500ml 1000ml	30ml	12th September, 2015 11-09-2019	Dy.No.16818-(R&I) DRAP dated 16-6-2021. Due to market need and demand. As we all know there is increase in prices of all medicinal products and now little farmers want to purchase smaller pack size as per dose required and not to purchase one kg or bigger pack sizes.
2.	087087	Alviflox Oral Liquid Each 100ml contains:- Enrofloxacine HCl…..…10g Colistin Sulphate…….50,000,000IU (As per Innovator's Specification*)	100ml 250ml 500ml 1000ml 2.5 Liter	30ml	05th January, 2018	-do-

3.	049728	Bacomall Oral Powder Each 100gm contains:- Tylosin Tartrate …..…. 10gm Doxycycline HCl…....20gm Bromhexine …….....10gm Colistin Sulphate …….3gm	100gm 250gm 500gm 1000gm 1500gm 2500gm 5000gm	10gm	14th October, 2008 02-10-2018	-do-
4.	058922	NEO.C.C Oral Powder Each Kg contains:- Neomycin Sulphate..…..70gm Colistin Sulphate…….....4gm Chlotetracycline HCL…80gm	100gm 250gm 500gm 1000gm	10gm	29th July, 2009 26-07-2019	-do-
5.	049566	Liso 10 Powder Each gm contains:- Lysozyme…….22% Vitamin E 50 SD…….0.5%	100gm 250gm 500gm 1000gm	10gm	07th August, 2008 17-07-2018	-do-

M/s. Mallard Pharmaceuticals (Pvt) Ltd., Multan has deposited the required fee of Rs.10,000 x 5 Rs.50,500/- and submitted following supporting documents:-

(i) Copies of initial registration letters/ renewal trail.
(ii) Details of previously granted pack size(s).
(iii) GMP inspection conducted by DRAP on 13-08-2020.
(iv) Justification.
(v) Undertaking that the provided information/documents are true/correct.

The demanded pack size(s) are not given to other firms.

Registration Board in its 312th meeting deferred the case for provision of requisite manufacturing facility/equipment of demand pack size.

Accordingly letter issued to the firm to provide manufacturing facility/equipment of demand pack size of below mentioned products at the earliest for further processing the case. In response the firm has provide details are as under:-

Powder Section (General) Equipment List

Sr. No.	Name	Quantity	Specification
1.	Sachet Filling Machine	01	Dose filling (5g-25g)
2.	Cone Mixer	01	500Kg
3.	Cone Mixer	01	300Kg
4.	Dose Filling Machine	**01**	
5.	Granulator Machine	**01**	
6.	Sealing Machine	**02**	
7.	Dehumidifier	**03**	
8.	Dust Collector	**01**	
9.	Hygrometer	**04**	
10.	Conveyer Belt	**01**	

Liquid Section Equipment List

Sr.No.	Name	Quantity	Specification
1.	Mixer Vessel with Silver Son	01	5,00 Litres
2.	Mixer Vessel with Slow Mixing	01	1,000 Litres
3.	Mixer Vessel with Silver Son	01	2,000 Litres
4.	Storage Tank	01	500 Litres
5.	Transfer Pump	01	
6.	Colloidal Mill	01	
7.	4 Nozzles Liquid Filling Machine	01	
8.	2 Nozzles Liquid Filling Machine	01	
9.	1 Nozzles Liquid Filling Machine (Small doses)	01	
10.	Conveyer Belt	01	
11.	Sealing Machine	02	
12.	Bottle Blowing Machine	01	

Decision:- Keeping in view available manufacturing facility, Registration Board approved grant of additional packs as per following details:-

S. No.	Regn. No.	Name of Drug(s)/ Composition	Already Pack Size Granted	New Approved Additional Pack Size(s)
1.	078361	ARTD FOARD Liquid	100ml 250ml 500ml 1000ml	30ml
2.	087087	Alviflox Oral Liquid	100ml 250ml 500ml 1000ml 2.5 Liter	30ml
3.	049728	Bacomall Oral Powder	100gm 250gm 500gm 1000gm 1500gm 2500gm 5000gm	10gm
4.	058922	NEO.C.C Oral Powder	100gm 250gm 500gm 1000gm	10gm
5.	049566	Liso 10 Powder	100gm 250gm 500gm 1000gm	10gm

Case No. 05:- Cancellation of Distribution Agreement of M/s. SS Associates, Lahore by their Principal Abroad (Turkey).

M/s. Medicavet, Turkey informed vide letter about termination of distribution agreement with M/s. SS Associates, S-77-R8/10 Ground Floor Back Side Nirala Sweet, Mozang Chungi Jail Road, Lahore ***w.e.f. 18-01-2019*** and further informed about appointment of *M/s. Unicare Enterprises, Faisalabad* (Head Office: M/s. Unicare Enterprises, Commercial -06, 1st Floor, Block-A, Kazimabad, Model Colony, Karachi, Pakistan-75100) (Regd. Office: Reg. Office: Plot No. 587/1-B, Street No.3, Punjab Small Industrial Estate, Nalka Kohala, Sargodha Road, Faisalabad) **Godown Address:**-Plot No. 587/B-2, Street No.03, Punjab Small Industrial Estate, Nalka Kohala, Sargodha Road, Faisalabad as their new distributor. M/s. Medicavet, Turkey also provided a copy of termination notice addressed to M/s. SS Associates, S-77-R8/10 Ground Floor Back Side Nirala Sweet, Mozang Chungi Jail Road, Lahore.Details of registration applications submitted by M/s. SS Associates, Lahore from the above mentioned principal is as follow:-

S. No	Name of Applicant/ Manufacturer	Name of Drugs/Composition / Meeting No.	Shelf Life and Pack Sizes	Remarks
1.	M/s. Unicare Enterprises, Plot No. 587/1-B, Street No.03, Punjab Small Industrial Estate, Nalka Kohala, Sargodha Road, Faisalabad. **Godown Address:-** Plot No. 587/B-2, Street No.03, Punjab Small Industrial Estate, Nalka Kohala, Sargodha Road, Faisalabad. **Manufacturer:-** M/s. Medicavet, Tarim Hayvancilik Ilac ve Kimya San. Ticaret Ltd. Sti. ITOSB Istanbul Tuzla Org. San. Bolg. Eski Ankara Asfalti 12. Cadde No: 1 Tepeoren Tuzla-Istanbul, Turkey.	Mediquinol 10% Oral Solution Each ml contains:- Enrofloxacin…...100mg **(M-277)**	2 years 100ml 1Litre 2.5 Litre Firm has claimed in house specification	Inspection of the manufacturer abroad has been carried by the nominated panel on 27th& 28th September, 2018 and recommended the facility.
2.	**-do-**	Medicol Oral Solution Each ml contains:- Colistin Sulfate…….4.800.000 IU (240mg) **(M-277)**	2 years 20ml 500ml 1Litre 5 Litre Firm has claimed in house	-do-

			specificatio n	
3.	**-do-**	Nemason Water Soluble Powder Each gm contains:- Levamisole Hydrochloride…150mg **(M-277)**	2 years 20g 100g 500g 1Kg 5Kg Firm has claimed in house specification	-do-
4.	**-do-**	Synercid Water Soluble Powder Each gm contains:- Amoxicillin (as Trihydrate)…720mg Colistin Sulphate…….180mg **(M-284)**	2 years 20gm 100gm 500gm 1Kg 5Kg Manufacturer Specifications	Panel for inspection of Penicillin Section of manufacturer has been constituted comprised of Mr. Abdullah and Mr. Ajmal Sohail Asif.

Keeping in view the termination of distribution agreement of M/s. SS Associates, Lahore by M/s. Medicavet, Turkey, Registration Board decided to issue show cause notice to M/s. SS Associates, S-77-R8/10 Ground Floor Back Side Nirala Sweet, Mozang Chungi Jail Road, Lahore as to why the approval for registration of veterinary products may not be cancelled because of termination of their distribution agreement.

Accordingly show cause notice issued to M/s. SS Associates, Lahore on 30th December, 2019 and letter is undelivered and again letter to the firm another company address but letter is again undelivered.

Registration Board in its 295th meeting decided to issue final reminder to M/s. SS Associates, Lahore. A copy of same will also be sent to concerned DRAP office for handing over to the firm.

Accordingly final reminder issued to M/s. SS Associates, Lahore to submit your reply within five days, failing to which it will be presumed that you have nothing to offer in your defense and ex-parte decision would be taken in Registration Board, but letter is undelivered.

Registration Board in its 296th meeting decided to issue final show cause notice to M/s. SS Associates, Lahore to submit reply within 15 days. DRAP Lahore will be advised to advise a copy of same will also be sent to concerned DRAP office for handing over to the firm.

Accordingly letter issued to M/s. SS Associates, Lahore on 18th November, 2020 to submit your reply within 15 days, failing to which it will be presumed that you have nothing to offer in your defense and ex-parte decision would be taken in Registration Board,

M/s. SS Associates, Lahore has submitted NOC DATED 2nd December 2020 to transfer of the following products in the name M/s. Unicare Enterprises, Faisalabad manufactured by M/s. Medicavet, Tarim HayvancilikIlacve Kimya San. Tic. Ltd. Sti. Itosb Eski Ankara Asfalti Uzeri 12. Cadde No: 1 34959 Tepeoren Tuzla Istanbul, Turkey.

M/s. Unicare Enterprises, Faisalabad has deposited the required fee of Rs.100,000 x 4 = Rs.400,000/- and submitted following supporting documents: -

(i) Original NOC submitted by M/s. SS Associates, Lahore dated 2nd December, 2020.

Remarks of Evaluator: M/s. Unicare Enterprises have not submitted complete applications on form 5A for registration in their name.

The case was again discussed in its 297th meeting and the Registration Board deferred the case for scrutiny and complete detail.

The firm has provided following documents. The details are as under:-

(i) Application on Form-5A
(ii) Original free sales certificates and certificate of origin for veterinary products of above mentioned products.
(iii) Photocopy of GMP certificate.
(iv) Copy of distribution agreement.
(v) Copy Drug Sale License valid upto 10-04-2027.
(vi) Side master files of above mentioned products.
(vii) Undertaking.

Decision:- Registration Board approved the above mentioned products as per policy for inspection of manufacturer abroad and verification of local storage facility. Details are as under:-

S. No.	Name of Applicant/ Manufacturer	Name of Drugs/Composition / Meeting No.	Pack Size(s)/ Shelf Life	Finished Product Specifications
1.	M/s. Unicare Enterprises, Plot No. 587/1-B, Street No.03, Punjab Small Industrial Estate, Nalka Kohala, Sargodha Road, Faisalabad. **Godown Address:-** Plot No. 587/B-2, Street No.03, Punjab Small Industrial Estate, Nalka Kohala, Sargodha Road, Faisalabad. **Manufacturer:-** M/s. Medicavet, Tarim Hayvancilik Ilac ve Kimya San. Ticaret Ltd. Sti. ITOSB Istanbul Tuzla Org. San. Bolg. Eski Ankara Asfalti 12. Cadde No: 1 Tepeoren Tuzla-Istanbul, Turkey.	Mediquinol 10% Oral Solution Each ml contains:- Enrofloxacin……...100mg	2 years 100ml 1Litre 2.5 Litre	Firm has claimed in house specification
2.	**-do-**	Medicol Oral Solution Each ml contains:- Colistin Sulfate…4.800.000IU (240mg)	2 years 20ml 500ml 1Litre 5 Litre	Firm has claimed in house specification
3.	**-do-**	Nemason Water Soluble Powder Each gm contains:- Levamisole Hydrochloride…….150mg	2 years 20g 100g 500g 1Kg 5Kg	Firm has claimed in house specification

4.	**-do-**	Synercid Water Soluble Powder Each gm contains:- Amoxicillin (as Trihydrate)…….720mg Colistin Sulphate……..180mg	2 years 20gm 100gm 500gm 1Kg 5Kg	Manufacturer Specifications

Case No. 06:- Registration of Drugs under the Drugs Act, 1976.

Following non-drug diluents are registered in different meeting of Registration Board and processed.

S. No.	Reg. No.	Manufacturer	Name of Drug(s) & Composition.
1.	111532	M/s. ISIS Pharmaceuticals & Chemical Works, 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi.	ISIS Diluent (for eye drops vaccines) Each ml contains:- Monobasic Potassium Phosphate……0.37mg Disodium Phosphate Dihydrate……0.72mg Sodium Chloride……7.65mg (As per Innovator's Specification)*
2.	112108	M/s. Intervac (Pvt) Ltd., 18 Km Lahore Sheikhupura Road, Sheikhupura.	DILUENT VAC Each ml contains:- Monobasic Potassium Phosphate…….....0.37mg Disodium Phosphate Dihydrate…….....0.72mg Sodium Chloride……..7.65 mg Disodium Edetate Dihydrate…….…….0.50mg (As per Innovator's Specification)*

Registration Board approved API of drug products only.

Decision:- The Registration Board deferred the case for further deliberation.

Case.No.07:- Request of M/s. Bio-Labs (Pvt) Ltd., Plot No.145, Industrial Triangle, Kahuta Road, Islamabad Registration of Drugs.

M/s. Bio-Labs (Pvt) Ltd., Plot No.145, Industrial Triangle, Kahuta Road, Islamabad has requested for registration of following veterinary products for local manufacture in their name and cancellation of same from the name of M/s. Breeze Pharma (Pvt.) Ltd., Islamabad.

S. No.	Reg. No.	Name of Drug(s)/ Composition	Already Approved Pack Size(s)	Initial Date of Registration
1.	063788	Lincamox-S Water Soluble Powder Each gm contains:- Amoxicillin Trihydrate…….200mg Lincomycin base…….....88mg Spectinomycin base…….....88mg	100gm 500gm 1 Kg	27-10-2010 (i)Initial registration letter incomplete. (ii) Last renewal not provided.

		Vitamin E Acetate……..30mg		
2.	059176	Strepcin Injection Each ml contains:- Procain Penicillin G…...200mg Streptomycin Sulfate….250mg	10ml 20ml 50ml 100ml	18-08-2009 31-07-2019
3.	059150	Alincospectin Water Soluble Powder Each gm contains: - Amoxicillin Trihydrate…..200mg Lincomycin base……..88mg Spectinomycin base…….88mg	100gm 250gm 500gm 1Kg 5Kg 25Kg	01-08-2009 (i)Initial registration letter incomplete. 30-07-2019
4.	059117	ZPS-100 Powder Each Kg contains:- Procaine Penicillin……12gm Streptomycin Sulphate…..36gm Zinc Bacitracin……..52gm	100gm 250gm 500gm 1Kg 5Kg 25Kg	01-08-2009 (i)Initial registration letter incomplete. 30-07-2019
5.	059135	Amoxicure LA Injection Each ml contains:- Amoxicillin Trihydrate is eq to Amoxicillin base……..150mg	50ml 100ml	01-08-2009 (i)Initial registration letter incomplete. 30-07-2019
6.	059181	Comox Water Soluble Powder Each Kg contains:- Amoxycillin Trihydrate….150gm Colistin Sulphate…….500MIU	100gm 250gm 500gm 1Kg 5Kg 25Kg	18-08-2009 (i)Initial registration letter incomplete. 30-07-2019
7.	059162	Provet 40 Lac Dry Injection Each dry vial contains: - Procaine Penicillin…40,00,000IU	30ml	01-08-2009 (i)Initial registration letter incomplete. 31-07-2019

M/s. Bio-Labs (Pvt) Ltd., Plot No.145, Industrial Triangle, Kahuta Road, Islamabad has deposited the required fee Rs.20,000 x 7 = Rs.140,000/- and submitted following supporting documents:-

(i) Original NOC **dated 15-01-2021** from M/s. Breeze Pharma (Pvt.) Ltd., Islamabad.
(ii) Copy of initial registration letters and renewal status.
(iii) Copy of Drug Manufacturing License.
(iv) Variation for change of brand name Colimox Water Soluble Powder to Comox Water Soluble Powder
(v) GMP panel inspection report conducted on 18th & 23rd April, 2019 DML No.000296 (Formulation).
(vi) Copy of approved sections.
(vii) Applications on Form 5.
(viii) Undertaking.

- NOC issued by M/s. Breeze Pharma (Pvt) Ltd., Islamabad on 15-01-2021 to M/s. Bio-Labs (Pvt) Ltd., Islamabad.
- The firm M/s. Bio-Labs (Pvt) Ltd., Islamabad deposit fee of above mentioned drugs on 19th April, 2021.
- The applications submitted by M/s. Bio-Labs (Pvt) Ltd., in R&I-DRAP on 28th April, 2021.
- The Drug Manufacturing License cancelled of M/s. Breeze Pharma (Pvt) Ltd., Islamabad on 26th -27th April, 2021.

Legal Division opinion: the Legal Division has informed that as per available facts/record of the case, M/s. Breeze Pharma, Islamabad issued various NOC's to different firms for transfer of registration of products from its name to other manufacturer. Central Licensing Board cancelled the Drug Manufacturing License of the said firm in its 280th meeting held on 26th & 27th April, 2021. Hence, this Division is opined that those from who got NOC's from M/s. Breeze Pharma, Islamabad and applied well within time for transfer of registration to PE&R Division before cancellation of Drug Manufacturing License, their cases for transfer of registration may be processed by the Division in accordance with law.

Decision:- Registration Board did not exceed request of the firm M/s. Bio-Labs (Pvt) Ltd., Islamabad as firm submitted application dated 28th April 2021 after the cancellation of M/s Breeze pharma DML.

Case No.08: Request of M/s. Aptly Pharmaceuticals, Faisalabad for change of composition of veterinary drug(s).

Registration Board in its 285th meeting approved following veterinary drugs in favor of M/s. Aptly Pharmaceuticals, Faisalabad. Registration letter has already been issued to the firm. The firm has requested to change the compositions are as under:-

S. No.	Regn.No.	Name of Manufacturer	Name of Drug(s) / Composition Granted	Composition Requested by the Firm	Approved Packs Size	Remarks
I		II	III	IV	V	VI
1.	093869	M/s. Aptly Pharmaceuticals, 5-Km Sargodha-Sidhar Bypass Road, Faisalabad.	Closul-5 Oral Powder **Each Kg contains:-** Colistin Sulphate…5,000,000 IU (As per Innovator's Specification)*	Closul-5 Oral Powder **Each gm contains:-** Colistin Sulphate…5,000,000 IU	500g 1Kg 2.5Kg 5Kg in plastic jar	Dy.No.18373-R&I DRAP dated 23-06-2022

M/s. Aptly Pharmaceuticals, Faisalabad has deposited fee of Rs.20,000/- for the said purpose along with form-5 and requested to change the compositions. Furthermore, the requested composition has already been granted registration to various firms.

The case was discussed in its 295th meeting of Registration Board advised to get justification for reason for change of composition and its approval status accordingly.

Accordingly letter issued to the firm to get justification for reason for change of composition. In response the firm has inform that mathematically it is impossible that 1kg of powder could contain 263.1mg of active of active which is too much low for its therapeutic effect. Required composition detail is as follows which a "me-too products".

S.No.	Registration No.	Product Name	Composition Registered	Manufacturer

1.	049616	Colisel-50 Powder	Each gm contains:- Colistin Sulphate…5,000,000 IU	M/s. Selmore Pharmaceuticals (Pvt) Ltd. Lahore.

International units' converter

5,000,000 IU = 263.1mg per gran which is effective.

Decision:- Registration Board did not exceed request of the firm M/s. Aptly Pharmaceuticals, Faisalabad, as the same formulation is already registered in the name of various firms including M/s. Nawan Laboratories (Pvt) Ltd., Karachi vide Regn.No. 035059.

Case No.09:- Request of M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura for change of composition of already registered veterinary drugs.

M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura has requested for change of composition of their registered products. Details are as under:-

S. No.	Regn.No.	Product Granted Composition	Previous Demanded Composition	Remarks/ Diary No. R&I
I	**II**	**III**	**IV**	**VI**
1.	063652	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide……0.06gm Oxfendazole……0.0226gm**	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…..…60gm Oxfendazole…..…22.6gm**	Dy. No. 21308-R&I DRAP dated 28-07-2022
2.	063649	Avi-Dex Liquid Each 1000ml contains:- **Triclobendazole……..0.05gm Levamisole HCl……0.015gm**	Avi-Dex Liquid Each 1000ml contains:- **Triclabendazole……..50gm Levamisole HCl…..…15gm**	-do-
3.	063654	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....0.025gm Sodium Selenite…...0.0015gm Cobalt Sulphate….0.00382gm**	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....25gm Sodium Selenite..….1.5gm Cobalt Sulphate…..3.82gm**	-do-

M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura deposited **fee of Rs.5000 x 3 = Rs.15000/- and again deposited fee of Rs.25000 x 3 = Rs.75000/-** and submitted following supporting documents:-

(i) Copies of registration letters.
(ii) Renewal trails.
(iii) Copy of Drug Manufacturing License.
(iv) GMP panel inspection report conducted by panel of inspector on 22nd October, 2018.
(v) Comparison of me-too.
(vi) Undertaking.

The firm has informed that giving the approval for registration mistakenly registered some of the drugs other them our requirement may be it was due to clerical mistake on the part of DRAP.

The case was discussed in its 313th meeting of Registration Board deferred for confirmation of already approved generic drugs and details of renewal.

The firm has provided details of already approved generic drugs are as under:-

S. No.	Regn.No.	Product Granted Composition	New Demanded Composition
1.	063652	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…….….0.06gm** **Oxfendazole……0.0226gm**	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…..…..62.50gm** **Oxfendazole…..……22.65gm**
2.	063649	Avi-Dex Liquid Each 1000ml contains:- **Triclobendazole……..0.05gm** **Levamisole HCl……0.015gm**	Avi-Dex Liquid Each 1000ml contains:- **Triclabendazole……....50gm** **Levamisole HCl…...…37.50gm**
3.	063654	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....0.025gm** **Sodium Selenite…...0.0015gm** **Cobalt Sulphate….0.00382gm**	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....25gm** **Sodium Selenite..….0.35gm** **Cobalt Sulphate…...0.75gm**

The above mentioned products already registered in various firms M/s. Mediexcel Pharmaceuticals, Islamabad, M/s. Star Laboratories (Pvt) Ltd., Lahore and M/s. Mylab (Pvt) Ltd., Bahawalpur vide Registration No.031412,031454 & 073903 respectively.

Decision:- Registration Board considered and approved the standardization of composition of already registered drugs of M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura. The details are as under: -

S. No.	Regn.No.	Existing Name of Drug & Composition	New Approved Name of Drug & Composition
1.	063652	Boxer Liquid Each 1000ml contains:- **Oxyclozanide…….….0.06gm** **Oxfendazole……0.0226gm**	Boxer Liquid Each 1000ml contains:- **Oxyclozanide…….…..62.50gm** **Oxfendazole…..…22.65gm**
2.	063649	Avi-Dex Liquid Each 1000ml contains:- **Triclobendazole……..0.05gm** **Levamisole HCl……0.015gm**	Avi-Dex Liquid Each 1000ml contains:- **Triclabendazole……....50gm** **Levamisole HCl….37.50gm**
3.	063654	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....0.025gm** **Sodium Selenite…...0.0015gm** **Cobalt Sulphate….0.00382gm**	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....25gm** **Sodium Selenite..….0.35gm** **Cobalt Sulphate…...0.75gm**

MIMUTES OF 11H MEETING OF EXPERT WORKING GROUP ON VETERINARY DRUGS SCHEDULED ON 12TH AUGUST, 2022.

Case No. 01: Deferred cases of (M-316)

1.	Name and address of manufacturer / Applicant	M/s. Mylab Pvt Ltd. Khankah Sharif Bahawalpur.
	Brand Name +Dosage Form + Strength	Aspire-C Water Soluble Powder
	Composition	Each gm contains:- Acetylsalicylic Acid…...….67mg Vitamin C……200mg
	Diary No. Date of R& I & fee	Dy No. 23783: 12-12-2017 PKR 20,000/-: 08-12-2017
	Pharmacological Group	Analgesic and vitamin
	Type of Form	Form-5
	Finished product Specifications	In house specification
	Pack size & Demanded Price	500g, 1000g, 5000g
	Approval status of product in Reference Regulatory Authorities	NA
	Me-too status (with strength and dosage form)	Gesix-C (**Reg.# 043286**) Water Soluble Powder by Prix Pharma
	GMP status	Last GMP inspection conducted on 13-09-2018 and 14-09-2018 recommending the renewal of DML.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case to Expert Working Group on Veterinary Drugs.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Salicylic Acid with Vit C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
2.	Name and address of manufacturer / Applicant	M/s. Decent Pharma Plot No. 30, Street SS 3, National Industrial Zone, Rawat.
	Brand Name +Dosage Form + Strength	Vital-C Oral Powder
	Composition	Each 100g contains:- Vitamin C……...…..20g Acetyl Salicylic……...…20g Vitamin K3……..…2.5g
	Diary No. Date of R& I & fee	14-11-2016, Dy. No.2185, Rs.20,000/-, 10-11-2016
	Pharmacological Group	Analgesic and antipyretic (NSAIDs)
	Type of Form	Form-5
	Finished product Specifications	In house specification
	Pack size & Demanded Price	100g, 500g, 1Kg, 2.5Kg, 5Kg, 10Kg,20Kg, 25Kg; Decontrolled
	Approval status of product in Reference Regulatory Authorities	NA
	Me-too status (with strength and dosage form)	C-Plus Powder of M/s. Intervac Pharma (Reg#046598)

	GMP status	QA Division vide letter No.F.8-6/2018-QA dated 18th September, 2018 concluded that the firm M/s. Decent Pharma, Rawat is allowed to resume production in oral dosage forms. However, production in sterile area shall remain suspended till the installation of distillation assembly, verification by the panel of experts and subsequent approval for resumption of production.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case to Expert Working Group on Veterinary Drugs.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Salicylic Acid with Vit C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
3.	Name and address of manufacturer / Applicant	M/s. Ras Pharmaceuticals Pvt Ltd, 25km, Lahore Road, Multan.
	Brand Name +Dosage Form + Strength	RZL-150 Fee Premix Powder
	Composition	Each Kg contains:- Zinc Bacitracin……..100gm Lincomycin (Lincomycin as HCl)…....50gm
	Diary No. Date of R& I & fee	Dy. No. 57; 29-4-2016; Rs.20,000/- (29-4-2016)
	Pharmacological Group	Anti-bacterial
	Type of Form	Form-5
	Finished product Specifications	In-house
	Pack size & Demanded Price	100gm, 500gm, 1Kg, 2.5Kg, 5Kg, 25Kg, Decontrolled
	Approval status of product in Reference Regulatory Authorities	
	Me-too status (with strength and dosage form)	ZL-150 by Intervac Reg # 069663
	GMP status	16-10-2018 Firm was operating at the fair level of GMP Compliance.
	Remarks of the Evaluator	Fee challan Photocopy attached.
	Previous Decision	Registration Board referred the applied formulation to Expert Working Group on Veterinary Drugs for review.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. Decision of EWGVD: The EWGVD deliberated the cases and decided to recommend the product for the registration. **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
4.	Name and address of manufacturer / Applicant	M/s. Farm Aid Group, Plot # 3/2, Phase I & II, Hattar Industrial Estate, Haripur.

	Brand Name +Dosage Form + Strength	Para-20 Powder
	Composition	Each 100gm contains:- Paracetamol……..…….20.0gm Vitamin C…….5.0gm Potassium Carbonate…….…....12.5gm Sodium Bicarbonate……..…...12.5gm Vitamin E…….……..…...12.5gm
	Diary No. Date of R& I & fee	Dy.No. 23816 dated 10-07-2018 Rs.20,000/- 06-07-2018
	Pharmacological Group	Antioxodant, analgesic, antipyretic
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	1gm, 200gm, 30gm, 50gm, 100gm, 250gm, 500gm, 1Kg,5Kg, 10Kg, 15Kg, 20Kg, 25Kg ; Decontrolled
	Me-too status (with strength and dosage form)	Para Ce Oral Powder. Of Biogen Pharma
	GMP status	Last GMP inspection conducted on 16-03-2017 and report concludes that firm was considered to be operating at good level of GMP Compliance."
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the applied formulation to Expert Working Group on Veterinary Drugs for review.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of paracetamol with Vit C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
5.	Name and address of manufacturer / Applicant	M/s. Ras Pharmaceuticals (Pvt.) Ltd. 25, Km Lahore Road Multan.
	Brand Name +Dosage Form + Strength	CINA-ES Oral Liquid
	Composition	Each ml contains:- Enrofloxacin……..……75mg Sulphamethoxypyridazine……..……...50mg Sulphamethazine……50mg Trimethoprim……..…...25mg
	Diary No. Date of R& I & fee	Dy. No. 23021 dated 03-07-2018 Rs. 20,000/-Dated 03-07-18
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	100ml, 250ml, 500ml, 1 Liter, 5Liter, 10 Liter, 25 Liter & Decontrolled

	Me-too status	Sulphacina Oral Liquid of M/s Bio-Oxime Pharmaceuticals
	GMP status	Date of Inspection: 16-10-2018. The firm is a small manufacturing unit (veterinary) and was operating at the fair level of GMP compliance. However, it is advised to overcome the shortcomings and submit the compliance accordingly.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case regarding the composition to the expert working group on veterinary drugs.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
6.	Name and address of manufacturer / Applicant	M/s. Ras Pharmaceuticals (Pvt.) Ltd. 25, Km Lahore Road Multan.
	Brand Name +Dosage Form + Strength	Paralyte-C Oral Powder
	Composition	Each 100gm contains:- Paracetamol…….....2gm Vitamin C (Ascorbic Acid)……..…....20gm Calcium Carbonate……..4.5gm Magnesium Sulphate……..…..3.5gm Potassium chloride…….….4gm
	Diary No. Date of R& I & fee	Dy. No. 23026 dated 03-07-2018 Rs. 20,000/-Dated 03-07-18
	Pharmacological Group	NSAID+ Vitamin+ electrolyte
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	50gm, 100gm, 250gm, 500gm, 1Kg, 2.5Kg, 5Kg 10Kg, 25Kg & Decontrolled
	Me-too status	Spin-C Powder of M/s Leads Pharma (Pvt) Ltd.
	GMP status	Date of Inspection: 16-10-2018. The firm is a small manufacturing unit (veterinary) and was operating at the fair level of GMP compliance. However, it is advised to overcome the shortcomings and submit the compliance accordingly.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case regarding the composition to the expert working group on veterinary drugs.

	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of paracetamol with Vit C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
7.	Name and address of manufacturer / Applicant	M/s. Mylab Pvt. Ltd. Khankah Shariff Bahawalpur.
	Brand Name +Dosage Form + Strength	Duralin Complex Injection
	Composition	Each ml contains:- Oxytetracycline Hydrochloride……..……10mg Dexamethasone as Sodium Phosphate…….0.5mg
	Diary No. Date of R& I & fee	Dy. No 13038, dated 06-04-2018, Rs.20,000/- Dated 27-02-2018
	Pharmacological Group	Anti-Inflammatory-Antibiotic combination
	Type of Form	Form-5
	Finished product Specifications	Manufacturer‘s specifications
	Pack size & Demanded Price	10 ml Clear Glass vial 20 ml Clear Glass vial 30 ml Clear Glass vial 40 ml Clear Glass vial 50 ml Clear Glass vial Decontrolled.
	Me-too status	OXY COMPLEX INJECTION 150MG
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case regarding the composition to the expert working group on veterinary drugs.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of oxytetracycline with Dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
8.	Name and address of manufacturer / Applicant	M/s. Aamster Laboratories, Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	FEBROL-C Oral Water Soluble Powder
	Composition	Each 100g contains:-

		Vitamin C ……..…20g Paracetamol……..…2g Potassium Chloride ……..…..4g Calcium Carbonate ……..45g Magnesium Sulphate …… 3.5g
	Diary No. Date of R& I & fee	Dy. 19059, 30-09-2019, Rs.20,000/- dated 27-09-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100gm,250gm,500gm,1Kg,5Kg,10Kg,25Kg / Decontrolled
	Me-too status	Paravit-C (D-Maarson Pharma) 074081
	GMP status	CLB in its 271st meeting held on 12th September 2019 approved the grant of Drug Manufacturing License (Formulation) with following section: Oral Powder Section-I (Veterinary)
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case regarding the composition to the expert working group on veterinary drugs.
	Decision:- Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of paracetamol with Vit C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
9.	Name and address of manufacturer / Applicant	M/s. Farm Aid Group, Plot # 3/2, Phase I & II, Hattar Industrial Estate, Haripur.
	Brand Name +Dosage Form + Strength	Asper Fam Powder
	Composition	Each Kg contains:- Acetylsalicylic Acid……...67gm Ascorbic Acid……...200gm Citric Acid……....125gm Sodium Bicarbonate…….250gm
	Diary No. Date of R& I & fee	Dy. No 16297 Dated 03-05-2018, Rs. 20,000/-
	Pharmacological Group	Antipyretic, analgesic
	Type of Form	Form-5
	Finished product Specifications	In-house
	Pack size & Demanded Price	10gm, 20gm, 30gm, 50gm, 100gm, 250gm, 500gm, 1Kg, 5Kg, 10Kg, 15Kg, 20Kg, 25Kg; Decontrolled
	Me-too status	S.B. Asper-C effervescent granules of m/s S.B.Pharma Islamabad
	GMP status	Last GMP inspection conducted on 16-03-2017 and report concludes that firm was considered to be operating at good level of GMP Compliance.

	Remarks of the Evaluator	
	Previous Decision	Registration Board deferred as formulation is under review of expert working group on veterinary drugs (M-293).
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of acetylsalicylic Acid with ascorbic acid and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
10.	Name and address of manufacturer / Applicant	M/s. Aamster Laboratories, Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	BRONCO FAST Oral Water Soluble Powder
	Composition	Each 1000g contains:- Doxycycline HCl ……..…..…200g Tylosin Tartrate ……..…100g Colistin Sulphate ……..……450MIU Bromhexine HCl……..……..5g Streptomycin Sulphate ……...36g
	Diary No. Date of R& I & fee	Dy. 19086, 30-09-2019, Rs.20,000/- dated 27-09-2019
	Pharmacological Group	Antibiotic, Mucolytic, Expectorant
	Type of Form	Form-5
	Finished product Specifications	In-house
	Pack size & Demanded Price	100gm,250gm,500gm,1Kg,5Kg,10Kg,25Kg/ decontrolled
	Me-too status	Pulmodox-S (Attabak Pharma) 071069
	GMP status	First Inspection for grant of license conducted on 05/09/2019, Panel unanimously approved for the grant of License.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case regarding the composition to the expert working group on veterinary drugs (M-293).
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
11.	Name and address of manufacturer / Applicant	M/s. Aamster Laboratories, Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Bronco Plus Oral Water Soluble Powder

	Composition	Each 1000g contains:- Doxycycline HCl …… 20% Tylosin Tartrate ……10% Colistin Sulphate ……450MIU Bromhexine HCl……0.5% Streptomycin Sulphate ……..3.5%
	Diary No. Date of R& I & fee	Dy. 19086, 30-09-2019, Rs.20,000/- dated 27-09-2019
	Pharmacological Group	Antibiotic, Mucolytic, Expectorant
	Type of Form	Form-5
	Finished product Specifications	In-house
	Pack size & Demanded Price	100gm,250gm,500gm,1Kg,5Kg,10Kg,25Kg/ decontrolled
	Me-too status	Becto-5 (Noble Pharma) 075609
	GMP status	First Inspection for grant of license conducted on 05/09/2019, Panel unanimously approved for the grant of License.
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case regarding the composition to the expert working group on veterinary drugs (M-293).
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
12.	Name and address of manufacturer / Applicant	M/s. Alina combine Pharmaceuticals (Pvt.) Ltd, A-127, S.I.T.E., Super Highway, Karachi.
	Brand Name +Dosage Form + Strength	Aceto-Vit Water Soluble Powder
	Composition	Each 100gm contains:- Acetylsalicylic acid……6.7gm Vitamin C……20gm
	Diary No. Date of R& I & fee	Dy. No.27; 7-7-2015; Rs.20,000/- (6-7-2015)
	Pharmacological Group	Analgesic, Vitamin
	Type of Form	Form-5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 500gm, 5Kg
	Me-too status	Aspersym-C Water Soluble Powder (Reg # 079109)
	GMP status	Last inspection report 15-12-2016 The management is putting all efforts to bring a team of qualified staff together and putting resource together for continuous improvement of their system.
	Remarks of the Evaluator	
	Previous Decision:	Deferred for following: (M-277)

		Registration Board referred the case to QA & LT Division to conduct GMP inspection of Firm on priority. Registration Board directed the firm to submit clarification/justification regarding compatibility of Vitamin C with Acetyl salicylic acid. Registration Board referred the case to expert working group on veterinary drugs for review of formulation (M-293).
	Evaluation by PEC	Panel inspection conducted on 03-10-2019 recommends renewal of DML No. 000441. The firm has submitted stability summary sheets of 6 months accelerated and 36 months real time stability study data of applied product.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of acetylsalicylic Acid with vit. C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
13.	Name and address of manufacturer / Applicant	M/s. A & K Pharmaceutical, 94-A, Punjab Small Industrial Estate, Sargodha Road, Faisalabad
	Brand Name +Dosage Form + Strength	Acevit C Plus Powder
	Composition	Each Kg contains:- Aspirin…….....67.0gm Vitamin C…….……200.0gm Potassium Chloride……...3gm Sodium Citrate…….…….....7gm
	Diary No. Date of R& I & fee	Dy. No.376; 08-10-2015; Rs.20,000/- (08-10-2015)
	Pharmacological Group	NSAID/Vitamin/Electrolyte
	Type of Form	Form-5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 500gm, 1Kg, 2.5Kg & 5Kg ; Decontrolled
	Me-too status	Asper-Cool Water Soluble Powder Of Attabak Pharma
	GMP status	Last GMP inspection report
	Remarks of the Evaluator	
	Previous Decision:	Deferred for following: (M-279) Evidence of approval of approval of required manufacturing facility from Licensing Division Submission of latest GMP inspection report conducted within a period of last 1 year by DRAP. Details of Primary Packaging Material for the applied formulation. Registration Board referred the case to expert working group on veterinary drugs for review of formulation **(M-293)**.
	Evaluation by PEC	Panel inspection conducted on 03-10-2019 recommends renewal of DML No. 000441.

		The firm has submitted stability summary sheets of 6 months accelerated and 36 months real time stability study data of applied product.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of aspirin with vit. C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
14.	Name and address of manufacturer / Applicant	M/s. A & K Pharmaceutical, 94-A, Punjab Small Industrial Estate, Sargodha Road, Faisalabad
	Brand Name +Dosage Form + Strength	Pyradin Injection
	Composition	Each ml contains:- Diminazine Aceturate……...105mg Antipyrine…….…….131mg
	Diary No. Date of R& I & fee	366,08-10-2015, 20,000/-, 08-09-2015
	Pharmacological Group	Anti-tripanosoma
	Type of Form	Form-5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	10ml, 20ml, 50ml, & 100ml; Decontrolled
	Me-too status	Pronil Injection of Selmore Pharma
	GMP status	Last GMP inspection report
	Remarks of the Evaluator	
	Previous Decision:	Deferred for following: (M-279) Evidence of approval of approval of required manufacturing facility from Licensing Division Submission of latest GMP inspection report conducted within a period of last 1 year by DRAP. Details of Primary Packaging Material for the applied formulation. Registration Board referred the case to expert working group on veterinary drugs for review of formulation **(M-293)**.
	Evaluation by PEC	The firm has provided Liquid Injection (vial) section. Copy of Panel inspection dated 09-11-2018 recommends renewal of DML except in oral powder penicillin section.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of antipyrine combinations with their dosage form at length and decided to obtain scientific rationale of combination, pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species, Difference between chemical structure of antipyrine, metamizole and novaminsulfone and Confirmation of causing of "agranulocytosis" by antipyrine in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

15.	Name and address of manufacturer / Applicant	M/s. Mediexcel Pharmaceuticals Islamabad, Plot # 282 Industrial Triangle, Kahuta Road Humak, Islamabad.
	Brand Name +Dosage Form + Strength	Panidex Liquid Injection
	Composition	Each ml contains:- Benzyl Penicillin Procaine…..……125,000IU Benzathine Penicillin G……..…..125,000IU Dihydrostreptomycin Sulphate……0.25gm Dexamethasone Sodium Phosphate…….0.20mg Dexamethasone-21-Isonicotinate……0.20mg
	Diary No. Date of R& I & fee	Dy. No 32426 dated 31-01-2020 Rs. 20,000/- 18-12-2019
	Pharmacological Group	Antibacterial/Steroid
	Type of Form	Form-5
	Finished product Specification	Mfg specifications
	Pack size & Demanded Price	50ml/ Decontrolled
	Me-too status	BDEX Liquid Injection of M/s. Selmore Pharmaceuticals Pvt Ltd, (Reg.# 080952)
	GMP status	GMP certificate issued on the basis of inspection conducted on 08/10/2019.
	Remarks of the Evaluator	
	Previous Decision:	Registration Board referred the case to expert working group on veterinary drugs for review of formulation (M-293).
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
16.	Name and address of manufacturer / Applicant	M/s. D-Haans Pharmaceuticals, Plot No. 9/A, Industrial Estate, Bhimber.
	Brand Name +Dosage Form + Strength	Bem-Cool Water Soluble Powder
	Composition	Each 100g contains:- Vitamin C…….20g Aspirin…….6.7g
	Diary No. Date of R& I & fee	Dy.No 2066 dated 20-02-2020 Rs.20,000/- (20-02-2020)
	Pharmacological Group	Anti-oxidant, Analgesic, Antipyretic
	Type of Form	Form-5
	Finished product Specification	In-house
	Pack size & Demanded Price	100g, 250g, 500g,1Kg,5Kg,10Kg ; Decontrolled
	Me-too status	049778; Bursa Gold Water Soluble Powder
	GMP status	CLB in its 273rd meeting held on 15th Jan, 2020 considered the case of M/s D-Haans Pharmaceuticals, Plot No. 9/A, Industrial Estate,

		Bhimber Pakistan and approved the grant of DML by way of formulation with following four sections.
	Remarks of the Evaluator	
	Previous Decision:	Registration Board referred the case to expert working group on veterinary drugs for review of formulation.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of aspirin with vit. C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
17.	Name and address of manufacturer / Applicant	M/s. D-Haans Pharmaceuticals, Plot No. 9/A, Industrial Estate, Bhimber.
	Brand Name +Dosage Form + Strength	Broncho-EZ Water Soluble Powder
	Composition	Each gm contains:- Doxycycline HCl……200mg Tylosin Tartrate……100mg Colistin Sulphate…..…....0.5MIU Bromhexine HCI……..……..5mg Streptomycin Sulphate..…..20mg
	Diary No. Date of R& I & fee	Dy.No 2062 dated 20-02-2020 Rs.20,000/- (20-02-2020)
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specification	In-house
	Pack size & Demanded Price	100g, 250g, 500g,1Kg,5Kg,10Kg ; Decontrolled
	Me-too status	078296; Riz Wan-S Water Soluble Powder
	GMP status	CLB in its 273rd meeting held on 15th Jan, 2020 considered the case of M/s D-Haans Pharmaceuticals, Plot No. 9/A, Industrial Estate, Bhimber Pakistan and approved the grant of DML by way of formulation with following four sections.
	Remarks of the Evaluator	
	Previous Decision:	Registration Board referred the case to expert working group on veterinary drugs for review of formulation.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

18.	Name and address of manufacturer / Applicant	M/s Farm Aid Group, Plot # 3/2, Phase I & II, Hattar Industrial Estate, Haripur.
	Brand Name +Dosage Form + Strength	Aspo C Powder
	Composition	Each Kg contains:- Acetylsalicylic Acid……..67gm Ascorbic Acid……..200gm
	Diary No. Date of R& I & fee	Dy.No 44455 dated 31-12-2018 Rs.20,000/-,27-12-2018
	Pharmacological Group	Antioxidant, Analgesic, Antipyretic
	Type of Form	Form-5
	Finished product Specification	In-house
	Pack size & Demanded Price	10gm, 20gm, 30gm, 50gm, 100gm, 250gm, 500g, 1Kg, 5Kg, 10Kg: Decontrolled
	Me-too status	Acetyle-C 20 Oral Powder Of M/S Kohinoor Industries
	GMP status	Last GMP inspection conducted on 03-10-2018 report concludes that firm was considered to be maintaining satisfactory level of the cGMP
	Remarks of the Evaluator	
	Previous Decision:	Registration Board referred the case to Expert Working Group on Veterinary Drugs.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Acetylsalicylic Acid with Ascorbic Acid and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
19.	Name and address of manufacturer / Applicant	M/s. Grand Pharma Pvt Ltd Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi.
	Brand Name +Dosage Form + Strength	ZipcoStrep Powder
	Composition	Each Kg contains:- Zinc Bacitracin…….……....52gm Procaine Penicillin……..……..…...12gm Streptomycin Sulphate….……...…36gm Colistin Sulphate….…….……..60MIU
	Diary No. Date of R& I & fee	Dy.No 21184 dated 18/10/2019; Rs.20,000/-18/10/2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 250gm, 500g, 1Kg, 5Kg, 10Kg, 25Kg; Decontrolled
	Me-too status	Zeptocol Powder of M/s Selmore Pharma (Reg. #080962)

	GMP status	New Section of Veterinary Oral Powder Penicillin was approved on 12th September, 2019 by CLB.
	Remarks of the Evaluator	The firm has claimed for manufacturer's specifications but the product is present in USP as oral suspension. Firm has replied that the ratio between Amoxicillin and Clavulanic acid is 5:1 which is being marketed internationally and in local market.
	Previous Decision:	Deferred in 293rd DRB meeting for review of formulation. Registration Board referred the case regarding the composition/strength to the expert working group on veterinary drugs (M-295).
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

20.	Name and address of manufacturer / Applicant	Mallard Pharmaceuticals (Pvt) Ltd., 23-Km Lahore Road, Multan, Pakistan
	Brand Name +Dosage Form + Strength	Vetizine Injection
	Composition	Each ml contains:- Diminazene Acetorate……105mg Antipyrine……..131mg
	Diary No. Date of R& I & fee	Dy No. 6869: 22.02.2018 PKR 20,000/-: 22.02.2018
	Pharmacological Group	Pyrazolones + Diminazene aceturate (Not mentioned in ATC)
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	50ml; the firm has mentioned that the price is decontrolled
	Me-too status	Antiprotoz injection ("each vial contains:- Diminazine aceturate…1050mg, phenazone…1312mg). Reg. No. 43122. 30ml, 50ml, 100ml.
	GMP status	The firm was inspected on 13.08.2020 with the following conclusion: As the firm has rectified most of the shortcomings and improved the condition of the GMP, panel of inspection is of the opinion to recommend the resumption of the production in Liquid Injectable Section (General Veterinary) of the firm M/s Mallard Pharmaceuticals Multan.
	Remarks of the Evaluator.IX	•
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs.	

	Decision of EWGVD: **The EWGVD deliberated the cases of antipyrine combinations with their dosage form at length and decided to obtain scientific rationale of combination, pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species, Difference between chemical structure of antipyrine, metamizole and novaminsulfone and Confirmation of causing of "agranulocytosis" by antipyrine in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
21.	Name and address of manufacturer / Applicant	M/s. International Pharma Labs, Raiwind Road, Bhoptian Chowk, Defence road, 1Km towards Kahna, Lahore.
	Brand Name +Dosage Form + Strength	Cytoget Injection
	Composition	Each 100ml solution contains:- Oxytetracycline as HCI……..…..15gm Tripelennamine HCI……..….1gm Dexamethasone ……..0.050gm
	Diary No. Date of R& I & fee	68, 06-03-2015, Rs.8000/- (Photocopy attached), 31-05-2012, 12000/- (photocopy attached) 06-03-2015
	Pharmacological Group	Antibiotic with Analgesic, Anti-pyretic & Anti-Inflammatory
	Type of Form	Form-5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	50ml ; Decontrolled
	Me-too status	Oxy-TD of Selmore Pharmaceuticals (Reg # 029666)
	GMP status	Panel inspection dated 19-12-2017 & 02-03-2018 unanimously recommends for renewal of DML.
	Previous remarks of the Evaluator.	
	Previous decision(s)	Deferred for rationale of Dexamthasone in the applied formulation (M-285).
	Evaluation by PEC-XIV	The firm has referred to the document of "Essential drug data for rational therapy in veterinary practice" for rationality of Dexamethasone. However, the document referred that the drug is available as dexamethasone sodium phosphate solution for injection and no reference/rationale provided for combination therapy.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

22.	Name and address of manufacturer/ Applicant	M/s Elegance Pharmaceuticals, Chak Belli Pandori Road, Distt. Rawalpindi (Oral Dry Powder veterinary).
	Brand Name + Dosage Form + Strength	Paramol C Powder
	Composition	Each 100gm contains:- Paracetamol……20gm Vitamin C…….5gm Potassium Carbonate……...12.5gm Sodium Bicarbonate……12.5gm Vitamin E…….……12.5gm
	Diary No. Date of R & I & fee	Dy. No 4965 dated 04-02-2019; Rs.20,000/- dated 04-02-2019 vide deposit slip No. 0622350 (Duplicate). Rs. 5000/- dated 16-07-2019 for revision of formulation.
	Pharmacological Group	Analgesic, Anti pyretic, Vit. C, and Vitamin E deficiency.
	Type of Form	Form-5.
	Finished product Specification	Manufacturer's specifications.
	Pack size & Demanded Price	100gm, 500gm, 1000g, & price is decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Pozadol powder, Leads Pharma, Reg. No. 084969.
	GMP status	Same as above.
	Remarks of the Evaluator [XIII]	• Firm has revised their initial formulation with fee of Rs.5,000/- submitted vide challan No. 1953361 dated 12-07-2019 wherein they have changed concentration of Vit. E from 1.25gm to 12.5gm. • Fee for registration application is required.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Paracetamol with Vitamin C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
23.	Name and address of manufacturer / Applicant	M/s. Grand Pharma Pvt Ltd, Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	KanCo Dex Injection
	Composition Each ml contains:	Each ml contains:- Kanamycin Sulphate……..…50mg Neomycin Sulphate……...50mg Colistin Sulphate……..…100,000 I.U Dexamethasone……..…0.5mg
	Diary No. Date of R& I & fee	Dy No 34798, dated 30-12-2020, Rs 20,000/-
	Pharmacological Group	Steroid / Amino glycoside
	Type of Form	Form-5

	Finished Product Specification	Manufacturer's specification
	Pack size & demanded price	50ml; Decontrolled
	Me-too status	Kono Dex Injection (Reg. # 052347) by Alina Combine Pharmaceutical Pvt. Ltd., Karachi.
	GMP status	New Section Veterinary Liquid Injection Vial (Steroid)
	Remarks of the Evaluator-VI	Salt for of Dexamethasone has not been submitted as per me-too reference.
	Previous Decision 297th	Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Remarks	The firm has revised the formulation as : Each ml contains: Kanamycin Sulphate…….……50mg Neomycin Sulphate…….……...50mg Colistin Sulphate……100,000 I.U Dexamethasone sodium phosphate……0.5mg With submission of Rs 5,000 vide slip#2052333 dt:15-3-2021.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
24.	Name and address of manufacturer / Applicant	M/s. Grand Pharma Pvt Ltd Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	KanCo Dex Injection
	Composition Each ml contains:	Each ml contains: Kanamycin Sulphate……50mg Neomycin Sulphate……..50mg Colistin Sulphate…….100,000 I.U Dexamethasone……0.5mg
	Diary No. Date of R& I & fee	Dy no 34798, dated 30-12-2020, Rs 20,000/-
	Pharmacological Group	Steroid / Amino glycoside
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's specification
	Pack size & demanded price	100ml; Decontrolled
	Me-too status	Kono Dex Injection (Reg. # 052347) by Alina Combine Pharmaceutical Pvt. Ltd., Karachi.
	GMP status	New Section Veterinary Liquid Injection Vial (Steroid)
	Remarks of the Evaluator-VI	Salt for of Dexamethasone has not been submitted as per me-too reference.
	Previous Decision 297th	Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too

		status) alongwith registration number, brand name and name of firm.
	Remarks	The firm has revised the formulation as : Each ml contains:- Kanamycin Sulphate…….……...50mg Neomycin Sulphate…….…...…..50mg Colistin Sulphate…….100,000 I.U Dexamethasone Sodium Phosphate……0.5 mg With the submission of Rs 5,000 fee Deposit slip no2052334 dated 15-3-2021.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
25.	Na me and address of manufacturer / Applicant	M/s. Grand Pharma Pvt Ltd Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Genta Mix IM Injection
	Composition Each ml contains:	Each 50ml contains:- Tylosin……7.5gm Dexamethasone…….…..0.01325gm Gentamycin Sulphate…….3gm Chlorpheniramine Maleate..0.375gm
	Diary No. Date of R& I & fee	Dy no 34805, dated 30-12-2020, Rs 20,000/-
	Pharmacological Group	Steroid / Antibiotic / Antihistamine
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's specification
	Pack size & demanded price	50ml; Decontrolled
	Me-too status	Genta Combisone Injection (Reg. # 046696) by Leads Pharma.
	GMP status	New Section Veterinary Liquid Injection Vial (Steroid)
	Remarks of the Evaluator-VI	Submitted me too reference contains chlorpheniramine whereas firm has applied for Chlorpheniramine maleate.
	Previous Decision 297th	Deferred for evidence of applied formulation/drug already approved by DRAP (generic /me-too status) alongwith registration number, brand name and name of firm.
	Remarks	The firm has revised the formulation as : Each 50ml contains:- Tylosin……..…..7.5gm Dexamethasone……0.01325gm Gentamycin Sulphate…….3gm Chlorpheniramine……0.375gm With the submission of Rs 5,000 fee Deposit slip no2052335 dated 15-3-2021

	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
26.	Name and address of manufacturer / Applicant	M/s. Grand Pharma Pvt Ltd, Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Genta Mix IM Injection
	Composition Each ml contains:	Each 50ml contains:- Tylosin…….……7.5gm Dexamethasone……..…0.01325gm Gentamycin Sulphate……...3gm Chlorpheniramine Maleate…0.375gm
	Diary No. Date of R& I & fee	Dy no 34805, dated 30-12-2020, Rs 20,000/-
	Pharmacological Group	Steroid / Antibiotic / Antihistamine
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's specification
	Pack size & demanded price	100ml; Decontrolled
	Me-too status	Genta Combisone Injection (Reg. # 046696) by Leads Pharma.
	GMP status	New Section Veterinary Liquid Injection Vial (Steroid)
	Remarks of the Evaluator-VI	Submitted me too reference contains chlorpheniramine whereas firm has applied for Chlorpheniramine maleate.
	Previous Decision 297th	Deferred for evidence of applied formulation/drug already approved by DRAP (generic/me-too status) alongwith registration number, brand name and name of firm.
	Remarks	The firm has revised the formulation as : Each 50ml contains:- Tylosin……..…...7.5gm Dexamethasone……0.01325gm Gentamycin Sulphate.…….3gm Chlorpheniramine ….....0.375gm With the submission of Rs 5,000 fee Deposit slip no2052336 dated 15-3-2021
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

27.	Name and address of manufacturer / Applicant	M/s. Aamster Laboratories, Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Prozin Mix-1000 Water Soluble Powder
	Composition	Each Kg contains:- Procaine Penicillin ……..… 12g Streptomycin Sulphate ……....……..… 36g Colistin Sulphate ….....… 60MIU Zinc Bacitracin ……..…….....52g
	Diary No. Date of R& I & fee	Dy No.12128 : 22.04.2021 PKR. 20,000/-; 22.04.2021
	Pharmacological Group	Antibacterial
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's Specification
	Pack size & Demanded Price	100g, 250g, 500g, 1Kg/Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Zeptocol W/S Powder (Selmore Pharma) Reg # 080962
	GMP status	Liquid Injection (General) (Veterinary-New Section) Oral Powder (Penicillin) (Veterinary-New Section) Inspection for grant of additional sections conducted on 11/03/2021. Panel unanimously recommended approval of additional sections.
	Remarks of the Evaluator	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
28.	Name and address of manufacturer / Applicant	M/s. Aamster Laboratories, Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Prozin Mix-2000 Water Soluble Powder
	Composition	Each Kg contains:- Procaine Penicillin …… 16g Streptomycin Sulphate ……....…… 40g Colistin Sulphate ….....80MIU Zinc Bacitracin 10%……100g
	Diary No. Date of R& I & fee	Dy No.12129: 22.04.2021 PKR. 20,000/-; 22.04.2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's Specification
	Pack size & Demanded Price	100g, 250g, 500g, 1Kg/Decontrolled

	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Colibak-SP 160 W/S Powder (Nawan Pharma) Reg # 082488
	GMP status	Liquid Injection (General) (Veterinary-New Section) Oral Powder (Penicillin) (Veterinary-New Section) Inspection for grant of additional sections conducted on 11/03/2021. Panel unanimously recommended approval of additional sections.
	Remarks of the Evaluator	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
29.	Name and address of manufacturer / Applicant	M/s. Aamster Laboratories, Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Neo Pen-Z Water Soluble Powder
	Composition	Each gm contains:- Procaine Penicillin ……..……..… 12mg Streptomycin Sulphate.....… .36mg Neomycin Sulphate ……...……10mg Zinc Bacitracin 52mg
	Diary No. Date of R& I & fee	Dy No.12127 : 22.04.2021 PKR. 20,000/-; 22.04.2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's Specification
	Pack size & Demanded Price	100g, 250g, 500g, 1Kg, 10Kg, 25Kg/Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Biocillin SN W/S Powder (Bio Labs Pharma) Reg # 097941
	GMP status	Liquid Injection (General) (Veterinary-New Section) Oral Powder (Penicillin) (Veterinary-New Section) Inspection for grant of additional sections conducted on 11/03/2021. Panel unanimously recommended approval of additional sections.
	Remarks of the Evaluator	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed**	

	countries for use in variety of animal species as applied by the firms in their applications for product registration. **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
30.	Name and address of manufacturer / Applicant	M/s. Ras Pharmaceuticals (Pvt) Ltd. 25-Km Lahore Road, Multan
	Brand Name +Dosage Form + Strength	Protoras Oral Powder
	Composition	Each 100gm contains:- Procain Penicillin……1.2g Streptomycin Sulphate……3.6g Zinc Bacitracin……5.2g Colistin Sulphate……..6MIU
	Diary No. Date of R& I & fee	Dy No.13605, 20-05-2021, 30,000/- 19-05-2021
	Pharmacological Group	Penicillin (Antibacterial)
	Type of Form	Form-5
	Finished product Specifications	Manufacturer Specification
	Pack size & Demanded Price	100gm,500gm,1Kg,2.5Kg, 5Kg,10Kg,25Kg : Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Zeptocol Powder of Selmore Pharm Lahore Reg.No#080962
	GMP status	New Section Approval Dated 27 May 2021
	Remarks of the Evaluator	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
31.	Name and address of manufacturer / Applicant	M/s. Mylab Pvt Ltd. Khankah Sharif Bahawalpur
	Brand Name +Dosage Form + Strength	PSN-Pred Injection
	Composition	Each 5gm contains:- Procaine Penicillin…..…….100,000 IU Streptomycin Sulphate……..…100mg Neomycin Sulphate……..…..100mg Prednisolone……...…..10mg
	Diary No. Date of R& I & fee	Dy. No 40584: 06-12-2018 PKR 20,000/-: 04-12-2018
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished Product Specification	Firm has claimed in house specification
	Pack size & Demanded Price	5gm amber coloured glass vial: Decontrolled
	Approval status of product in Reference Regulatory Authorities.	N.A

	Me-too status	Multiject IM Injection by Nawan Trading Corp. (Reg#018871)
	GMP status	Last inspection report dated 13-9-2018 to 14-09-2018, panel recommended the renewal of DML along with grant of additional 7 sections.
	Remarks of the Evaluator[3].	•
	Decision of 287th meeting of Registration Board	Deferred for evidence of approval of required manufacturing facility of "Liquid Injectable (Steroidal) section" From Central Licensing Board.
	Response by the firm	Firm has again submitted section approval letter dated 3rd December 2018 specifying Liquid Injectable (Steroid) veterinary section.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with Prednisolone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
32.	Name and address of manufacturer/ Applicant	M/s Bio-Oxime Pharmaceuticals, Plot.No.31,32 Millat Garment City, Dry Port Road, Faisalabad.
	Brand Name + Dosage Form + Strength	Biowan S Oral Powder
	Composition	Each 1000gm contains:- Doxycycline HCL……200gm Tylosin Tartrate…..…..100gm Colistin Sulphate……..50MIU Bromhexine HCL……..…5gm Streptomycin Sulphate…20gm
	Diary No. Date of R & I & fee	Dy. No. 7972; 22.02.2019 PKR. 20,000/-; 22.02.2019
	Pharmacological Group	Antibiotics + mucolytics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	500g; 1000g, 5000g; Decontrolled
	Me-too status	RIZ WAN-S WATER SOLUBLE POWDER. Reg. No. 78296 (colistin sulphate 0.5MIU/g)
	GMP status	The firm was inspected on 24.02.2021, wherein the renewal of DML was recommended.
	Remarks of the Evaluator	The firm revised the strength of colistin sulphate in line with the me-too product without submission of applicable fee.
	Previous decision	The board in its 295th meeting deferred the case for: • Updated status of GMP since submitted inspection report is not within the period of three years.

		• Submission of fee for revision of formulation.
	Evaluation by PEC	• Reply dated 03.06.2021: • The firm submitted Rs. 30,000/- fee (challan; 20985124132)
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
33.	Name and address of manufacturer/ Applicant	M/s Bio-Oxime Pharmaceuticals, Plot.No.31,32 Millat Garment City, Dry Port Road, Faisalabad
	Brand Name + Dosage Form + Strength	Specto Plus Oral Powder
	Composition	Each 100gm contains:- Lincomycin HCL……5gm Spectinomycin HCL….7.5gm Spiramycin Adipate.…2.5gm Bromohexime HCL..…0.5gm
	Diary No. Date of R & I & fee	Dy. No. 7967; 22.02.2019 PKR. 20,000/-; 22.02.2019
	Pharmacological Group	Antibiotics and mucolytics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	500g, 1000g, 5000g; Decontrolled
	Me-too status	SPECLINX ORAL POWDER, Reg. No. 80714
	GMP status	The firm was inspected on 24.02.2021, wherein the renewal of DML was recommended.
	Remarks of the Evaluator	
	Previous decision	The board in its 295th meeting deferred the case for updated status of GMP since submitted inspection report is not within the period of three years.
	Evaluation by PEC	Reply dated 03.06.2021: • GMP status updated. •
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to request to the applicant firms for scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

34.	Name and address of manufacturer/ Applicant	M/s. Selmore Pharmaceuticals (Pvt.) Ltd., 36-Km, Multan Road Lahore (Veterinary Oral powder).
	Brand Name + Dosage Form + Strength	Bioresp Powder.
	Composition	Each Kg contains:- Doxycycline HCl ……..……...200gm Tylosin Tartrate ……..……...100gm Colistin Sulphate …….……500 MIU Bromhexine HCl …….……..….5gm Streptomycin Sulphate ….……20gm
	Diary No. Date of R & I & fee	Dy. No 12780 dated 06-03-2019; Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic.
	Type of Form	Form-5.
	Finished product Specification	Manufacturer's specifications.
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 10Kg, 25Kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Respi Dox Water Soluble Powder, D-Maarson Pharmaceuticals, Reg. No. 072684.
	GMP status	Conclusion: (05-03-2018,17-08-2018 & 16-10-2018) In the light of the inspection conducted by the panel and based on the findings the panel of inspectors recommends grant of renewal of drug manufacturing license by way of formulation of M/s Selmore Pharma Lahore for following sections: 1- Veterinary Bolus 2- Veterinary Aerosol 3- Veterinary Oral powder 4- Veterinary Oral Liquid 5- Veterinary Liquid Injection 6- Veterinary Penicillin oral powder 7- Veterinary Penicillin dry powder for injection 8- Veterinary Penicillin liquid injection 9- Veterinary Hormone Liquid injection 10- Human Penicillin capsule 11- Human Penicillin dry powder suspension 12- Human Penicillin dry powder injection.
	Remarks of the Evaluator	• Firm has provided their master formulation, outline of method of manufacturing and finished product specifications with submission of 7500/- fee vide slip No. 86741441121 dated 02-09-2021.
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.**	

	Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.	
35.	Name and address of manufacturer/ Applicant	M/s. Grand Pharma Pvt. Ltd, Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi.
	Brand Name + Dosage Form + Strength	ZipcoStrep Powder
	Composition	Each Kg contains:- Zinc Bacitracin……...52gm Procaine Penicillin…….....12gm Streptomycin Sulphate…….……36gm Colistin Sulphate…..……60 MIU
	Diary No. Date of R & I & fee	Dy.No.21184; 18-10-2019; Rs.20,000 (18-10-2019)
	Pharmacological Group	Antibiotic.
	Type of Form	Form-5.
	Finished product Specification	Manufacturers' specifications.
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 2.5Kg, 5Kg, 10Kg, 25Kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Zeptocol Powder of M/s Selmore Pharma (Reg. #080962)
	GMP status	New Section of Veterinary Oral Powder Penicillin was approved on 12th September, 2019 by CLB.
	Remarks of the Evaluator	•
	Decision of 293rd meeting:	Deferred for the review of formulation.
	Submission of the firm:	Firm submitted their reply that same formulation with same strength was approved in 294th meeting of Registration Board to M/s Mediexcel Pharmaceuticals, Islamabad. They further submitted that same formulation with same strength was approved in 296th meeting of Registration Board to M/s Aptly Pharmaceuticals, Sargodha. They requested to consider their product for registration in the upcoming meeting of Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	

36.	Name and address of manufacturer / Applicant	M/s. Bioskills Pharmaceuticals, 4-Km Tamboly, GT Road, Sadhoke, District Gujranwala.
	Brand Name +Dosage Form + Strength	Streptoskill-36 Powder
	Diary No. Date of R& I & fee	Dy. No:18638 (02-07-2021), Rs.30,000/-
	Composition	Each 1000gm contains:- Tylosin Tartrate……...100gm Doxycycline HCl…….200gm Colistin sulphate…….. 450 MIU Bromhexine HCl……..5gm Streptomycin Sulfate ……..…...36g
	Pharmacological Group	Antibiotic/ Expectorant
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's Specifications
	Pack Size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 2.5Kg ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	NA
	Me-too Status	Strepto Dox Powder (Veterinary), Reg No: 071069 by M/S Attabak Pharmaceutical
	GMP Status	First Inspection for Grant of license conducted on 18/02/2021, Panel unanimously approved for grant of license.
	Remarks of the Evaluator.	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
37.	Name and address of manufacturer / Applicant	M/s. Bioskills Pharmaceuticals, 4-Km Tamboly, GT Road, Sadhoke, District Gujranwala.
	Brand Name +Dosage Form + Strength	Streptoskill-20 Powder
	Diary No. Date of R& I & fee	Dy. No:18671 (02-07-2021), Rs.30,000/-
	Composition	Each 1000gm contains:- Tylosin Tartrate……....100gm Doxycycline HCl…….….200gm Colistin Sulphate……...500 MIU Bromhexine HCl…….....5gm Streptomycin Sulfate …….....20g
	Pharmacological Group	Antibiotic/ Expectorant
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's Specifications
	Pack Size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 2.5Kg ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	NA
	Me-too Status	SP DOX Powder (Veterinary), Reg No: 087960 by M/S : FARM AID GROUP

	GMP Status	First Inspection for Grant of license conducted on 18/02/2021, Panel unanimously approved for grant of license.
	Remarks of the Evaluator.	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
38.	Name and address of manufacturer / Applicant	M/s. Vetec Laboratories, Plot No. 20, Street S-5, National Industrial Zone, Rawat, Rawalpindi.
	Brand Name +Dosage Form + Strength	PARA-Cool Powder
	Composition	Each 100gm contains:- Paracetamol…….….20gm Vitamin C……...5gm Potassium Carbonate…….12.5gm Sodium Bicarbonate……..12.5gm Vitamin E……...1.25gm
	Diary No. Date of R& I & fee	Dy. No. 11636; 06-03-2019; Rs. 20,000/- (01-03-2019)
	Pharmacological Group	Analgesic
	Type of Form	Form-5
	Finished product Specification	Firm has claimed In-house specification
	Pack size & Demanded Price	100gm, 500gm, 1Kg, 2.5Kg, 5 Kg, 25 Kg : Decontrolled
	Me-too status	PARACE by Biogen Pharmaceuticals (Reg. No. 063812)
	GMP status	New License (Inspection Date: 04-10-2018 & 05-11-2018). DML issued on 05.03.19
	Remarks of the Evaluator	Firm was asked to correct API Strength in Master formulation as per Me-too or justify the formulation. Firm in reply submitted same formulation which is not as per Me-too.
	Decision of 289th meeting: Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. **Submission by the firm:** • The firm has submitted revised formulation according to available me too along with the revised Form 5. • The revised label claim is given in the following; Each 100gm contains:- Paracetamol……..…....20gm Vitamin C…….…..…....5gm Potassium Carbonate…....…...12.5gm Sodium Bicarbonate…….…....12.5gm Vitamin E…….……12.5gm	

	*Strength of Vitamin E is changed from 1.25gm to 12.5gm. • Me too: PARA CE ORAL POWDER by M/s. Biogen Pharma, Reg. no. 063812 • The firm has not submitted any fee for revision of formulation.	
	Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Paracetamol with vit. C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
39.	Name and address of manufacturer / Applicant	M/s. Mylab Pvt Ltd., Khankah Sharif, Bahawalpur.
	Brand Name +Dosage Form + Strength	Dexum Injection
	Composition	Each ml contains:- Dexamethasone Sodium Phosphate……0.265gm
	Diary No. Date of R& I & fee	Dy.No. 14090, 16-04-2018, 20,000/-, 19-02-2018
	Pharmacological Group	Corticosteroid
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	100ml glass vial; Decontrolled
	Me-too status	Dexacare Injection of M/s Vety care (Reg # 026528)
	GMP status	GMP inspection report conducted on 24-02-2021 to 25-02-2021 concluded that the firm was found to be operating at a satisfactory level of GMP compliance.
	Previous remarks of the Evaluator.	The firm has provided Liquid Injectable (Steroid) Section.
	Previous decision(s)	Registration Board referred the case to QA & LT to update GMP status of the firm on priority (M-293).
	Evaluation by PEC	The firm has submitted Form-5 with revised strength of applied formulation as follows: Each ml contains: Dexamethasone sodium phosphate…….2mg Me-too: Dexamethasone sodium phosphate injection of M/s Orient Laboratories (Reg # 041253) Fee challan of PKR 30,000/- (slip # 2447234655) dated 30-12-2021 has been submitted.
	Decision: Deferred for review of formulation by expert working group on veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Dexum Injection and decided to obtain dosage form and dosage regimen with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
40.	Name and address of manufacturer / Applicant	M/s. Grand Pharma Pvt Ltd, Plot No. 5-A, Street No. N5, National Industrial Zone, Rawat, Rawalpindi.

	Brand Name +Dosage Form + Strength	Pred DX Injection
	Composition	Each ml contains:- Prednisolone…....….....7.5mg Dexamethasone….....2.5mg
	Diary No. Date of R& I & fee	Dy no 34816, dated 30-12-2020, Rs 20,000/-
	Pharmacological Group	Steroid
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's specification
	Pack size & demanded price	50ml; Decontrolled
	Me-too status	CORTINOL-P Injection (Reg. # 014570) by Star laboratories, Animal division Lahore
	GMP status	New Section Veterinary Liquid Injection Vial (Steroid)
	Remarks of the Evaluator-VI	• Me too reference in applied fill volume could not be verified.
	Decision 297th : Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. **Evaluation by PEC VI**: The firm has submitted CORTINOL-P microcrystalline suspension Injection (Reg. # 014570) by Star laboratories, Animal division Lahore, in 50ml pack size.	
	Decision: Deferred for review of the product/molecule by expert working group on veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Prednisolone with Dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
41.	Name and address of manufacturer/ Applicant	M/s Alina Combine Pharmaceuticals Pvt Ltd A-127, S.I.T.E Super Highway, Karachi
	Brand Name + Dosage Form + Strength	Neoxy F Water soluble powder
	Composition	Each Kg contains:- Oxytetracycline HCL…..50gm Neomycin Sulphate…….14gm Furaltadone HCL…….30gm
	Diary No. Date of R & I & fee	Dy. No. 11684; 06.03.2019 PKR. 20,000/-; 05.03.2019
	Pharmacological Group	Antibiotics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed manufacturer's specifications
	Pack size & Demanded Price	100g, 500g, 1Kg, 2.5Kg; decontrolled
	Me-too status	O-NEFUR ORAL POWDER. Reg. No. 35120
	GMP status	The firm was inspected on 30.06.2021 wherein GMP status was rated satisfactory.

	Remarks of the Evaluator	The API in the reference product is Furaltadone. You have mentioned Furaltadone HCl. Justify.
	Previous decision (M-307)	• Deferred for consideration on its turn, updated GMP status of the firm from QA & LT division and review of formulation by expert working group for veterinary drugs.
	Evaluation by PEC	• Updated inspection report submitted.
	Decision: Deferred for review of formulation by expert working group for veterinary drugs. **Decision of EWGVD:** **The Expert Working Group on Veterinary Drugs decided to recommend to reject veterinary formulations containing Furaltadone due to strong potential of causing genotoxicity, cytotoxicity and possible residual effects.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
42.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	C-Lyte P Oral Powder
	Composition	Each 100g contains:- Paracetamol ……..……20g Vitamin C……..……..……5g Potasium Carbonate……..…..12.5g Sodium Bi Carbonate ……...12.5g Vitamin E …….. …...12.5g
	Diary No. Date of R& I & fee	Dy No.14358: 27.05.2021 PKR. 30,000/-; 26.05.2021
	Pharmacological Group	NSAID, Vitamin, Minerals
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100g, 250g, 500g, 1Kg, 5Kg, 10Kg, 25Kg/Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Parascorbic Powder (Baariq Pharma) Reg # 087140
	GMP status	Oral Powder Section-I (Veterinary)-General Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for clarification regarding the use of fat soluble vitamin (Vitamin E) in water soluble powder.
	Evaluation by PEC	Firm has submitted the reply:

		'We use Vitamin E 50% Acetate (DL-Alpha-Tocopherol acetate). This form of API is only used in water soluble powder.'
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary Drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases of Paracetamol with Vitamin C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
43.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Tylopremsone Plus Injection
	Composition	Each ml contains:- Colistin Sulphate ……..1250mg Tylosin Tartrate ……..10mg Bromhexine HCl ……..…100mg Dexamethasone …….. ….50mg
	Diary No. Date of R& I & fee	Dy No.14731 : 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic, Mucolytic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	10ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Colitylo Plus Injection (Alina Combine) Reg # 052336
	GMP status	Liquid Injection Section (Veterinary)-(Steroid) Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation: Each ml contains:- Colistin Sulphate ……1250mg Tylosin Tartrate ……..……..…..……10mg Bromhexine HCl ……..…..100mg Dexamethasone Sodium Phosphate……50mg

		As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA and FDA Center for Veterinary Medicine Tylosin is approved as Tylosin base for injectable dosage form. Benzyl alcohol is used as excipient and tylosin only injection is administered via the intramuscular route only.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
44.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Tylopremsone Plus Injection (50ml)
	Composition	Each ml contains:- Colistin Sulphate ……..1250mg Tylosin Tartrate ……...10mg Bromhexine HCl ……100mg Dexamethasone ……50mg
	Diary No. Date of R& I & fee	Dy No.14732: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic, Mucolytic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Colitylo Plus Injection (Alina Combine) Reg # 052336
	GMP status	Liquid Injection Section (Veterinary)-(Steroid) Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation:

		Each ml contains:- Colistin Sulphate …….. 1250mg Tylosin Tartrate …… 10mg Bromhexine HCl ……..... .100mg Dexamethasone Sodium Phosphate…….. 50mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA and FDA Center for Veterinary Medicine Tylosin is approved as Tylosin base for injectable dosage form. Benzyl alcohol is used as excipient and tylosin only injection is administered via the intramuscular route only.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
45.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Tylopremsone Plus Injection
	Composition	Each ml contains:- Colistin Sulphate……..1250mg Tylosin Tartrate ……...10mg Bromhexine HCl……100mg Dexamethasone ……..….. 50mg
	Diary No. Date of R& I & fee	Dy No.14733: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic, Mucolytic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Colitylo Plus Injection (Alina Combine) Reg # 052336
	GMP status	Liquid Injection Section (Veterinary)-(Steroid). Inspection for grant of License conducted on 12/04/2021.Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	

	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation: Each ml contains:- Colistin Sulphate ……..…..1250mg Tylosin Tartrate ……10mg Bromhexine HCl ……..….100mg Dexamethasone Sodium Phosphate….. 50mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA and FDA Center for Veterinary Medicine Tylosin is approved as Tylosin base for injectable dosage form. Benzyl alcohol is used as excipient and tylosin only injection is administered via the intramuscular route only.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
46.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Tylo Premson G Injection
	Composition	Each ml contains:- Tylosin Tartrate……..150mg Gentamycin Sulphate ……60mg Dexamethasone ……. 0.265mg Chlorpheniramine ……...7.5mg
	Diary No. Date of R& I & fee	Dy No.14728: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic, Anti Histamine
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	10ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Genta Combisone Injection (Leads Pharma) Reg # 046696
	GMP status	Liquid Injection Section (Veterinary)-(Steroid)

		Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation: Each ml contains:- Tylosin Tartrate……....150mg Gentamycin Sulphate ……....60mg Dexamethasone Sodium Phosphate… 0.265mg Chlorpheniramine ……..7.5mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA Chlorpheniramine is approved as Chlorpheniramine maleate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA and FDA Center for Veterinary Medicine Tylosin is approved as Tylosin base for injectable dosage form. Benzyl alcohol is used as excipient and tylosin only injection is administered via the intramuscular route only.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
47.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi
	Brand Name +Dosage Form + Strength	Tylo Premson G Injection (50ml)
	Composition	Each ml contains:- Tylosin Tartrate…….150mg Gentamycin Sulphate ……..…… 60mg Dexamethasone ……. 0.265mg Chlorpheniramine..…….7.5mg

	Diary No. Date of R& I & fee	Dy No.14729: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic, Anti Histamine
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Genta Combisone Injection (Leads Pharma) Reg # 046696
	GMP status	Liquid Injection Section (Veterinary)-(Steroid) Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation: Each ml contains:- Tylosin Tartrate……...150mg Gentamycin Sulphate……... 60mg Dexamethasone Sodium Phosphate …0.265mg Chlorpheniramine…….7.5mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA Chlorpheniramine is approved as Chlorpheniramine maleate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA and FDA Center for Veterinary Medicine Tylosin is approved as Tylosin base for injectable dosage form. Benzyl alcohol is used as excipient and tylosin only injection is administered via the intramuscular route only.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.**	

	Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.	
48.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Tylo Premson G Injection
	Composition	Each ml contains:- Tylosin Tartrate……..…..150mg Gentamycin Sulphate……....…60mg Dexamethasone ……....0.265mg Chlorpheniramine…….7.5mg
	Diary No. Date of R& I & fee	Dy No.14730: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic, Anti Histamine
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Genta Combisone Injection (Leads Pharma) Reg # 046696
	GMP status	Liquid Injection Section (Veterinary)-(Steroid) Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation: Each ml contains:- Tylosin Tartrate…….. 150mg Gentamycin Sulphate……..…60mg Dexamethasone Sodium Phosphate ….0.265mg Chlorpheniramine…….7.5mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA Chlorpheniramine is approved as

		Chlorpheniramine maleate for injectable dosage form. As per Product Information Database of Veterinary Medicines Directorate, MHRA and FDA Center for Veterinary Medicine Tylosin is approved as Tylosin base for injectable dosage form. Benzyl alcohol is used as excipient and tylosin only injection is administered via the intramuscular route only.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
49.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Kena Premsone N Injection
	Composition	Each ml contains:- Kanamycin Sulphate ……...50mg Colistin Sulphate ……..…100,000IU Neomycin Sulphate …….50mg Dexamethasone ……..0.5mg
	Diary No. Date of R& I & fee	Dy No.14721: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	I-Kency Injection (International Pharma) Reg # 096810
	GMP status	Liquid Injection Section (Veterinary)-(Steroid) Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.

	Evaluation by PEC	Firm has revised the formulation: Each ml contains:- Kanamycin Sulphate……...50mg Colistin Sulphate ……100,000IU Neomycin Sulphate ……50mg Dexamethasone sodium phosphate ……0.5mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. Fee challan required for this amendment.
	Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
50.	Name and address of manufacturer / Applicant	M/s. Kayans Pharmaceuticals, Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi.
	Brand Name +Dosage Form + Strength	Kena Premsone N Injection (100ml)
	Composition	Each ml contains:- Kanamycin Sulphate ……..50mg Colistin Sulphate ……100,000IU Neomycin Sulphate ……50mg Dexamethasone …….0.5mg
	Diary No. Date of R& I & fee	Dy No.14722: 28.05.2021 PKR. 30,000/-; 28.05.2021
	Pharmacological Group	Steroid, Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	I-Kency Injection (International Pharma) Reg # 096809
	GMP status	Liquid Injection Section (Veterinary)-(Steroid) Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Previous decision **(M-308)**	Deferred for correction of the salt form of Dexamethasone in label claim along with submission of applicable fee.
	Evaluation by PEC	Firm has revised the formulation:

		Each ml contains:- Kanamycin Sulphate ……..……50mg Colistin Sulphate ……..…..100,000IU Neomycin Sulphate …….…. 50mg Dexamethasone Sodium Phosphate …… 0.5mg As per Product Information Database of Veterinary Medicines Directorate, MHRA Dexamethasone is approved as Dexamethasone sodium phosphate for injectable dosage form. Fee challan required for this amendment.
	Decision: Decision: Deferred for further deliberation by Expert Working Group on Veterinary. **Decision of EWGVD:** **The EWGVD deliberated the cases of different antibiotic with dexamethasone and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
51.	Name and address of Manufacturer / Applicant	M/s. Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name, Dosage Form, Strength	AMCOLI-480 Oral Water Soluble Powder
	Composition	Each 100g contains:- Colistin Sulphate ……48,000,000IU
	Diary No., Date of R & I & Fee	Dy.No. 19101, 30-09-2019, Rs.20,000
	Pharmacological Group	Antibiotic
	Type Of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack Size and Demanded Price	100gm,250gm,500gm,1Kg,5Kg,10Kg / Decontrolled
	Me-Too Status	Colibak water soluble powder (Attabak Pharma) Reg No. 049707
	GMP Status	First Inspection for grant of license conducted on 05/09/2019 Panel unanimously approved for the grant of License.
	Remarks of Evaluator	The firm has applied for In-House specifications and the product is not present in available pharmacopoeia (USP, BP, IP, JP).
	Decision: Registration Board in its 293 meeting referred to expert working group for rationalization of colistin formulations. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.**	

	Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.	
52.	**Name and address of manufacturer / Applicant**	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No.8C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK
	Brand Name +Dosage Form + Strength	Huddy Spray-25
	Composition	Each ml contains:- Oxytetracycline ……..25mg Gentaian Violet…….5mg
	Diary No. Date of R& I & fee	Dy.No 30157 dated 11-11-2020 Rs.20,000 dated 11-11-2020
	Pharmacological Group	Antibotic Antiseptic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer Specification
	Pack size & Demanded Price	100ml & 200ml
	Me-too status	TERAGEN 2.5% AEROSOL SPRAY (043300) STAR LABS
	GMP status	First Inspection for grant of license conducted on 09/10/2020 Panel unanimously approved for the grant of License.
	Remarks of the Evaluator[II].	
	Decision: Registration Board in its 307th meeting deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
53.	Name and address of manufacturer / Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK
	Brand Name +Dosage Form + Strength	Huddy Spray-4
	Composition	Each gm contains:- Oxytetracycline HCl……..40mg Gentaian Violet……..….4mg
	Diary No. Date of R& I & fee	Dy. No.30155 dated 11-11-2020 Rs.20,000 dated 11-11-2020
	Pharmacological Group	Antibotic Antiseptic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer Specification
	Pack size & Demanded Price	200g
	Me-too status	TERAGEN AEROSOL SPRAY(026430) STAR LABS
	GMP status	First Inspection for grant of license conducted on 09/10/2020 Panel unanimously approved for the grant of License.
	Remarks of the Evaluator.	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:**	

	The EWGVD deliberated the cases and decided to recommend the product for the registration. **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
54.	**Name and address of manufacturer / Applicant**	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK
	Brand Name +Dosage Form + Strength	CTC Spray
	Composition	Each ml contains: - Chlortetracycline Hydrochloride ….. 995.3mg
	Diary No. Date of R& I & fee	Dy.No 30151 dated 11-11-2020 Rs.20,000 dated 10-11-2020
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished Product Specification	Manufacturer Specification
	Pack size & Demanded Price	100ml,150ml,200ml
	Me-too status	STROM SPRAY (078336) WIMITS PHARMACEUTICALS
	GMP status	First Inspection for grant of license conducted on 09/10/2020 Panel unanimously approved for the grant of License.
	Remarks of the Evaluator.	
	Decision: Registration Board in its 307th deferred for scientific rationale regarding solubility of 995.3mg of Chlortetracycline hydrochloride in 1 ml of solvent. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	

55.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No. 58C, 59C, 60C, 61C, 62C, 63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Rolds PSB- 150 W/S Powder
	Composition	Each Kg contains:- Procain Pencillin ……..…..12gm Streptomycin Sulphate……..…..36gm Zinc Bacitracin ……..50gm
	Diary No. Date of R & I & fee	Dy No 29155; Dated 04-11-2020; Rs.20,000 Date 04-11-2020.
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 10Kg, 25Kg & Decontrolled
	Me-too status	Isogin Powder of M/s International Pharma Labs, Raiwind Road, Lahore 099066
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•

	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has submitted as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
56.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Harry Col-23 Oral Liquid
	Composition	Each 100ml contains:- Florfenicol ……23g
	Diary No. Date of R & I & fee	Dy.No.29502; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 450ml, 500ml, 1Litre, 2.5Litre / Decontrolled
	Me-too status	Nafloxin- 23 Oral Liquid (Ras Pharma) 079867
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has submitted as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.**	

	Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.	
57.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Harry COl-11 Oral Liquid
	Composition	Each 100ml contains: - Florfenicol……11% w/v
	Diary No. Date of R & I & fee	Dy.No.29560; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 450ml, 500ml, 1Litre, 2.5Litre / Decontrolled
	Me-too status	Rofin Liquid (Biorific Pharma) 083825
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has submitted as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
58.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Flor- Rold C 16% Oral Liquid
	Composition	Each 100ml contains: - Florfenicol …….……11g Colistin Sulphate.....50MIU
	Diary No. Date of R & I & fee	Dy.No.29586; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 500ml, 1Litre, 2.5Litre & Decontrolled
	Me-too status	F- Col Liquid (D- Maarson Pharma) 072679

	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has submitted as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
59.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Flor- Rold C 28% Oral Liquid
	Composition	Each 1000ml contains: - Florfenicol……23gm Colistin Sulphate.....50MIU
	Diary No. Date of R & I & fee	Dy.No.29585; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 500ml, 1Litre, 2.5Litre & Decontrolled
	Me-too status	Maxiflor Plus Liquid (Biogen Pharma) 075617
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has submitted as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	

	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
60.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK
	Brand Name + Dosage Form + Strength	COF Rold 2% Oral Liquid
	Composition	Each ml contains:- Bromhexine Hydrochloride …..…20mg
	Diary No. Date of R & I & fee	Dy.No.29588; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Mucolytics
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml,150ml,250ml,500ml,1Litre,2.5Litre & Decontrolled
	Me-too status	Could not be confirmed
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	• Me- too status could not be confirmed.
	Decision of 297th meeting of Registration Board:	Deferred for following: • Scientific rationale of related strength of the same formulation. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Submission of the firm:	Firm has provided AVIXIN-M 2% ORAL LIQUID Reg. No. 099038, as me too for the applied formulation and further submitted as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	

61.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Enrolds C- 148 Oral Liquid
	Composition	Each 100ml contains: - Enrofloxacin……10g Colistine Sulphate…….48 MIU
	Diary No. Date of R & I & fee	Dy.No.29493; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 500ml, 1Litre, 2.5Litre / Decontrolled
	Me-too status	Eflin-VL 10% Oral Liquid of M/s Vetec Laboratories, National Industrial Zone, Rawat, Rawalpindi 099309
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
62.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Enrolds C- 65 Oral Liquid
	Composition	Each 100ml contains:- Enrofloxacin……20g Colistine Sulphate……..….4,500,000 I.U
	Diary No. Date of R & I & fee	Dy.No.29578; 05-11-2020; Rs.20,000 (05-11-2020)
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 450ml, 500ml, 1Litre, 2.5Litre & Decontrolled

	Me-too status	Eflin- Kk 20% Oral Liquid of M/s Vetec Laboratories, National Industrial Zone, Rawat, Rawalpindi 099311
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	• M/s Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
63.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Roldzen Forte Oral Suspension
	Composition	Each ml contains:- Oxyclozanide……..….30mg Levamisole HCl……..…..…...15mg Cobalt Chloride ……..…..……7.6mg Sodium Sel…….……3.4mg
	Diary No. Date of R & I & fee	Dy.No.29516; 05-11-2020; Rs.20,000/- 05-11-2020
	Pharmacological Group	Anthelmintic
	Type of Form	Form- 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ML ,250ML, 500ML, 1000ml, 2.5Litre & Decontrolled
	Me-too status	Biowerm Oral Liquid of M/s Bio- Oxime (074781)
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths.

		• Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
64.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Harryzen Forte Oral Suspension
	Composition	Each 100ml contains: - Oxyclozanide……..…6.000gm Levamisole HCl……..3.0gm Sodium Selenite.....0.076gm Cobalt Sulphate…….....0.764gm
	Diary No. Date of R & I & fee	Dy.No.29509; Dated 5-11-2020; Rs.20,000/-5-11-2020
	Pharmacological Group	Anthelmintic Minerals
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml, 150ml, 250ml, 500ml, 1000ml, 2.5Litre & Decontrolled
	Me-too status	Verminil Plus Oral Drench of M/s Vetz Pharma (080504)
	GMP status	First Inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved the grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.**	

	Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.	
65.	Name and address of manufacturer/ Applicant	M/s Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Ben Rold 11.25% Oral Suspension
	Composition	Each 100ml contains: - Albendazole……11.25gm
	Diary No. Date of R & I & fee	Dy.No.29515; Dated 05-11-2020; Rs.20,000 Dated 05-11-102020
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specifications
	Pack size & Demanded Price	100ml, 150ml, 250ml, 500ml, 1000ml, 2.5Litre & Decontrolled
	Me-too status	Albensure Drench of Biogen Pharma (069609)
	GMP status	First Inspection for grant of license was conducted on 09-10-2020 and the panel unanimously approved the grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
66.	Name and address of manufacturer/ Applicant	M/s Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK
	Brand Name + Dosage Form + Strength	Rold Oxfen DS Drench
	Composition	Each ml contains: - Oxfendazole……22.70mg
	Diary No. Date of R & I & fee	Dy No. 29554 Dated 05-11-2020; Rs.20,000 Dated 05-11-2020
	Pharmacological Group	Anthelmintic, Minerals
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specification
	Pack size & Demanded Price	100ml,150ml,250ml,500ml,1000ml,2.5litre & Decontrolled
	Me-too status	Oxfenda -D Drench (084933) Divine Pharma

	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	
67.	Name and address of manufacturer/ Applicant	M/s. Haarolds Pharmaceutical Pvt Ltd Plot No 58C,59C,60C,61C,62C,63C, and 64C Small Industrial Estate Bhimber AJK.
	Brand Name + Dosage Form + Strength	Ben Rold 12.5% Oral Suspension
	Composition	Each ml contains: - Albendazole……125mg
	Diary No. Date of R & I & fee	Dy No. 29528, 05-11-2020; Rs.20,000, 05-11-2020
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specification	Manufacturers Specifications
	Pack size & Demanded Price	100ml, 150ml, 250ml, 500ml, 1000ml, 2.5litre & Decontrolled
	Me-too status	Vetazole 12.5% Oral Liquid (079280) of Vetz Pharma
	GMP status	First inspection for grant of license was conducted on 09-10-2020 and the panel approved grant of License.
	Previous Remarks of the Evaluator PEC-XIII (a)	•
	Decision of 297th meeting of Registration Board:	Deferred for scientific rationale of related strength of the same formulation.
	Submission of the firm:	Firm has as under: • This is for marketing purpose as different clients demands different strengths. • Me too is available for the applied strengths approved by DRAP. • We have applied the strength as per existing policy of the Registration Board.
	Remarks of the Evaluator PEC-XIII	
	Decision: Registration Board in its 307th deferred for review by expert working group for veterinary drugs. **Decision of EWGVD:**	

	The EWGVD deliberated the cases and decided to recommend the product for the registration. **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**

ITEM NO.III IMPORTED VETERINARY

1.	Name and address of Applicant	M/s. Mehran International, 498-C, Feroz Shah Mehta Road, Karachi.
	Detail of Drug Sale License	**Address:** M/s. Mehran International, 498-C, Feroz Shah Mehta Road, Karachi. **Validity: 0**1/08/2019 **Status:** Drug License by way of Wholesale
	Name and address of manufacturer	M/s Hebei New Century Pharmaceutical Co., Ltd. No.189 Taihang Street Hi-tech Zone Shijiazhuang City, Hebei China.
	Name and address of marketing authorization holder	M/s Hebei New Century Pharmaceutical Co., Ltd. No.189 Taihang Street Hi-tech Zone Shijiazhuang City, Hebei China.
	Name of exporting country	China
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No.2588 Dated 26/01/2017
	Fee including differential fee	Rs. 100,000/- Dated 25/01/2017
	Brand Name +Dosage Form + Strength	Diminazine and Antipyrine granules for injection
	Composition	Each 2.36g bag contains:- Diminazene …….. 1.050gm Antipyrine …….. 1.31gm
	Target Species	(for horse, cattle and sheep use)
	Finished Product Specification	Manufacturer‘s specification
	Pharmacological Group	Antiprotozoal agent
	Shelf life	3 years
	Demanded Price	De-controlled
	Pack size	2.36g
	International availability	-
	Me-too status	Diminol powder for injection of M/s Star Labs Lahore (Reg.# 017066)
	Detail of certificates attached	Original Legalized CoPP (certificate no. 2016030519) issued by *Shijiazhuang Animal Husbandry and Aquatic Product Bureau* confirms the free sale of the product in exporting country. The facilities and operations conform to GMP as recommended by WHO as per CoPP. The certificate remains valid until 04-03-2021
	Remarks of the Evaluator.	
	Previous Decision:	Registration Board referred the case to Expert Working Group on Veterinary drugs for review of formulation **(M-283)**.
Decision of Expert Working Group in its 5th meeting: Deferred for further evaluation with respect to withdrawal period and safety profile of antipyrine.		

Decision of Expert Working Group in its 6th meeting: *Fixed dose combination of Diminazene aceturate & Antipyrine (Phenazone) are available and marketed in countries having heamatozoons infections, where the principle of disease therapy intends requirement of 'antiprotozoal' and 'antipyratic' together for ease and convenience of use and therapeutic effect. However, withdrawal period is advised for strict observance on label when used in food producing animals. The combination is recommended for registration.*

Decision of Registration Board in 289th meeting:-

Registration Board in its 289th meeting deferred the case for further deliberation on the matter.

Decision of Expert Working Group in its 08th meeting:

The Committee deferred the case till getting the following information relating to the formulation;

a. Evidence of availability of said formulation in any reference regulatory authority.
b. Difference between chemical structure of antipyrine, metamizole and novaminsulfone.
c. Confirmation of causing of "agranulocytosis" by antipyrine.

Decision of EWGVD:

a. **The EWGVD deliberated the cases of antipyrine combinations with their dosage form at length and decided to obtain scientific rationale of combination, pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species, Difference between chemical structure of antipyrine, metamizole and novaminsulfone and Confirmation of causing of "agranulocytosis" by antipyrine in their applications for product registration.**

Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.

2.	Name and address of Applicant	M/s. Mustafa Brothers 186-D Peoples Colony No.1 Faisalabad.
	Detail of Drug Sale License	Address: P-1860-D, Peoples Colony No.1 Faisalabad. Validity : 12/2/2019 Status: License to sell drugs as a distributor
	Name and address of manufacturer	M/s. Asia Animal Pharmaceutical Co. Ltd Address: No.130-1A Highway-Ba Lang Ward – Cai Rang District – CanTho City: Viet Nam.
	Name and address of marketing authorization holder	M/s Asia Animal Pharmaceutical Co. Ltd Address: No.130-1A Highway-Ba Lang Ward – Cai Rang District – CanTho City: Viet Nam.
	Name of exporting country	Viet Nam
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy No : 14758 Dated : 12/09/2017
	Fee including differential fee	Rs : 100,000 Dated : 12/09/2017
	Brand Name +Dosage Form + Strength	Analgin C Solution for Injection
	Composition	Each ml contains:- Analgin……250mg Vitamin C……100mg
	Finished Product Specification	In-House
	Pharmacological Group	Antipyretic, Antiinflammatory
	Shelf life	3 Years (As packaged for sale) 14 days (After first opening the immediate packaging)
	Demanded Price	Decontrolled

	Pack size	100ml
	Me-too status	Could not be confirmed
	Detail of certificates attached	**Free sale Certificate:** Issued by Ministry of Agriculture and Rural development and is valid until 29-3-2019 **GMP certificate** Copy of GMP certificate issued from Ministry of Agriculture and Rural development/Socialist Republic of Viet Nam and is valid until 31 July 2022.
	Remarks of the Evaluator.	3 batches tested at Accelerated stability (40'C+-2'C and 75% RH +-5%) for 6 months and Long term stability (30'C+-2'C and 65% RH +-5%) for 3 years or 36 months a) 0111 Manufacturing date March 2011 b) 0211 Manufacturing date March 2011 c) 0311 Manufacturing date March 2011 Analgin is a synonym of metamizole (a banned drug)
	Previous Decision: Registration Board referred the case to expert Working Group of veterinary drugs for review of formulation (M-288). **Decision of Expert working group in 08th meeting:** The expert working group after thorough deliberation decided not to recommend the formulation due to the presence of banned ingredient "Analgin". **Decision of EWGVD:** **The Expert Working Group on Veterinary Drugs recommended the rejection of drugs containing salt Analgin/Novaminsulfom/Dipyrone /Metamizole etc. for Veterinary drugs for being associated with serious adverse effects like agranulocytosis.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
3.	Name and address of Applicant	M/s. Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No. 1, Miran Muhammad Shah Road, Karachi-75350, Pakistan.
	Detail of Drug Sale License	Address: M/s. Ghazi Brothers, Gazi House D-35, KDA Scheme No.1. Miran Muhammad Shah Road, Karachi. Validity: 25 May, 2020 Status: License to sell drugs as a Distributor
	Name and address of manufacturer	Life Come Biochemistry Co., Ltd. No. 19 Nanpu Ecological Industrial Park, Pucheng, Fujian, China.
	Name and address of marketing authorization holder	Life Come Biochemistry Co., Ltd. No. 19 Nanpu Ecological Industrial Park, Pucheng, Fujian, China.
	Name of exporting country	China
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No.1325 Dated 14/02/2017
	Fee including differential fee	Rs.50,000/- Dated 20/12/2017
	Brand Name +Dosage Form + Strength	Sinomd 15% Powder (for oral use)
	Composition	Each Kg of powder contains:- Bacitracin (as methylene disalicylate)… 150g

		750g of bacitracin methylene disalicylate eq. to 150g of bacitracin base)
	Target Species	Chickens, Hen & growing turkeys
	Finished Product Specification	In House
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	De-Controlled
	Pack size	1Kg, 2Kg, 5Kg & 10Kg
	International availability	Could not be confirmed
	Me-too status	N/A
	Detail of certificates attached	*Original legalized free sale certificate:* Issued by: Pucheng administration of Animal Husbandry & Veterinary & Aquatic Products. Issued on: 14-01-2016. Free sale in exporting country: Confirms the free sale of the product in exporting country. GMP Certificate (Copy): Issued by: Ministry of Agriculture of the People Republic of china, Fujian Province. Certificate No. (2015) S.Y.GMP Z.ZI, No.13003. Issued on: August 21, 2015 Valid till: August 20, 2020.
	Remarks of the Evaluator.	
	Previous Decision: Registration Board referred the case to the Expert committee on the veterinary drugs for their comments regarding need of this medicine within the country (M-286). **Decision of Expert working group in 08th meeting:** Deferred for confirmation of safety and rationality of Bacitracin and indications for applied formulation. **Decision of EWGVD:** **The EWGVD deliberated the case of Sinomd 15% Powder with their dosage form at length and decided to obtain scientific rationale of pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.** **Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.**	
4.	Name and address of Applicant	M/s. Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No. 1, Miran Muhammad Shah Road, Karachi-75350, Pakistan.
	Detail of Drug Sale License	Address: M/s. Ghazi Brothers, Gazi House D-35, KDA Scheme No.1. Miran Muhammad Shah Road, Karachi. Validity: 25 May, 2020 Status: License to sell drugs as a Distributor
	Name and address of manufacturer	M/s. Life Come Biochemistry Co., Ltd. No. 19 Nanpu Ecological Industrial Park, Pucheng, Fujian, China.
	Name and address of marketing authorization holder	M/s. Life Come Biochemistry Co., Ltd. No. 19 Nanpu Ecological Industrial Park, Pucheng, Fujian, China.
	Name of exporting country	China

	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No.1325 Dated 14/02/2017
	Fee including differential fee	Rs. 50,000/- Dated 20/12/2017
	Brand Name +Dosage Form + Strength	Sinobac 15% Powder (for oral use)
	Composition	Each Kg of powder contains:- Bacitracin (as zinc)… 150g (750g of bacitracin zinc eq. to 150g of bacitracin base)
	Target Species	Broiler, Hen , Cattle/Buffalo, Aquaculture
	Finished Product Specification	In House
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	De-Controlled
	Pack size	1Kg, 2Kg, 5Kg & 10Kg & 25Kg
	International availability	Could not be confirmed
	Me-too status	N/A
	Detail of certificates attached	*Original legalized free sale certificate:* Issued by: Pucheng administration of Animal Husbandry & Veterinary & Aquatic Products. Issued on: 14-01-2016. Free sale in exporting country: Confirms the free sale of the product in exporting country. GMP Certificate (Copy): Issued by: Ministry of Agriculture of the People Republic of china, Fujian Province. Certificate No. (2015) S.Y.GMP Z.ZI, No.13003. Issued on: August 21, 2015 Valid till: August 20, 2020.
	Remarks of the Evaluator.	
	Previous Decision: Registration Board referred the case to the Expert committee on the veterinary drugs for their comments regarding need of this medicine within the country (M-286). **Decision of Expert working group in 08th meeting:** Deferred for confirmation of safety and rationality of Bacitracin and indications for applied formulation. **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**	

5.	Name and address of manufacturer / Applicant	M/s. ICI Pakistan Ltd, ICI House , 5 West Wharf, Karachi.
	Detail of Drug Sale License	Address: 5 West Wharf, Karachi Validity: 19-02-2020 Status: Drug License by way of Wholesale.
	Name and address of manufacturer	M/s Intervet Productions SA Rue De Lyons, 27460 Igoville, France.
	Name and address of marketing authorization holder	M/s. Intervet International BV Wim de Korverstraat 35, 5831 AN Boxmeer, The Netherlands.
	Name of exporting country	France
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No Dated 26/05/2017
	Fee including differential fee	Rs. 100,000/- Dated 23/02/2018

Brand Name +Dosage Form + Strength	Exzolt Solution 10mg/ml for use in Drinking Water
Composition	Each ml contains: Fluralaner…10mg
Target Specifications	Chickens (pullets, breeders, layer hen)
Finished Product Specification	In-House
Pharmacological Group	Ectoparasitcides
Shelf life	3 years
Demanded Price	As per SRO
Pack size	Bottle of 1 Litre, 4 Litre
International availability	Approved in ANSM
Me-too status	N/A
Detail of certificates attached	Original Legalized COPP Certificate No. 06/17/113733 Certified by: EMA Free sale: Yes GMP : GMP Complaint Issue Date: 12-10-2017 Letter of Authorization M/s Intervet International BV Wim de Korverstraat 35, 5831 AN Boxmeer, The Netherlands & M/s ICI Pakistan LTD ICI House , 5 West Wharf, Karachi Dated: Nov, 2017
Remarks of the Evaluator.(VI)	Withdrawal Period Meat and Offal: 14 days. Eggs: Zero days In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing
Evaluation by PEC:	**Decision of 291st**:- Deferred for further deliberation regarding use of applied formulation in chickens. Firm has submitted EPAR stating that Exzolt is a veterinary medicine used to treat poultry red mite (Dermanyssus gallinae) infestation in pullets (Young female chickens), breeders and layer hens.

Decision of 293rd : Deferred for further deliberation regarding use of applied formulation in chickens

Decision of 295th: Deferred for the justification of safety parameters in accordance with the withdrawl period.

Firm's response: The withdrawl period(s) for exzolt 10mg/ml solution for use in drinking water for chickens were determined based on the following MRL of fluralaner as established by the Committee for Medicinal Products for Veterinary Use (CVMP).

Table :MRL(s) for fluralaner

Active Substance	Marker residue	Animal Specie	MRL	Target tissue	Other provision
Fluralaner	Fluralaner	Poultry	65ug/kg 650ug/kg 420ug/kg 650ug/kg 1300ug/kg	Muscle Liver Kidney Skin with fat Eggs	No Entry

Based on the results of the residue depletion studies and taking into the account the MRL established for fluralaner, the MAH proposes the following WHPs for exzolt 10mg/ml solution for use in drinking water for chickens:
Meat and offal: 13days
Eggs: 0 days.
Nevertheless, it is up to the competent authority to assess residue depletion data and come to a conclusion on the with-drawl periods. Therefore, with-drawl periods as registered nationally in

	different countries (e.g. Country of origin) might deviate from what has been proposed by the MAH.					
	Recommendation of 10th EWG:- **The Expert Working Group on Veterinary Drugs deferred for further deliberation.** **Decision of EWGVD:** **The EWGVD deliberated the cases and decided to recommend the product for the registration.** **Decision:- Keeping in view the decision of EWGVD, Registration Board approved the product.**					
6.	M/s. Ghazi Brothers, Ghazi House, D-35. K.D.A. Scheme No.1, Miran Muhammad Shah Road, Karachi./ **Manufactured by:** M/s. CEVASA S.A. 23rd Street Nº 293 - Pilar Industrial Park, Pilar, State of Buenos Aries, Argentina.	Antitermyl Water Soluble Powder **Dosage form:** Water Soluble oral Powder Each 100 gram contains:- Acetyl Salicylic Acid…17gm Caffeine..2gm Vitamin C (Ascorbic acid)……3gm (Non-steroidal Anti-inflammatory, Xanthine derivative, Vitamin).	Form 5-A Dy No. 7655 PKR 50,000/- Dated: 16-05-2013 **Pack size**: 100g, 1 Kg, 5Kg Price: De controlled	International availability not provided N/A Original legalized free sale certificate of Argentina is attached which confirms the free sale of product in country of origin. **GMP Status:** Certificate issues on 11October 2012 by Argentina	Firm has claimed Mfg. Specs and the product is not present in available versions of BP and USP (**B.P 2013** and **USP 39**)	Deferred for review of formulation by Dr. Qurban Ali. (Member Registration Board)

Recommendation of 10th EWG:-

The Expert Working Group on Veterinary Drugs deferred for further deliberation.

Decision of EWGVD:
The EWGVD deliberated the cases of Acetyl Salicylic Acid with vit. C and similar combinations with their dosage form at length and decided to obtain scientific rationale of combination and pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.

Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.

Case No.07: Rejection of Registration of Oxyone Powder-Case Remanded Back by the Appellate Board.

The registration application of Oxyone Powder filed by M/s. Ghazi Brothers, Karachi was rejected by the Drug Registration Board in its 249th meeting held on 18th May, 2015 as per following details:-

S. No.	Name of Applicant/Manufacturer	Name of Drug(s)/ Composition	Decision of Registration Board
1.	M/s. Ghazi Brothers, Karachi. / Manufactured by M/s. Cheilbio Co. Ltd. Gyeonggi-Do, KoreA.	Oxyone Powder Each Kg contains:- Oxytetracycline Quaternary Ammonium Salts……200gm	The Board rejected the product due to Potential of misuse on feed additive & drug interaction. The Board also decided to issue show cause Notice to already Registered Products for cancellation (If applicable).

The firm filed appeal before the Appellate Board which was considered in its 45th meeting. The decision of the Appellate Board and further proceeding are as under:-

(i) "Keeping in view of the arguments of the Appellate Board and Defendants, the Appellate Board decided to give 15 days' time to the Appellant to submit documentary evidence that their applied product Oxyone Powder containing Oxytetracycline Quaternary Ammonium Salt is available in the US FDA in the same packaging as applied by the Appellant. Chairman was authorized to refer back the case to Registration Board, if documentary evidence is provided by the Appellant. Otherwise, if no such evidence is provided by the Appellant, case shall be placed in the next meeting of the Appellate Board for final decision on the Appeal".

(ii) Resultantly, M/s. Ghazi Brothers, Karachi has provided the documentary evidence that Oxytetracycline quaternary ammonium salt is available in US FDA and the packing is also same as applied by the firm (provided date is enclosed). Data provided by the firm was also verified from FDA website.

(iii) As authorized by the Appellate Board, Chairman (Appellate Board) has decided to refer back the case to the Registration Board for re-consideration in light of documentary evidence provided by the firm.

As per information submitted by the firm to the Appellate Board the pack size approved by the USFDA is 50 lb (22.6 Kg) for the brand of M/s. Phirbro Animal Health, New Jersey.

Registration Board in its 274th meeting referred the case to Veterinary expert Dr.Qurban Ali for evaluation and subsequent recommendations for consideration of Board.

Decision of EWGVD:
The EWGVD deliberated the cases of Oxyone Powder decided to request to the applicant firms for pharmacokinetics with examples of such products registered at scientifically developed countries for use in variety of animal species as applied by the firms in their applications for product registration.

Decision:- Registration Board endorsed the decision of Expert Working Group on Veterinary Drugs.

HUMAN IMPORT

Case No.01: REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CHANGE IN PACKAGING SITE, CHANGE OF ADDRESS OF IMPORTER AND PRODUCT STATUS CHANGE FROM BULK IMPORT TO FINISHED IMPORT.

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has applied for a change in packaging site, change of address of the importer, and product status change from bulk import to finished import for the following already registered products as per details given below: -

Name & Composition / Reg. No.	**Existing approved Site (as per approval) 19-10-2018**	**New Proposed Sites as per COPP**
Ultravist Injection 370 Solution for Injection Each ml contains: - Lopromide solution 0.769gm Reg. No. 009865	**Manufacturer: -** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Status:** Bulk Import & locally repack at**:** M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Bayer Vital GmbH 51368 Leverkusen, Germany. **Bulk Manufacturer, Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

The firm has submitted the following supporting documents: -

Change of Address of Manufacturing Site/Source/Marketing Authorization Holder (MAH).	
Documents required as per SOPs	**Submitted documents by firm**
a) Application with required fee as per relevant SRO. b) Copy of registration letter and last renewal status.	a) Fee of Rs.150,000/- b) Reg. Letter and renewal trail • Copy of registration letter issued from the then Reg-I Section on 13-06-1988. • Transfer of Reg. to to M/s Medipharm (Pvt) Ltd, 7-A, Gulberg-II, Lahore on 12-03-1992. • Change of source from M/s Schering AG,Germany to M/s Schering, Korea in packs of 10x30ml for local-repacking at M/s Medipharm (Pvt) Ltd, Lahore in packs of 1x30ml on 02-01-1998.

c) Original and legalized Certificate of Pharmaceutical Product. d) Revised Sole Agency Agreement when there is change in MAH. e) Undertaking that the provided information/ documents are true/ correct.	• Approval for change parent company name form Schering Ag Germany to Bayer Schering Pharma Pharma AG Germany on **28-12-2010.** • Approval for change of name of Manufacturer to Bayer Pharma AG, Berlin Germany on 13-02-2014. • Approval for change of address of manufacturer on 19-10-2018. • Change of registration status to new title i.e. M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore on 25-07-2019. • Renewal due date (according to company name change) • 27-12-2020 • Renewal submit on 12-06-2018 **c)** Original & legalized CoPP issued by Germany**.** d) Provided e) provided.

Decision: **Registration Board considered and approved request of the firm for change in packaging site, change of address of the importer and product status change from bulk import to finished import for the already registered products as per details given below: -**

Name & Composition / Reg. No.	**Previous approved Site (as per approval) 19-10-2018**	**New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status**
Ultravist Injection 370 Solution for Injection Each ml contains: - Lopromide solution 0.769gm Reg. No. 009865	Manufacturer: - M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. Status: Bulk Import & locally repack at: M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	Product License Holder: M/s Bayer Vital GmbH 51368 Leverkusen, Germany. Bulk Manufacturer, Packaging and Final Release: M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany Imported by (Registration Holder) M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. Status: Finished Import.

Case No.02: **REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CHANGE IN PACKAGING SITE, CHANGE OF ADDRESS OF IMPORTER AND PRODUCT STATUS CHANGE FROM BULK IMPORT TO FINISHED IMPORT.**

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has applied for change in packaging site, change of address of importer and product status change from bulk import to finished import for their following already registered products as per details given below: -

Name & Composition / Reg. No.	**Existing approved Site (as per approval) 19-10-2018**	**New Proposed Sites as per COPP**
Ultravist Injection 300 Each 1 ml contains: - Lopromide solution 623mg Reg. No. 009866	**Manufacture: -** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Status:** Bulk Import & locally repack at M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Bayer Vital GmbH 51368 Leverkusen, Germany. **Bulk Manufacturer, Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

The firm has submitted the following supporting documents: -

Change of Address of Manufacturing Site/Source/Marketing Authorization Holder (MAH).	
Documents required as per SOPs	**Submitted documents by firm**
a) Application with required fee as per relevant SRO. b) Copy of registration letter and last renewal status.	a) Fee of Rs.150,000/- b) Reg. Letter and renewal trail • Copy of registration letter issued from the then Reg-I Section on 14-12-2012. • Approval for change of name of Manufacturer from M/s Bayer Schering Pharma AG, Germany to M/s Bayer AG Pharma AG Berlin, Germany on 08-09-2014 • Approval for change parent company name form Schering Ag Germany to Bayer Schering Pharma Pharma AG Germany on **28-12-2010.** • Approval for change of name of Manufacturer to Bayer Pharma AG, Berlin Germany on 13-02-2014. • Approval for change of address of manufacturer on 19-10-2018. • Change of registration status to new title i.e. M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore on 25-07-2019. • Renewal due date (according to Manf. Change name)

c) Original and legalized Certificate of Pharmaceutical Product. d) Revised Sole Agency Agreement when there is change in MAH. e) Undertaking that the provided information/ documents are true/ correct.	08-09-2019 • Renewal submit on 23-01-2017 **c)** Original & legalized CoPP issued by Germany**.** d) Provided e) Sole agency agreement provided.

Decision: **Registration Board considered and approved the firm request for change in packaging site, change of address of importer and product status change from bulk import to finished import for their following already registered products as per details given below: -**

Name & Composition / Reg. No.	**Previous approved Site (as per approval) 19-10-2018**	**New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status**
Ultravist Injection 300 Each 1 ml contains: - Lopromide solution 623mg Reg. No. 009866	**Manufacture: -** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Status:** Bulk Import & locally repack at M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Bayer Vital GmbH 51368 Leverkusen, Germany. **Bulk Manufacturer, Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

Case No.03: REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CHANGE IN PACKAGING SITE, CHANGE OF ADDRESS OF IMPORTER AND PRODUCT STATUS CHANGE FROM BULK IMPORT TO FINISHED IMPORT.

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has applied for change in packaging site, change of address of importer and product status change from bulk import to finished import for their following already registered products as per details given below: -

Name & Composition / Reg. No.	**Existing approved Site (as per approval) 19-10-2018**	**New Proposed Sites as per COPP**

Ultravist ®300 Solution for Injection Each ml contains: - Lopromide …….623mg (equivalent to 300mg Iodine) Reg. No. 072542 100ml	**Manufacture: -** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Status:** Bulk Import & locally repack at M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Bayer Vital GmbH 51368 Leverkusen, Germany. **Bulk Manufacturer, Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

The firm has submitted the following supporting documents: -

Change of Address of Manufacturing Site/Source/Marketing Authorization Holder (MAH).	
Documents required as per SOPs	**Submitted documents by firm**
a) Application with required fee as per relevant SRO. b) Copy of registration letter and last renewal status. c) Original and legalized Certificate of Pharmaceutical Product d) Revised Sole Agency Agreement when there is change in MAH. e) Undertaking that the provided information/ documents are true/ correct.	a) Fee of Rs.150,000/- b) Reg. Letter and renewal trail • Copy of registration letter issued 14-12-2012. • Change of registration status to new title i.e. M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore on 25-07-2019. • Renewal submit on 23-01-2017 c) Original & legalized CoPP issued by Germany**.** d) Provided e) Sole agency agreement provided.

Decision: Registration Board considered and approved the firm request for change in packaging site, change of address of importer and product status change from bulk import to finished import for their following already registered products as per details given below: -

Name & Composition / Reg. No.	**Previous approved Site (as per approval) 19-10-2018**	**New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status**

Ultravist ®300 Solution for Injection Each ml contains: - Lopromide …….623mg (equivalent to 300mg Iodine) Reg. No. 072542	**Manufacture: -** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Status:** Bulk Import & locally repack at M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Bayer Vital GmbH 51368 Leverkusen, Germany. **Bulk Manufacturer, Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

Case No.04: REQUEST OF M/S NOVARTIS PHARMA (PAKISTAN) LTD, KARACHI FOR PERMISSION FOR PRINTING LABELLING PARTICULARS ON OUTER BOX IN COMPLIANCE WITH DRUG (LABELLING AND PACKAGING) RULES, 1986 ON IMPORT OF REGISTERED PRODUCTS.

M/s Novartis Pharma (Pakistan) Ltd, C-21, SITE, Manghopir Road, Karachi has stated that due to very specific and limited usage in Pakistan and due to production constraints, they are unable to supply these products in the country-specific packs in low volumes.

Details of Products:

S. No.	Reg. No.	Name of Product	Remarks
1.	069519	Afinitor 5mg Tablets. Each tablet contains:- Everolimus …….5mg.	Reg. Letter date 26.02.2011. Renewal due date 12.11.2018. Renewal submit date 27.01.2016
2.	069520	Afinitor 10mg Tablets. Each tablet contains:- Everolimus ….10mg.	Reg. Letter date 26.02.2011. Renewal due date 12.11.2018. Renewal submit date 27.01.2016
3.	072543	Tasigna Capsules 150mg. Each capsule contains:- Nilotinib……150mg.	Reg. Letter date 20.12.2012 Renewal due date 19.12.2017 Renewal submit on 29.01.2018 Frim submit Rs.40,000/-
4.	052256	Tasigna 200mg Capsules. Each hard gelatin capsule contains:- Nilotinib…..200mg.	Reg. Letter date 13.11.2008. Renewal due date 12.11.2018. Renewal submit date 19.09.2018
5.	074855	Exelon Transdermal Patch. Each patch of 15 cm^2 contains:- 27mg rivastigmine base, in vivo release rate of 13.3mg/24 hours.	Reg. Letter date 18.08.2015 Renewal due date 17.08.2020 Renewal submit date 21.07.2020
6.	059068	Exelon 4.6mg Transdermal Patch. Each transdermal patch of 5cm^2 contains:- Rivastigmine 9mg and releases rivastigmine at the rate of 4.6mg/24hours.	Reg. Letter date 05.10.2009 Renewal due date 04.10.2019 Renewal submit date 04.09.2019

7.	059069	Exelon 9.5mg Transdermal Patch. Each transdermal patch of $10cm^2$ contains:- Rivastigmine 18mg and releases rivastigmine at the rate of 9.5mg/24hours.	-do-
8.	027321	Exelon capsules 6.0mg Each capsule contains carbamoylatine hydrogen tartrate 6.0mg	Reg. Letter date: 22-03-2002 due date: 21-03-2017 Renewal submit on:28-12-2016
9.	027322	Exelon capsules 4.5mg Each capsule contains carbamoylatine hydrogen tartrate 4.5mg	-do-
10.	023119	Exelon capsules 1.5mg Each capsule contains carbamoylatine as hydrogen tartrate 1.5mg	Reg. Letter date: 10-02-1999 due date: 09-02-2019 Renewal submit on: 21-01-2019.
11.	023120	Exelon capsules 3mg Each capsule contains carbamoylatine as hydrogen tartrate 3mg	-do-
12.	088393	Ultibro Breezhaler Inhalation Powder Capsule Each capsule contains: Indacaterol maleate.143mcg (eq. to 110mcg of Indacaterol) Glycopyrronium bromide.63mcg (eq to 50mcg Glycopyrronium)	Reg. Letter date 22.03.2018 Renewal due date 21.03.2023
13.	078119	Jakavi 5mg Tablets. Each tablet contains:- Ruxolitinib……5mg.	Reg. Letter date 20.03.2014 Renewal due date 19.03.2019 Renewal submit on 22.01.2019.
14.	078120	Jakavi 15mg Tablets. Each tablet contains:- Ruxolitinib……..15mg.	-do-
15.	078121	Jakavi 20mg Tablets. Each tablet contains:- Ruxolitinib……..20mg.	-do-
16.	014961	Sandimmum Neoral -Drink Solution 100mg/ml Each ml contains Ciclosporin 100mg	Reg. Letter date: 19-05-1994. Approval for change of name form Sandoz to Novartis: 23-06-2007 Due date: 22-06-2017 Submit date: 30-03-2017
17.	033196	Glivec 100mg Film Coated Tablets. Each tablet contains:- Imatinib mesylate 100mg.	Reg. Letter date 14-03-2005. Due date: 13-03-2020 Submit date 10-02-2020 Dy. No.1158 R&I dated 13-01-2022.
18.	033197	Glivec 400mg Film Coated Tablets. Each tablet contains:- Imatinib mesylate 400mg.	Reg. Letter date: 14-03-2005. Due date: 13-03-2020 Submit date: 19-01-2015

19.	069586	Onbrez Breezhaler Inhalation Powder Hard Capsule Each capsule contains: Indacaterol maleate equivalent to 150mcgIndacaterol	Dy.No.6680 R&I dated 10-03-2022 Reg. letter on 22-04-2011 Renewal submit on 09-03-2021 Due date 21-04-2021
20.	069587	Onbrez Breezhaler Inhalation Powder Hard Capsule Each capsule contains: Indacaterol maleate equivalent to 300mcg Indacaterol	**-do-**
21.	027324	Sandostatin Lar Injection 20mg Each vial contains:- Octreotide acetate 20mg.	Reg. Letter date: 22-03-2002 due date: 20-03-2017 Renewal submit on:28-12-2016
22.	027325	Sandoslatin Lar Injection 30mg Each vial contains: Octreotide acetate 30mg.	-do-
23.	072551	Zometa 4mg/100ml Solution for Infusion. Each 100ml contains:- Zoledronic Acid Monohydrate 4.264mg corresponds to 4.0mg of Zoledronic Acid Anhydrous.	Reg. Letter date: 13-03-2013 due date: 12-03-2018 Renewal submit on:13-11-2017
24.	008008	Sandimmum Infusion 50mg Each ml contains: - Cyclosporin 50mg	Reg. Letter date: 27-02-1985. Approval for change of name form Sandoz to Novartis: 23-06-2007 Approval for change of brand name on 08-05-2008. Due date: 07-05-2018 Submit date: 22-04-2018
25.	090523	Kisqali 200mg Film Coated Tablet. Each Film Coated Tablet Contains: Ribociclib (as succinate)…200mg	Reg. Letter date 25.06.2018 Renewal due date 24.06.2023

The firm has requested to allow them to print the following components on outer box of product locally at their licensed premises (DML No.000003, C-21, SITE, Area, Karachi) as per labeling and packaging rules 1986.

- Urdu text.
- Registration number.
- Maximum retail price.
- Name and address of sole agent.
- Other information (as per labeling requirements)

The firm has provided the following documents along with the application: -

a. Fee challan of Rs.10,000/- for each product.
b. Copy of registration letters, post registration variation & renewal trail.
c. Copy of valid drug manufacturing license No.000003 by way of formulation.

Decision: **Registration Board acceded to the request of firm for import of already registered above products in standard export packs. The Board advised the firm to locally print MRP and Registration Number along with Urdu text before sale of drug at their Licensed Premises of M/s Novartis Pharma (Pakistan) Ltd, C-21, SITE, Manghopir Road, Karachi (DML No.000003) to**

comply requirement as per drugs (labelling & packing) rules, 1986. This permission shall be valid for two (02) years only. The firm shall submit future plan regarding the import of drugs (labelling & packing) rules, 1986 compliant packs.

Case No.05: REQUEST OF M/S NOVARTIS PHARMA (PVT) LTD, KARACHI FOR EXTENSIONIN SHELF LIFE FROM 21 MONTHS TO 36 MONTHS OF ASUNRA 100MG DISPERSIBLE TABLETS (REG.NO.047517).

The subject case was discussed & deferred in 316th meeting of Registration Board as per following details.

M/s Novartis Pharma (Pakistan) Limited, Karachi has requested for extension in shelf life of registered product from 21 Months to 36 Months as per following details.

Reg. No.	Name/ Composition	Approved sites (as per approval)	Name of Sites (as per CoPP)	Initial registration letter with shelf life
047517	Asunra Dispersible tablets Each Dispersible tablet contains: Deferasirox…100mg	**Manufacturer: -** M/s. Novartis Pharma Stein AG, Switzerland.	**Manufacturer: -** M/s. Novartis Pharma Stein AG, Schaffhauserstrasse 4332 Stein, Switzerland	15-12-2007 Shelf life not mentioned in Reg. letter. Dy.No.16100 R&I DRAP 09-06-2021

The firm has submitted following documents as per SOP's

Documents required as per SOP's	Documents submitted by the firm
Application on Form 5A with required fee as per relevant SRO.	The firm has deposited a fee of Rs.7500/-
Copy of registration letter and last renewal status.	Registration letter issued on 15-12-2007 Due date of renewal is 14-12-2017 Submission of renewal is 10-11-2017
Proposed shelf-life, justification & data of long-term stability testing (as per conditions of zone IV-A) including chromatograms for a minimum of 3 commercial scale batches or development scale batches upto the proposed shelf-life.	Provided
Approval of regulatory body of country of origin or Original and legalized Certificate of Pharmaceutical Product as per WHO format.	Original & legalized CoPP issued by Swissmedic showing shelf life 36 Months
Undertaking that: i. Provided information is true & correct. ***For extension in shelf life:*** • No change to the primary packaging type in direct contact with the FPP and to the recommended conditions of storage. • No change in formulation and specification either of finished product, API and excipients etc.	Provided

• In case both the above conditions are involved then manufacturer will submit complete requisite information as per procedure.	

Remarks: -
As per provided CoPP the product is not on free sale in country of origin.

Decision 66th PRVC
The Committee evaluated the case and Chairman Registration Board, on the recommendations of the committee, decided to defer the request for confirmation of free sale status in any country of origin.

Fresh Proceedings
The firm has stated as under:
We are submitting an undertaking on stamp paper that Asunra 100mg tablets is registered and currently marketed in India, Sri Lanka, Ghana and Kenya with approved extended shelf life i.e. 36 months.

Decision 76th PRVC.
Keeping in view of above, Committee refer the case to Registration Board.

Decision:
Registration Board deferred the above case for confirmation of availability in exporting country or any RRA.

Reply of the firm:
The firm has submitted their reply as under: -
"Our principals, M/s. Novartis Switzerland, has declared that we had initially developed and registered 3 dose strengths of deferasirox dispersible tablets available in 125 mg, 250 mg, and 500 mg under the registered tradename "Exjade®" in Switzerland and many countries worldwide. Subsequent, to the initial registration of "Exjade®", Novartis further developed 100 mg and 400 mg deferasirox dispersible tablets and registered these additional dose strengths under the tradename "Asunra®" in Pakistan and a few other countries* worldwide. The 100 mg and 400 mg dose strengths of deferasirox dispersible tablets were registered for "export only" purposes in Switzerland under the tradename Exjade® dispersible tablets 100 mg and 400 mg. As a result, the tradename product Asunra® is listed for export only purposes in Switzerland and has never been marketed in this country".

Decision: Registration Board deliberated that availability of drug product either in country of origin or in reference regulatory authorities is prior condition of registration but in instant case the product does not qualify either of aforementioned parameter. Accordingly, the Board decided to seek guidance from DRAP Authority on the matter.

Case No.06: REQUEST OF M/S PFIZER PAKISTAN LIMITED, KARACHI FOR CHANGE IN REGISTRATION STATUS FROM BULK IMPORT TO FINISHED IMPORT WITH CHANGE IN MANUFACTURING SITE-ADRIBLASTINA 10MG&50MG.

M/s Pfizer Pakistan Ltd, 12 Dockyard Road, West Wharf, Karachi has applied for change in registration status from bulk import to finished import with change in manufacturing site for their following already registered products as per details given below: -

Name & Composition / Reg. No.	Existing approved Site (as per approval)	New Proposed Site / Manufacturer/ Product License Holder (as per COPP)
Adriblastina Injection 10mg Reg. No. 002580 Solvent ampoule Each ampoule contains: Nacl….47.7 Water for Injection…5.3ml q.s	**Manufacturer:** M/s Actavis Italy S.p.A., Italy.	**Product License Holder:** Pfizer Italia S.r.I. - Via lsonzo, 71 - 04100 Latina **Manufacturer:** M/s Corden Pharma Latina S.p.A Via del Murillo, Km 2,800 04013 Sermoneta, Latina, Italy **Manufacturer for Diluent for Adriblastina Injection 10mg only** M/s Alfasigma S.p .a. - Via E. Fermi 1- 65020 Alanno (PE) - Italy
Adriablastina RD (Rapid Dissolution) 50mg Freeze-dried powder for Injection Each vial contains: - Doxorubicin HCl 50mg Reg. No. 014606		

The firm has submitted the following supporting documents: -

Change of Address of Manufacturing Site/Source/Marketing Authorization Holder (MAH).	
Documents required as per SOPs	**Submitted documents by firm**
a) Application with required fee as per relevant SRO.	a) Fee of Rs.150,000/- for each product
b) Copy of registration letter and last renewal status.	b) Copy of Reg letter (22-04-1977). Approval for change of Name of Manf. Site on 9th Sept 2010. Approval for transfer of registrations from M/s Park Davis & Company to M/s Pfizer Pakistan Ltd, Karachi on 1st June, 2011. Last renewal on 28-05-2021 (due date 30-05-2021).
c) Original and legalized Certificate of Pharmaceutical Product.	c) Original & legalized CoPP for both products issued by EMA.
d) Revised Sole Agency Agreement when there is change in MAH.	d) Provided
e) Undertaking that the provided information/ documents are true/ correct.	e) Copy of sole agency authorization

Decision: Registration Board considered and approve request for change in registration status from bulk import to finished import with change in manufacturing site for their already registered products as per details given below: -

Name & Composition / Reg. No.	Previous approved Site (as per approval)	New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status
Adriblastina Injection 10mg Reg. No. 002580 Solvent ampoule Each ampoule contains: Nacl….47.7 Water for Injection…5.3ml q.s	**Manufacturer:** M/s Actavis Italy S.p.A., Italy. Repacked by: Pfizer Pakistan Limited B-2 S.I.T.E Karachi Pakistan	**Product License Holder:** Pfizer Italia S.r.I. - Via lsonzo, 71 - 04100 Latina **Manufacturer:** M/s Corden Pharma Latina S.p.A Via del Murillo, Km 2,800 04013 Sermoneta, Latina, Italy **Manufacturer for Diluent for Adriblastina Injection 10mg only** M/s Alfasigma S.p .a. - Via E. Fermi 1- 65020 Alanno (PE) - Italy Finished Import
Adriablastina RD (Rapid Dissolution) 50mg Freeze-dried powder for Injection Each vial contains: - Doxorubicin HCl 50mg Reg. No. 014606		

Case No.07: REQUEST OF M/S PFIZER PAKISTAN LIMITED, KARACHI FOR CHANGE IN REGISTRATION STATUS FROM BULK IMPORT TO FINISHED IMPORT WITH CHANGE IN ADDRESS (ADMINISTRATIVE) OF MANUFACTURING SITE –CYTOSAR INJECTION 100MG&500MG.

M/s Pfizer Pakistan Ltd, B-2, SITE, Karachi has applied for change in registration status **from bulk import to finished import** with **change in manufacturing site address (administrative)** for their following already registered products as per details given below: -

Name & Composition / Reg. No.	Existing approved Site (as per Letter No.F312-RB/2021-PR-I dated 03-11-2021)	New Proposed change in Administrative address
Cytosar Injection 100mg (IV) Each vial contains: - Cytarabine….100mg (Manufacturer Specification) Reg. No. 005771	**Manufacturer:** M/s Corden Pharma Latina S.p.A Via del Murillo, Km 2,800 04013 Sermoneta, Latina, Italy **Labelling, Repacking & Quality Control Site:** M/s Pfizer Pakistan Ltd, B-2, SITE, Karachi.	**Product License Holder:** Pfizer Holding France 23-25, avenue du docteur lannelongue 75014 paris France **Manufacturer:** M/s Corden Pharma Latina S.p.A Via del Murillo, km 2800 04013-Sermoneta (Latina) Italy
Cytosar Injection 500mg (IV) Each vial contains: - Cytarabine….500mg (Manufacturer Specification) Reg. No. 022545	**-do-**	**-do-**

The firm has stated that the change in address is purely administrative in nature & the firm has also submitted regional approval for the same.

The firm has submitted the following supporting documents: -

a) Fee of Rs.150,000/- for each product
b) Copy of Reg. Transfer letter (01-06-2011).
   Approval for change in Manf. of bulk import & Local repacking of drugs on 03-11-2021.

Last renewal on 28-05-2021 (due date 01-06-2021).
Approval of country of origin.

c) Original legalized CoPP

Decision: **Registration Board considered and approved request of the firm for change in registration status from bulk import to finished import with change in manufacturing site address (administrative) for their already registered products as per details given below: -**

Name & Composition / Reg. No.	Previous approved Site (as per Letter No.F312-RB/2021-PR-I dated 03-11-2021)	New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status
Cytosar Injection 100mg (IV) Each vial contains: - Cytarabine….100mg (Manufacturer Specification) Reg. No. 005771	**Manufacturer:** M/s Corden Pharma Latina S.p.A Via del Murillo, Km 2,800 04013 Sermoneta, Latina, Italy **Labelling, Repacking & Quality Control Site:** M/s Pfizer Pakistan Ltd, B-2, SITE, Karachi.	**Product License Holder:** Pfizer Holding France 23-25, avenue du docteur lannelongue 75014 paris France **Manufacturer:** M/s Corden Pharma Latina S.p.A Via del Murillo, km 2800 04013-Sermoneta (Latina) Italy
Cytosar Injection 500mg (IV) Each vial contains: - Cytarabine….500mg (Manufacturer Specification) Reg. No. 022545	**-do-**	**-do-**

Case No.08: REQUEST OF M/S AGP LIMITED, KARACHI FOR REGISTRATION OF DRUGS TO THEIR NAME.

M/s AGP Limited, B-23-C, SITE, Karachi has submitted an application for registration of following already registered products from M/s. Novartis Pharma (Pakistan) Ltd, 15 West Wharf Karachi to their name. Detail of each proposed product is as under: -

Product-1: Gemcitabin "Ebewe" 1g Injection (Reg.No. 066183)		
S. No.	**Name / Detail of Documents**	**Documents/information provided by the firm**
1.	Product Name/ Composition	**As per approval** Gemcitabin "Ebewe" 1g Injection. Each vial contains:- Gemcitabine……..1gm **As per CoPP** Gemcitabin "Ebewe 10mg/ml Concentrate for solution for infusion Each ml contains:- Gemcitabine HCL eq. to Gemcitabine……..10mg As per Form-5F Gemcitabine Fareva 1g Injection
	Reg. date / renewal status	Reg. Letter issued on 04-12-2010 (due date 03-12-2020) Renewal submit on 20-10-2020.

	Name and address of Applicant(Transferee)	M/s AGP Limited, B-23-C, SITE, Karachi.
	Name of Transferor	M/s. Novartis Pharma (Pakistan) Ltd, 15 West Wharf, Karachi.
	Detail of Drug Sale License	**DSL No.045 (valid upto 21-09-2023)** **Address:** M/s AGP Limited, B-23-C, SITE, Karachi. **Godown address:** 1. M/s AGP Limited, B-23-C, SITE, Karachi. 2. Burma Oil Mills Limited, TCW Plot No. 1&2 Boat Building Yard Area West Wharf, Karachi.
	Name and address of Manufacturer / Product License Holder	**As per approval** **Manufacturer**: M/s. Ebewe Pharma Ges.m.b.H. Unterach, Austria. **As per CoPP:** **Product License Holder:** M/s Ebewe Pharma Ges.m.b.H. Nfg KG, MondseestraBe 11, 4866 Unterach, am attersee, Austria. **Manufacturer.** **Manufacturer.** M/s Fareva Unterach GmbH, MondseestraBe 11, 4866 Unterach, am attersee, Austria.
	Name of exporting Country	Austria
	Diary No. & Date of R& I	Dy. No. 32493 Dated 08/12/2021.
	Finished Product Specification	Not mentioned in Reg. Letter.
	Shelf life	02 Years (as per Reg. Letter)
	Pack Size	Per Vial (as per Reg. Letter)
	Remarks: -	

The firm has submitted the following supporting documents / information for approval of above transfer of registrations: -

a) Fee of Rs.150,000/- for each product.
b) Applications on Form-5F.
c) Copy of Registration letters and renewal trail, detail as mentioned above table.
d) Original legalized CoPP issued by Austria for above products.
e) Copy of Termination letter from M/s Ebewe Pharma, MondseestraBe 11, 4866 Unterach am Attersee, Austria in the name of M/s. Novartis Pharma (Pakistan) Ltd, 15 West Wharf, Karachi for above products.
f) Copy of Letter of authorization in the name of M/s AGP Limited, B-23-C, SITE, Karachi from M/s Ebewe Pharma, MondseestraBe 11, 4866 Unterach am Attersee, Austria for above products.
g) Copy of NOC for transfer of registrations from M/s. Novartis Pharma (Pakistan) Ltd, 15 West Wharf, Karachi **(issued on 09-08-2021).**
h) An undertaking that annexed documents is correct and true is required

Decision: Keeping in view the above position, Registration Board decided as follow;

a. Approved the cancellation of registration of following product from the name of M/s Novartis Pharma (Pakistan) Ltd, 15 West Wharf, Karachi.

S. No	Reg. No.	Name & Composition

1.	**066183**	**Gemcitabin "Ebewe" 1g Injection Each ml contains:- Gemcitabine HCL eq. to Gemcitabine……..10mg**

b. Approved the registration of above product in the name of M/s AGP Limited, B-23-C, SITE, Karachi as per policy for imported finished drug registration (in accordance with details of composition and manufacturer as per CoPP) and firm will submit the fee as per SRO for correction in manufacturer in covering letter.

c. A reference shall be sent to Costing & Pricing Division for their comments regarding MRP of the said product.

Case No.09: REQUEST OF M/S ELI LILLY PAKISTAN LTD, KARACHI FOR UPDATE LEAFLET FOR NEW INDICATION OF REGISTERED PRODUCTS.

M/s Eli Lilly Pakistan Ltd, Karachi has submitted request for update leaflet for new indication for their registered products. Details of products are as under: -

S. No	Reg. No.	Name of Drug(s) & Composition.	Manufacturer & Marketing Authorization Holder
1	110560	Yulareb 50mg Film coated Tablets Each film coated tablet contains: Abemaciclib……..50mg	**Product License Holder:** M/s Eli Lilly Nederland B.V., Panendorpseweg 83, 3528BJ Utrecht, the Netherlands. **Manufacturer & Quality Control Site:** M/s Lilly del Caribe, Inc., 12.6Km, 65th Infantry Road, Carolina, 00985 Puerto Rico. **Packing and Released Site:** Lilly S.A., Avda. De la Industria 30, 28108 Alcobendas, Madrid Spain.
2	110561	Yulareb 100mg Film coated Tablets Each film coated tablet contains: Abemaciclib……..100mg	
3	110562	Yulareb 150mg Film coated Tablets Each film coated tablet contains: Abemaciclib……..150mg	

Previously approved Indication	New additional EMA-approved
Advanced or Metastatic Breast Cancer Verzenios is indicated for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a LHRH agonist	Early Breast Cancer Verzenios in combination with endocrine therapy is indicated for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence (see section 5.1). In pre- or perimenopausal women, aromatase inhibitor endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

Firm has submitted following documents: -

a) Application with a fee of Rs.10,000/- for each product (Reg. Letter issued on 23rd April, 2022).
b) Justification of proposed change.
c) Copy of EMA approval.
d) Copy of existing leaflet.
e) Copy of proposed leaflet.
f) An undertaking.

Decision: Registration Board considered and approve request of the firm for a new indication as per EMA approval.

Case No.10: REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CANCELLATION OF REGISTRATION OF IMPORTED DRUGS.

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has submitted request for cancellation of registrations of imported drugs which were registered at C-21, SITE, Karachi plant which has been divested.

S. No	Product(s) Name	Reg. No.	Reason for De-Reg. (stated by firm)	Alternative registered product
1.	Angeliq Tablet 2mg Each film coated tablets contains: - Estradiol ..... l.0mg. Drospirenone..... 2.0mg.	059088	The licensed facility of product registration holder / importer i.e. C-21, SITE, Karachi has already been divested in 2020-21 and transfer of registrations were also not processed (but applied for the issuance of cancellation of registration since Mar, 2021) as it was not feasible for a company to import, re-launch and market these products due to the availability of more advance therapies with better patient compliance in Pakistan Hence, registrations of both the products are already no more valid. Therefore, requesting for the issuance of formal letter for cancellation of registration.	Estranor(Saffron) Star-Gest (Mass Pharma)
2.	Nebido Solution for Injection 1000mg Each ampoule of 4ml contains: - Testosterone Undecanoate.....1000mg.	059089	-do-	Testonon (Zafa), Danabol (Danas), Lyssa (Mass Pharma), Testosterone (Geofman)
3.	Qlaira Tablet Each wallet (28 film coated tablets) contains: -	088370	The licensed facility of product registration holder / importer i.e. C-21, SITE, Karachi has already been divested in 2020-21 and transfer of registrations were also not processed	Desofam (Zafa), Hytrade-C (Hygeia),

	Part I (2 dark yellow film coated tablets-Core) Estradiol valerate...3.0mg. Part II (5 medium red film-coated tablets-Core) Estradiol valerate...2.0mg. Dienogest....2.0 mg. Part III (17 light yellow film-coated tablets-Core) Estradiol valerate...2.0mg. Dienogest....3.0 mg. Part IV (2 dark red film-coated tablets-Core) Estradiol valerate...1.0mg. Part V (2 white film-coated tablets-Core) Placebo		(but applied for the issuance of cancellation of registration since Mar, 2021) as it was not feasible for a company to import, re-launch (never launched before due to pricing / cost) and market Qlaria due to the very high production cost and low granted price (hardship was also not applied due to the fact that price will not be feasible for the patients in Pakistan as no reimbursement / out of pocket. Also alternative therapies / other oral contraceptives are available in a low price). Hence registrations of Qlaria is already no more valid. Therefore, requesting for the issuance of formal letter for cancellation of registration.	Geogynon (Geofman Pharma)

SOP Requirement	**Firms Response**
a) Application.	a. Application with a fee Rs.10,000/- for each product.
b) Copy of registration letter	b. Copy of registration letter Sr. No. 1 & 2 (Reg. Letter date 21-10-2009). Change of company name on 21-10-2010 Renewal submit on 24-06-2015. Sr. No.3, Reg. Letter issued on 28-02-2018.
c) Justification.	c. As mentioned above.
d) List of alternatives brands/ FPPs available in the country.	d. No alternative brands / FPPs is available in the Pakistan.
e) An undertaking that: i. No case is pending at any forum / court of law regarding this product. ii. Provided information/ documents are true/ correct.	e. Provided by the firm.

Decision: Registration Board referred the case for views of DRAP's committee on availability of life saving drugs regarding need of products and availability of alternate drug products/ brands.

Case No.11: REQUEST OF M/S NOVARTIS PHARMA FOR CANCELLATION OF REGISTRATION OF IMPORTED DRUGS.

M/s Novartis Pharma Pakistan has submitted request for cancellation of registration of imported drug as per following details.

S. No	Product(s) Name	Reg. No.	Reason for De-Reg. (stated by firm)	Alternative registered product
1.	Foradil Dry Powder Capsules for inhalation (with Inhaler). Each capsule contains: - Formoterol fumarate 12ug	028454	Due to global directives as we have divested this portfolio in Pakistan	Airease (Formoterol fumarate) Reg. No. 039306 of M/s Platinum Pharmaceutical

SOP Requirement	Firms Response
a) Application. b) Copy of registration letter. c) Justification. d) List of alternatives brands/ FPPs available in the country. e) An undertaking that: i. No case is pending at any forum / court of law regarding this product. ii. Provided information/ documents are true/ correct.	a. Application with a fee Rs.7,500/- for each product. b. Copy of registration letter (Reg. Letter date 07-05-2003). Renewal submit on 02-04-2018. c. As mentioned above. d. As mentioned above. e. Provided by the firm.

Decision: Registration Board referred the case for views of DRAP's committee on availability of life saving drugs regarding need of products and availability of alternate drug products/ brands

Case No.12: REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CANCELLATION OF REGISTRATION OF IMPORTED DRUGS.

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has submitted request for cancellation of registrations of imported drugs as per following details:

S. No	Product(s) Name	Reg. No.	Reason for De-Reg. (stated by firm)	Alternative registered product
1.	Bonefos 60mg/ml Each ml contains: - Dinatr.Clodron. tetrahydr. Respond Dinatr.clodron.anhydr 60mg.	013032	Manufacturing site is no more able to produce and supply Bonefos for Pakistan and also the availability of advance therapies better patient compliance, it is not possible for a company to import and market Bonefos.	Adronil Injection (M/s Searle) Bonviva Injection (M/s Roche) Ibnate (M/s Genix)

SOP Requirement	Firms Response
a) Application.	a. Application with a fee Rs.10,000/-.

b) Copy of registration letter	b. Transfer of Reg. (on 21-10-1998). Change of Manf site 10-02-2004 Change of name of source on 28-12-2010
c) Justification.	c. As mentioned above.
d) List of alternatives brands/ FPPs available in the country.	d. As mentioned above.
e) An undertaking that: i. No case is pending at any forum / court of law regarding this product. ii. Provided information/ documents are true/ correct.	e. Provided by the firm.

Decision: Registration Board referred the case for views of DRAP's committee on availability of life saving drugs regarding need of products and availability of alternate drug products/ brands.

Case No.13: REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CHANGE IN PACKAGING SITE, CHANGE OF ADDRESS OF IMPORTER AND PRODUCT STATUS CHANGE FROM BULK IMPORT TO FINISHED IMPORT.

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has applied for change in packaging site, change of address of importer and product status change from bulk import to finished import for their following already registered products as per details given below: -

Name & Composition / Reg. No.	Existing approved Site (as per approval) 19-10-2018	New Proposed Sites as per COPP (No.018/22)
Diane 35 Tablets Each coated tablet contains: - Cyproterone acetate..2mg Ethinyl estradiol… 0.035mg Reg. No. 011467	**Manufacturer:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Final Packing & Quality Control Release:** M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Jenapharm GmbH & Co. KG Otto-Schott-Strasse 15 07745 Jena, Germany. **Bulk Manufacturer:** M/s Bayer Weimar GmbH und Co. KG Dobereinerstrasse 20 99427 Weimar, Germany. **Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

The firm has submitted the following supporting documents: -

Change of Address of Manufacturing Site/Source/Marketing Authorization Holder (MAH).	
Documents required as per SOPs	**Submitted documents by firm**
a) Application with required fee as per relevant SRO.	a) Application with a Fee of Rs.150,000/-

b) Copy of registration letter and last renewal status.	b) Reg. Letter and renewal trail: • Copy of registration letter issued from the then Reg-I Section on 21-08-1990. • Transfer of Reg. to to M/s Medipharm (Pvt) Ltd, 7-A, Gulberg-II, Lahore on 12-03-1992. • Permission for import in bulk and repack locally on 11-03-1996. • Approval for change parent company name form Schering Ag Germany to Bayer Schering Pharma Pharma AG Germany on **28-12-2010.** • Approval for change of name of Manufacturer on 13-02-2014. • Approval for change of address of manufacturer on 19-10-2018. • Change of registration status to new title i.e. M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore on 25-07-2019. • Renewal due date (as per Reg. Letter) 20-08-2020 • Renewal submit on 08-06-2020
c) Original and legalized Certificate of Pharmaceutical Product. d) Revised Sole Agency Agreement when there is change in MAH. e) Undertaking that the provided information/ documents are true/ correct.	**c)** Original & legalized CoPP issued by Germany**.** d) Provided e) Sole agency agreement provided. f) Provided

Firm covering letter needs correction which shows previous address of manufacturer

Decision: **Registration Board considered and approved request of the firm for change in packaging site, change of address of importer and product status change from bulk import to finished import for their already registered products, as per details given below: -**

Name & Composition / Reg. No.	Previous approved Site (as per approval) 19-10-2018	New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status (No.018/22)
Diane 35 Tablets Each coated tablet contains: - Cyproterone acetate..2mg Ethinyl estradiol… 0.035mg Reg. No. 011467	**Manufacturer:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Final Packing & Quality Control Release:** M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore (approved on 25-07-2019)	**Product License Holder:** M/s Jenapharm GmbH & Co. KG Otto-Schott-Strasse 15 07745 Jena, Germany. **Bulk Manufacturer:** M/s Bayer Weimar GmbH und Co. KG Dobereinerstrasse 20 99427 Weimar, Germany. **Packaging and Final Release:** M/s Bayer AG Mullerstrasse 178 13353 Berlin, Germany. **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

Case No.14: REQUEST OF M/S BAYER PAKISTAN (PVT) LIMITED FOR CHANGE IN PACKAGING SITE, CHANGE OF ADDRESS OF IMPORTER AND PRODUCT STATUS CHANGE FROM BULK IMPORT TO FINISHED IMPORT.

M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi has applied for change in packaging site, change of address of importer and product status change from bulk import to finished import for their following already registered products as per details given below: -

Name & Composition / Reg. No.	Existing approved Site (as per approval) 08-05-2020	New Proposed Sites as per COPP (No.164/21)
Progynova Tablets Each coated tablet contains: - Estradiol Valerate 2.0mg Reg. No. 017864	**Product License Holder:** M/s Jenapharm GmbH & Co. KG Otto-Schott-Strasse 15 07745 Jena, Germany. **Bulk Manufacture:** M/s Bayer Weimar GmbH & Co. KG Weimar, Germany. **Packing & Final Release:** M/s Bayer Weimar GmbH & Co. KG Weimar, Germany. **Repacked by:** M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore.	**Product License Holder:** M/s Jenapharm GmbH & Co. KG Otto-Schott-Strasse 15 07745 Jena, Germany. **Bulk Manufacturer Packaging and Final Release:** M/s Bayer Weimar GmbH und Co. KG Dobereinerstrasse 20 99427 Weimar, Germany. **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

The firm has submitted the following supporting documents: -

Change of Address of Manufacturing Site/Source/Marketing Authorization Holder (MAH).	
Documents required as per SOPs	**Submitted documents by firm**
a) Application with required fee as per relevant SRO. b) Copy of registration letter and last renewal status.	a) Application with a Fee of Rs.150,000/- b) Reg. Letter and renewal trail: • Copy of registration letter issued from the then Reg-I Section on 27-09-1995. • Permission for import in bulk and repack locally on 18-01-1996. • Approval for change of Manf. Site on 12-05-2001. • Approval for change parent company name form Schering Ag Germany to Bayer Schering Pharma Pharma AG Germany on **28-12-2010.** • Approval for change of Manufacturer on 05-06-2017. • Change of registration status to new title i.e. M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore on 25-07-2019. • Approval of change of manufacturing /packaging site on 08-05-2020.

c) Original and legalized Certificate of Pharmaceutical Product. d) Revised Sole Agency Agreement when there is change in MAH. e) Undertaking that the provided information/ documents are true/ correct.	• Renewal due date (as per Reg. Letter) 26-09-2020 • Renewal submit on 08-06-2020 **c)** Original & legalized CoPP issued by Germany**.** d) Provided e) Provided

Decision: Registration Board considered and approve request of the firm for change in packaging site, change of address of importer and product status change from bulk import to finished import for their already registered products, as per details given below: -

Name & Composition / Reg. No.	**Existing approved Site (as per approval) 08-05-2020**	**New Approved Name of Manufacturer / Product License Holder (as per COPP)/import status (No.164/21)**
Progynova Tablets Each coated tablet contains: - Estradiol Valerate 2.0mg Reg. No. 017864	**Product License Holder:** M/s Jenapharm GmbH & Co. KG Otto-Schott-Strasse 15 07745 Jena, Germany. **Bulk Manufacture:** M/s Bayer Weimar GmbH & Co. KG Weimar, Germany. **Packing & Final Release:** M/s Bayer Weimar GmbH & Co. KG Weimar, Germany. **Repacked by:** M/s Bayer Pakistan (Pvt) Ltd, 108 Kot Lakhpat Industrial Estate, Lahore.	**Product License Holder:** M/s Jenapharm GmbH & Co. KG Otto-Schott-Strasse 15 07745 Jena, Germany. **Bulk Manufacturer Packaging and Final Release:** M/s Bayer Weimar GmbH und Co. KG Dobereinerstrasse 20 99427 Weimar, Germany. **Imported by (Registration Holder)** M/s Bayer Pakistan (Pvt) Ltd, Korangi Industrial Area, Plot No. 23, Sector No.22, Karachi. **Status:** Finished Import.

Case No.15: REQUEST OF M/S AJ MIRZA PHARMA (PVT) LTD, KARACHI FOR PERMISSION OF EXEMPTION OF URDU TEXT ON THE REGISTERED PRODUCT IMATIB-100MG CAPSULE (REG.NO.110582).

M/s AJ Mirza Pharma (Pvt) Ltd, First Floor, Shafi Court Merewether Road, Civil Lines, Karachi has stated that on the basis of demand we import registered product Imatib-100mg Capsule (Reg. No.110582) 2,047 boxes each containing 12 pack of 10's, standard export packs for one time only, as their manufacturer will be able to provide this medicine in country specific packs after 6 months.

Details of Product:

S. No.	**Reg. No.**	**Name of Product**	**Remarks**
1.	110582	Imatib Capsules 100mg Each Capsule contains: Imatinib (as mesylate) …..100mg	Reg. Letter date 20.07.2022.

The firm has requested to allow them to print the following components on outer box of product locally at licensed premises i.e. Plot no.44,Sector 27, Korangi Industrial Area, Karachi DML No.000234 as per labeling and packaging rules 1986.

- Urdu text.
- Registration number.
- Maximum retail price.
- Name and address of sole agent.
- Other information (as per labeling requirements)

The firm has provided the following documents along with the application: -

a. Fee challan of Rs.10,000/- for said product.
b. Copy of registration letter.
c. Copy of art work.
d. An undertaking.

Decision: **Registration Board acceded to the request for import of their already registered above product in standard export packs. The Board advised the firm for local printing of MRP and Registration Number along with Urdu text before sale of the drug at Licensed Premises of M/s AJ Mirza Pharma (Pvt) Ltd Plot No.44, Sector 27, Korangi Industrial Area, Karachi (DML No.000234) to comply requirement as per Drugs (labelling & packing) rules, 1986. This permission shall be valid for one time only. The firm shall submit future plan regarding the import of drugs (labelling & packing) rules, 1986 compliant packs.**

Case No.16: REQUEST OF M/S HOSPITAL SUPPLY CORPORATION, KARACHI FOR CHANGE OF ADDRESS OF MANUFACTURING SITE (MEDICAINE INJECTION REG. NO.023645)

M/s Hospital Supply Corporation, Karachi has applied for approval of change of address of manufacturing site for their already registered product medicaine injection (Reg. No. 023645) as per details given below:

Reg. No.	Name & Composition (as per approval)	Existing approved Manufacturing Site (as per approval)	New Proposed Site / Manufacturer & Product License Holder (as per COPP)
023645	**As per Approval** Kwang Myung Lidocaine HCL Injection. Each 1.8ml cartridge contains:- Lidocaine Hcl USP 36mg. Epinephrine Bitrtrate USP 0.324mg (Eq to 0.018mg of Epinephrine) **As per Transfer letter** Kwang Myung Lidocaine HCL Injection (Medicaine Injection)	M/s Kwang Myung Pharm. Co. Ltd 907, Sangshin – RI, Hyangnam – Myun, Hwaseong-Kun, KyuncGI-Do, Rep. of Korea.	**Manufacturer & Product License Holder: -** M/s Huons Co., Ltd, 100 Bio Valley-ro, Jecheon-si, Chungcheongbuk-do, Republic of Korea

The firm has submitted the following supporting documents: -

1. Fee of Rs. 100,000/- dated 09-07-2019.
2. Application on Form-5F
3. Copy of initial registration letter 26-05-1999 & transfer letter 15-05-2000 with renewal last renewal status.
4. Original & legalized COPP with free sale status of the product.
5. Original & legalized GMP certificate
6. Original & legalized Free Sale Certificate.
7. Original agent agreement
8. Letter of Authorization from product license holder.
9. Copy of DSL.
10. Prescribed undertaking.

Decision M-296: Registration Board approved the change of address of manufacturing site of following registered product medicaine injection (Reg. No. 023645) subject to policy for inspection of manufacturer abroad for imported finished drugs. Other terms and conditions will remain the same.

Reg. No.	Name & Composition (as per approval)	Existing approved Manufacturing Site (as per approval)	New approved Site / Manufacturer & Product License Holder (as per COPP)
023645	**As per Approval** Kwang Myung Lidocaine HCL Injection. Each 1.8ml cartridge contains:- Lidocaine Hcl USP 36mg. Epinephrine Bitrtrate USP 0.324mg (Eq to 0.018mg of Epinephrine) **As per Transfer letter** Kwang Myung Lidocaine HCL Injection (Medicaine Injection)	M/s Kwang Myung Pharm. Co. Ltd 907, Sangshin – RI, Hyangnam – Myun, Hwaseong-Kun, KyuncGI-Do, Rep. of Korea.	**Manufacturer & Product License Holder: -** M/s Huons Co., Ltd, 100 Bio Valley-ro, Jecheon-si, Chungcheongbuk-do, Republic of Korea

The comments /remarks of Legal Affair Division are as under:

> *"The instant case is of import of un-registered drug from a manufacturer which was not approved by the Registration Board yet. Moreover, mere approval by the Registration Board does not create any vested right of registration for any company / firm till the registration letter / post registration variation letter is issued. Therefore, the PE&R Division may process the case for prosecution of import of unregistered drug".*

Area FID Report

It is pertinent to mention that the clearance of the product under question was given in light of registration letter no.F.1-16/93-Reg-I dated 4th November, 2004 in which the name of manufacturer was changed from M/s Kwang Myung Pharm.Co.Ltd: 907, Sangshin-ri, Hyangnam-Myun, Hwaseong-city, Kyunggi-do. Rep.of Korea to M/s Huons Co. Ltd Korea whereas the address of the manufacturer is not mentioned.

In the light of above it is established that M/s Hospital Supply Corporation Karachi has imported consignment of Medicaine Injection from the new source before getting the approval letter.

Decision: Registration Board deliberated on the opinion of the Legal Affairs Division to prosecute the firm for import of unregistered . The Board after deliberation decided to issue show cause notices to the firm M/s Hospital

Supply Corporation, Karachi, under section 7 (11) read with 42 of the Drugs Act, 1976 for violation the condition of registration as reported by area FID.

Case No.17: REQUEST OF M/S NOVARTIS PHARMA (PAKISTAN) LIMITED, KARACHI FOR PERMISSION OF EXEMPTION OF URDU TEXT ON THE REGISTERED PRODUCT SANDOSTATIN 0.5mg/AMPOULE (REG. # 086485).

M/s Novartis Pharma (Pakistan) Limited, 15 West Wharf Dockyard Road, Karachi has stated that said product has very specific and limited usage in Pakistan and due to the production constraints, we are unable to supply this imported product in the country specific packs in low volumes.

Details of Product:

S. No.	Reg. No.	Name of Product	Remarks
1.	086485	Sandostatin 0.5mg/ml Ampoule Each 1 ml ampoule contains:- Octreotide…..0.5mg (As per Innovator's Specification)*	Reg. Letter date 12.02.2018.

The firm has requested to allow them to print the following components on outer box of product locally at licensed premises i.e. C-21, SITE, Karachi DML No.000003 as per labeling and packaging rules 1986.

- Urdu text.
- Registration number.
- Maximum retail price.
- Name and address of sole agent.
- Other information (as per labeling requirements)

The firm has provided the following documents along with the application: -

a. Fee challan of Rs.10,000/- for said product.
b. Copy of registration letter.

Decision: Registration Board acceded to the request of firm for import of their already registered above product in standard export packs. The Board advised the firm to locally print MRP and Registration Number along with Urdu text before sale of drug at their Licensed Premises of M/s Novartis Pharma (Pakistan) Ltd, C-21, SITE, Manghopir Road, Karachi (DML No.000003) to comply requirement as per drugs (labelling & packing) rules, 1986. This permission shall be valid for two (02) years only. The firm shall submit the future plan regarding the import of drugs (labelling & packing) rules, 1986 compliant packs.

Case No.18: REGISTRATION OF DRUGS.

Registration Board in its 261st meeting approved the following product of M/s. Amtul Pharmaceuticals, Lahore as per decision mentioned alongside each;

1	Importer M/s. Amtul Pharmaceuticals, 251-Sikandar Block Allama Iqbal Town, Lahore Manufacturer: M/s REYOUNG PHARMACEUTICAL CO.No.6, Erlangshan Road,Yiyuan County,Shandong Province, P.R. China. Priority # 85	Omulcer 40mg Injection Each vial of lyophilized powder contains:- Omeprazole Sodium 40mg Proton Pump Inhibitior Specifications:- Manufacturer	Pack size one vial Rs. 750/-	Approved as per Import Policy for Finished Drugs.

Now, M/s AMB HK Enterprises (Pvt) Ltd, Lahore has submitted request for registration of above product on their name and submitted following documents: -

- Original cancellation letter from REYOUNGE to M/s Amtul Pharmaceuticals, Lahore.
- Original agreement of REYOUNGE with M/s AMB HK Enterprises (Pvt) Ltd, Lahore.
- Original CoPP for Omeprazole 40mg Injection.

In view of above, a letter vide No.F.1-8/2020-I&V-II/Human Import dated 31st May, 2022 & reminder for the same dated 24th August, 2022 was conveyed to the firm and advised to submit fresh sole agency agreement letter in your name form product license holder and no reply from the M/s Amtul Pharmaceuticals, Lahore received.

Decision: **Registration Board considered the case and decided to issue a reminder to M/s. Amtul Pharmaceuticals, Lahore for submission of fresh sole agency agreement letter in their name form product license holder.**

Case No.19: REQUEST OF M/S SHAMCO TRADERS (PVT) LTD, LAHORE.

M/s Shamco Traders (Pvt) Ltd, 174-A, Ahmad Block, New Garden Town, Lahore has stated that they applied for registration of Lekarnitin IV Injection manufactured by Mefar Ilac Sanayii, Istambul, Turkey and got Registration letter on 13-12-2018 and company is since then importing and marketing this product.

Very recently another product with same salt and same manufacturer that is Mefar Ilac Sanayii, Istambul, Turkey is registered. Its brand name is metacartin imported by M/s Genome Pharma.

Details of above product as per I&V record is as under:

Imported by M/s Shamco Traders (Pvt) Ltd, Reg. letter issued on 13-12-2018 (M-284)		
Reg. No.	**Name of Drug**	**Manufacturer / PLH**
093928	Lekarnitin IV Injection 1g/5ml Each ml contains: Levocarnitine…**200mg** (USP Specification's)	**Manufacturer:** M/s mefar ilac sanayii a.s. Ramazanoglu mah. Ensar cad. No:20 kurtkoy pendik/ Istanbul, Turkey. **Product License Holder:** M/s Pharmada ilac sanayi. Ve ticaret a.s. Dem plaza, inonu mah. Kayisdagi cad no:172 b 34755 atasehir-Istanbul, Turkey
Imported by M/s M/s Genome Pharma, Reg. letter issued on 21-08-2020 (M-293)		
103770	Metacartin 1g/5ml Solution for I.M/ I.V Injection Each 5ml contains: Levocarnitine…..**1.00g** (USP Specification)	**Manufacturer :-** M/s Mefar Ilac Sanayi A.S. Ramazanoglu Mah. Ensar Cad. No: 20 34906 Kurtkoy-Pendik/ Istanbul. **Product License Holder:**

		M/s World Medicine Ilac San. Ve Tic. A.S. 15 Temmuz Mah. Cami Yolu Cad. No: 50 34212 Gunesli, Bagcilar/ Istanbul**.**

The firm is requested to know that is it legally correct to allow another brand with the similar active ingredient of the same foreign manufacturer to be registered and imported in Pakistan.

Decision of 79th meeting of PRVC:

On the recommendations of the committee, Chairman Registration Board considered and refer the case to Registration Board.

Proceeding of 278th meeting of Registration Board on such cases having same manufacturer is asunder:

Registration Board called up Deputy Director, Legal Affairs Division to further elaborate their opinion regarding the sole agency agreement. Deputy Director, Legal Affairs Division apprised the Board that Registration Board may grant registration of said product to any firm which produces sole agency agreement from the manufacturer, product license holder or authorized distributor of the product license holder and fulfill the requirements of Form-5A.

Decision: Registration Board endorsed proceeding of 278th meeting.

Case No.20: REQUEST OF M/S ATCO LABORATORIES LIMITED, KARACHI FOR CHANGE IN STORAGE CONDITIONS (PENTASA 500MG TABLET).

M/s. Atco Laboratories Limited, Karachi has requested for change in storage condition of registered product Pentasa 500mg Tab (Reg.No.031333). details are as under: -

S. No	**Change In Storage Condition**	
1.	**From**: "Store in dry place and at room temperature below 25°C".	**To:** "Do not store above 30°C, do not freeze, store in the original package in order to protect from light" The change in storage conditions is supported by stability data (30°C ± 2°C / RH 75 ± 5%) for two primary batches covering full shelf life 36 months, and one batch covering 24 months.
Adding The Full Address Of Manufacturing Site And Marketing Authorization		
2.	**From:** **Manufacture(as per approval)** M/s Pharbil Pharma GmbH, Germany. **Product License Holder (as per approval)** Not mentioned in Registration letter.	**To:** **Manufacture (as per COPP)** M/s Pharbil Pharma GmbH, Reichenberger Str. 43 33605 Bielefeld Germany. Or M/s Ferring International Center S.A. Chemin de la Vergognausaz 50 CH-1162 St. Prx Swiss Confederation. **Primary and Secondary Packaging** M/s Ferring International Center S.A. Chemin de la Vergognausaz 50 CH-1162 St. Prx Swiss Confederation. **Product License Holder (as per COPP)** M/s Ferring GmbH Wittland 11 24109 Kiel Germany

In support the firm has submitted the following documents;

a. Fee of Rs.5000/-
b. Initial registration letter and renewal status.
c. Original & legalized COPP issued by Germany.

Decision of 29th meeting of PRVC:

The Committee advised to take up the case in Registration Board meeting along with the application on CTD and with requisite fee of Rs.100,000/- as the manufacturing site is also changed.

M-245:

M/s. Atco Laboratories Limited, Karachi have requested to approve the change of manufacturing site of their registered imported drug "Pentasa 500mg Tablets (Mesalazine 500mg) (Reg. No.031333)" from M/s. Pharbil Pharma GmbH, Germany to M/s. Ferring International Center S.A., Switzerland.

The firm have deposited required fee Rs.100000/= and submitted following supporting documents:-

i) Copy of registration letter.
ii) Copy of last renewal.
iii) Copy of approval of change of manufacturing site.
iv) Copy of CRF Clearance Certificate.
v) Description of Manufacturing Process and Process Control (for new site).
Vi Original CPP confirming that change of manufacturing site from M/s. Pharbil Pharma GmbH, Germany to M/s. Ferring International Center S.A., Switzerland attested by Pakistan Embassy of Pakistan.
vii) Original GMP certificate of M/s. Ferring International Center S.A., Switzerland attested by Pakistan Embassy of Pakistan.
viii) Evidence copy of FDA approval for M/s. Ferring International Center S.A., Switzerland.

M/s. Atco Laboratories Limited, Karachi was advised to submit legalized proof of registration of the Pentasa 500mg Tablets manufactured by M/s. Ferring International Center S.A., Switzerland is approved by US-FDA. In response, the firm have submitted original legalized CoPP of "Pentasa 500mg Tablets (Reg. No.031333)" from Switzerland legalized by Pakistan Embassy.

M/s. Atco Laboratories Limited, Karachi was again advised to submit Form-5(A) and Site Mister File of Pentasa 500mg Tablets (Reg. N0.031333) from new site i.e. Switzerland. M/s. Atco Laboratories Limited, Karachi has submitted Form-5(A) and Site Mister File of new manufacturing site (Switzerland).

Decision of 245th meeting: Registration Board acceded to the request of firm.

Firm further submitted that on CoPP, under **2A.3.1** both manufacturing sites are mentioned i.e., M/s. Pharbil Pharma GmbH, Germany **OR** M/s. Ferring International Center S.A., Switzerland, it means that our principal has two approved sites as per CoPP but, our product, Pentasa 500mg tablet is now approved for M/s. Ferring International Center S.A., Switzerland as per DRAP policy.

Decision 307th meeting of RB:

Registration Board deferred the case for further deliberation**.**

Fresh proceeding:

we hereby declare that PENTASA 500mg TABLET is the innovator product of our principal manufacturer M/s. Ferring International Centre S.A., Switzerland.

Decision M-312:

Registration Board deferred the case for confirmation of requisite storage conditions approval from any RRA.

Firm submitted Germany official website link access on dated 26-08-2022 file:///C:/Users/sarfraz.nawaz/Downloads/FI_de_2127172_20210005419.pdf which shows " special precautions for storage
Do not store above 30°C."

Decision: Registration Board considered and approve the change in storage condition and detail as per CoPP of registered product Pentasa 500mg Tab (Reg.No.031333) details are as under: -

S. No	Change In Storage Condition	
1.	**From:** **"Store in dry place and at room temperature below 25°C".**	**To:** **"Do not store above 30°C, do not freeze, store in the original package in order to protect from light"** **The change in storage conditions is supported by stability data (30°C ± 2°C / RH 75 ± 5%) for two primary batches covering full shelf life 36 months, and one batch covering 24 months.**
Adding The Full Address Of Manufacturing Site And Marketing Authorization		
2.	**From:** **Manufacture(as per approval)** **M/s Pharbil Pharma GmbH, Germany.** **Product License Holder (as per approval)** **Not mentioned in Registration letter.**	**To:** **Manufacture (as per COPP)** **M/s Pharbil Pharma GmbH, Reichenberger Str. 43 33605 Bielefeld Germany.** **Or** **M/s Ferring International Center S.A. Chemin de la Vergognausaz 50 CH-1162 St. Prx Swiss Confederation.** **Primary and Secondary Packaging** **M/s Ferring International Center S.A. Chemin de la Vergognausaz 50 CH-1162 St. Prx Swiss Confederation.** **Product License Holder (as per COPP)** **M/s Ferring GmbH Wittland 11 24109 Kiel Germany**

Case No.21: DIFFERENCE IN MAH/MANUFACTURER OF APPROVED PRODUCTS IN 297TH MEETING OF REGISTRATION BOARD.

Registration Board in its 297th meeting approved the following product M/s Ahsan Pharma Importer and exporter, Zeenat Medicine Market, A-5, 1st Floor Napier Road Karachi, Pakistan as per decision mentioned alongside.

S. No	Name of Importer/Manufacturer	Product Name & Composition	Demanded Pack size & MRP

1.	M/s Ahsan Pharma Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi. **Manufacturer:** M/s Sichuan Huiyu Pharmaceutical Ltd. No. 5 Road Chengxi economic area, Neijiang, Sichuan-641000, China **Batch Releasing site:** M/s Seacross Pharmaceutical Limited, Bedford business centre, 61-63 st. peter's street, Bedford, Bedfordshire, MK40 2PR, United Kingdom. **Product License Holder:** M/s Seacross Pharmaceuticals Co., Ltd., Stanmore Bussiness & Innovation Centre, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK.	Paclitaxel 6mg/ml concentrate for solution for infusion. Each vial of 5ml contains: Paclitaxel……30mg Antineoplastic USP 24 months	As per SRO 1's 4th PAC Rs.8700.00/Vial
Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.			
2.	-do-	Paclitaxel 6mg/ml concentrate for solution for infusion Each vial of 16.7ml contains: Paclitaxel……100mg Antineoplastic USP 24 months	As per SRO 1's 4th PAC Rs.13000.00/Vial
Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.			
3.	-do-	Paclitaxel 6mg/ml concentrate for solution for infusion Each vial of 50ml contains: Paclitaxel……300mg Antineoplastic USP 24 months	As per SRO 1's 4th PAC Rs.29470.00/Vial
Decision: - Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.			

The names/address of Marketing Authorization Holder, Manufacturer & Batch Release Site as per Minutes & CoPP seems like different as per following details: -

Names/address of MAH, Manufacturer & Batch Release Site as per Minutes	Names/address of MAH, Manufacturer & Batch Release Site as per CoPP
Marketing Authorization Holder: - M/s Seacross Pharmaceuticals Co., Ltd., Stanmore Bussiness & Innovation Centre, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK. **Manufacturer:** - M/s Sichuan Huiyu Pharmaceutical Ltd. No. 5 Road Chengxi economic area, Neijiang, Sichuan-641000, China.	**Marketing Authorization Holder**:- M/s Seacross Pharmaceuticals Limited, Bedford Business Centre, 61-63 St. Peter's Street, Bedford, Bedfordshire, MK40 2PR, United King. **Manufacturer:-** M/s Sichuan Huiyu Pharmaceutical Company Limited, No. 5 Road Chengxi Economic

Batch Releasing site: - M/s Seacross Pharmaceutical Limited, Bedford business centre, 61-63 st. peter's street, Bedford, Bedfordshire, MK40 2PR, United Kingdom.	Zone, Neijiang, Sichuan, CN-641000, the people's Republic of China. **Batch Release Site: -** M/s Seacross Pharmaceutical Limited, Stanmore Bussiness & Innovation Centre, Stanmore Place, Howard Road, Stanmore, HA7 1BT, United Kingdom.

Decision: Registration Board noted the information.

Case No.22: DIFFERENCE IN MAH/MANUFACTURER OF APPROVED PRODUCTS IN 291ST MEETING OF REGISTRATION BOARD.

Registration Board in its 291st meeting approved the following product of M/s Roche Pakistan limited, 1st Floor, 37-B, Block-6, P.E.C.H.S, Karachi as per decision mentioned alongside.

S. No	Name of Importer/Manufacturer	Product Name & Composition	Demanded Pack size & MRP
1.	M/s Roche Pakistan limited, Ist floor, 37-B, Block-6, P.E.C.H.S, Karachi. **Manufacturing and analytical release testing:** Excella GmbH & Co. KG Nürnberger Strasse 12 90537 Feucht Germany **Analytical stability testing, primary and secondary packaging and release of Finished Drug Product:** Delpharm Milano, S.r.l.a Via Carnevale 1 20090 Segrate (MI) Italy **Release of Finished Drug Product:** F. Hoffmann□La Roche Ltd Viaduktstrasse 33 CH□4051 Basel Switzerland	Alecensa Capsule 150 mg Each capsule contains: Alectinib (as HCL)…… 150mg	To be provided 4's
Decision: Approved as per innovator's specification.			

The names/address of Marketing Authorization Holder & Manufacturer as per Minutes & CoPP seems like different as per following details: -

Names/address of MAH, Manufacturer as per Minutes	Names/address of MAH & Manufacturer as per CoPP
Manufacturing and analytical release testing: Excella GmbH & Co. KG Nürnberger Strasse 12 90537 Feucht Germany **Analytical stability testing, primary and secondary packaging and release of Finished Drug Product:** Delpharm Milano, S.r.l.a Via Carnevale 1 20090 Segrate (MI) Italy **Release of Finished Drug Product:** F. Hoffmann□La Roche Ltd Viaduktstrasse 33	**Marketing Authorization Holder**:- M/s Roche Pharma (Schweiz) Ltd, Schonmattstrasse 2, CH-4153 Reinach BL, Switzerland. **Manufacturer:-** M/s Excella GmbH & Co. KG Nürnberger Strasse 12 DE-90537 Feucht Germany.

CH□4051 Basel Switzerland	

Decision: Registration Board noted the information

Case No.23: REQUEST OF M/S FRESENIUS KABI PAKISTAN (PVT) LIMITED, KARACHI FOR REGISTRATION OF DRUGS TO THEIR NAME.

M/s Fresenius Kabi Pakistan (Pvt) Limited, Lahore has submitted an application for Registration of the following already registered product from M/s Muller & Phipps Pakistan (Pvt) Ltd, Karachi to their name. The detail of each proposed product is as under: -

Product-1: Zoledronic Acid Fresenius Kabi 4mg/5ml (Reg.No. 084867)		
S. No.	**Name / Detail of Documents**	**Documents/information provided by the firm**
1.	Product Name/ Composition	**As per approval** Zoledronic Acid Fresenius Kabi 4mg/5ml concentrate for solution for IV Infusion Each 5ml vial contains: - Zoledronic acid……4mg (As per Innovator's Specification) **As per CoPP** Zoledronic Acid Fresenius Kabi 4mg/5ml concentrate for solution for IV Infusion Each ml solution for infusion contains:- Zoledronic Acid monohydrate 0.853mg (corresponding to 0.8mg anhydrous substance)
	Reg. date / renewal status	Reg. Letter issued on 09-02-2018 (due date 08-02-2023)
	Name and address of Applicant(Transferee)	M/s Fresenius Kabi Pakistan (Pvt) Limited First Floor Tanwir Ahmed Medical Center (TAMC) MM Alam Road, 27-C/3, Gulberg-III, Lahore
	Name of Transferor	M/s Muller & Phipps Pakistan (Pvt) Ltd, Plot No.208&208/1, Sector 23 Korangi Industrial Area, Karachi.
	Detail of Drug Sale License	**DSL No.045 (valid upto 21-09-2023)** **Address:** M/s Fresenius Kabi Pakistan (Pvt) Limited First Floor Tanwir Ahmed Medical Center (TAMC) MM Alam Road, 27-C/3, Gulberg-III, Lahore. **Godown address:** 1. Agility Logistics (Pvt) Ltd, RLC-2, 26-KM, Multan Road, Opposite Hussaini Darbar, Near Shamshad Farm House, Lahore.
	Name and address of Manufacturer / Product License Holder	**As per approval** **Manufacturer**: M/S. FRESENIUS KABI AUSTRIA GMBH, HAFNERTRABE 36, A- 8055 GRAZ, AUSTRIA. **Product License Holder:** M/S. FRESENIUS KABI DEUTSCHLAND GMBH, D-61346 BAD HOMBURG V. D. H. / GERMANY. **As per CoPP (Germany):** **Manufacturer:** M/S. FRESENIUS KABI AUSTRIA GMBH, HAFNERTRABE 36, 8055 GRAZ, AUSTRIA. **Product License Holder:** M/S. FRESENIUS KABI DEUTSCHLAND GMBH, D-61346 BAD HOMBURG V. D. H. / GERMANY.

	Name of exporting Country	Germany
	Diary No. & Date of R& I	Dy. No. 1760 Dated 13/1/2021.
	Finished Product Specification	As per Innovator's Specification
	Shelf life	03 Years (as per Reg. Letter)
	Pack Size	5ml x 1's (as per Reg. Letter)
	Remarks: -	

The firm has submitted the following supporting documents / information for approval of above transfer of registrations: -

a) Fee of Rs.100,000/- for each product.
b) Applications on Form-5F.
c) Copy of Registration letter.
d) Original legalized CoPP issued by Germany for above products
e) Original of Termination letter.
f) Original Letter of authorization.
g) Original of NOC for transfer of registrations **(issued on 16-11-2020).**
h) An undertaking that annexed documents is correct and true is required

Decision: Keeping in view the above position, Registration Board decided as follow;

a. Approved the cancellation of registration of following product from the name of M/s Muller & Phipps Pakistan (Pvt) Ltd, Plot No.208&208/1, Sector 23 Korangi Industrial Area, Karachi.

S. No	Reg. No.	Name & Composition
1.	**084867**	**Zoledronic Acid Fresenius Kabi 4mg/5ml**

b. Approved the registration of above product in the name of M/s Fresenius Kabi Pakistan (Pvt) Limited First Floor Tanwir Ahmed Medical Center (TAMC) MM Alam Road, 27-C/3, Gulberg-III, Lahore as per policy for imported finished drug registration (in accordance with details of composition and manufacturer as per CoPP).

c. Reference shall be sent to Costing & Pricing Division for their comments regarding MRP of the said product.

Case No.24: REGISTRATION OF PRODUCT OF M/S IQBAL & COMPANY, ISLAMABAD.

Registration Board in its 291st meeting approved the following product of M/s Iqbal & Company, 1st floor, Al-Falah Manzil, Opp. National Police Foundation, St. No. 26, Sector E-11/4, Islamabad as per decision mentioned alongside.

Name of Importer/Manufacturer	**Product Name & Composition**	**Demanded Pack size & MRP**

M/s Iqbal & Company,1st floor, Al-Falah Manzil, Opp. National Police Foundation, St.No. 26, Sector E-11/4, Islamabad **Marketing Authorization Holder:** M/s Gambro Lundia AB Box ,Magistratsvagen 16, Lund, SE-22643, Sweden **Manufacturer:** M/s Bieffe Medital S.P.A Via Stelvio 94, 230 35 Sondalo (SO), I-23035, Italy	HEMOSOL B0 Solution for Haemodialysis/ Haemofiltration Each ml of 2 compartment bag contains: Medimar Electrolyte solution (Small Compartment A-250ml) lactic acid ……. 5.4mg Calcium chloride dehydrate …… 5.145mg Magnesium chloride hexahydrate…. 2.033mg Buffer Solution (Large Compartment B-4750 ml) Sodium Chloride……..…6.450mg Sodium hydrogen carbonate…. 3.090mg After Reconstitution Calcium (Ca+2)….. 1.75 mmol/L Magnesium (Mg+2)……0.5 mmol/L Sodium (Na+)…… 140 mmol/L Chloride (Cl-)…….. 109.5 mmol/L Lactate……..... 3 mmol/L Hydrogen carbonate (HCO3-)…….. 32mmol Hemofiltrates BP 18 months (Polyolefin bag)	(2 x 5000ml) polyolefin bags, in a box Not proposed
Decision: Approved as per policy of inspection of manufacturer abroad.		

Registration Board in its M-293rd meeting deliberated in light of Rule 24 (10) of Drugs (L, R & A) Rules, 1976 and authorized Chairman for nomination of inspector for product storage verification of local premises. Accordingly, Chairman RB nominate to Assistant Director (I&V) & Assistant Director (Reg-II) PE&R Division DRAP, Islamabad to inspect the above local storage facility. Inspection of premises M/s Iqbal & Company,1st floor, Al-Falah Manzil, Opp. National Police Foundation, St. No. 26, Sector E-11/4, Islamabad was conducted on 24th September, 2020 with status **Not Recommended** on the following points: -

Sr.No.	Observations / Shortcomings	Remarks
1.	Checklist for personal safety.	No
2.	Is there a cleaning schedule in place	No
3.	Are all the products are properly placed or arrangments are made for systematic storage	No
4.	Are the temperature logs readily available for a minimum of two years	One week record available
5.	Check the alarm system. Is it ok	No.
6.	Is there any routine and emergency maintenance plan	No
7.	Check if there is any maintenance agreement with an ourside agency	No.
8.	Is routine maintenance being perfomed correctly at the internvals stated in theagreeement	No
9.	When emergencies occur, does the maintennacne technician arrive with the maximum stipulated in the agreement	No.
10.	Does the importer have established the Re-Call system of drugs	No

Furthermore, Ten Cotton of drug HEMOSOL B0 Solution for Haemodialysis/ Haemofiltration which is under registration was found in storage premises of M/s Iqbal & Sons Company.
Accordingly, above position was conveyed to Additional Director (QA/LT) Division vide letter No.F.1-11/2020-I&V-II/Human Import dated 23rd December, 2020 for further necessary action at their end.

Decision of 291st meeting: Registration Board advised QA/LT Division to finalize the case and inform PE&R Division for further processing of case.

Updated Status: -

Area FID-IV has submitted vide letter No.F.4-5/2021-FID(IV) dated 29-07-2022 as under: -

I have honor to refer to the letter No. F- 3-312021-l & VII (M312) there dated 25ft Nov. 2021, which is in continuation to the previous letter No.F.l-lll2}20 (I & VII) Human Import dated 23'd December,2020 on the subject cited above. The detail of the matter /case after scrutiny of the documents is as under:

The Registration Board in its 312 meeting refers the case to QA Division. The firm has submitted documents which have been reviewed in light of decision of Registration Board which indicted the following details for consideration;

i. The firm has applied for the registration of Product namely "Hemosol BO solution for Heamodialysis/Flaemofiltration in 2016. the case was first presented before Registration Board in its 279th meeting.

ii. The case has finally decided by the Registration Board in its 291't meeting as under approved as per policy by the manufacture observed " (copy attached)

iii. Accordingly, Chairman Registration Board constituted the panel for verification of local storage facility comprising of
a) Assistant Director (I&V)
b) Assistant Director (Reg-II)

The panel conducted inspection on 24-09-2020 and observed series of shortcoming along with the observation that 10 carton of the same product (viz under registration) was present there but didn't refer the same in the shortcoming for clarification.(copy attached/. The case was referred to QA< Division on 23'd December 2020, (copy attached) mentioning that they have forwarded the pictures of the same to the predecessor FID ,which she explain that information was received on 30-09-2020 (after a weak of inspection) & no written complaint provided with detail so action can't initiated (copy attached). The letter was again received on 25th November 2021 (after laps of almost one year).

The undersigned scrutinized the available documents and Board meetings which indicate that product is categorized as medical Devices in Italy (where actually manufacturing takes place) and referred as medicinal product in Sweden (actual maker authorization holder) (copy attached). The documents further indicate that product actually imported in the year of 2018 &2019 for Shaukat Khanum Hospital (institutional supply (copy attached/ and since its fate at that time was not decided/declare whether it is medical devices or otherwise the firm thus avails the opportunity of category of Medical Devices (as in Italy) and Rules 52 of MEDICAL Device Rules 2018 provide exemption to these class of products which is further amended vide SRO526(1) 12021 and exemption is extended S.R.O NOC not proceeded.(copy attached)

In the light of above in is worth mentioning here that no action from QA&LT Division at this point is required and case may please be processed at the end of Registration Division in the light of provided documents.

Decision: **Registration Board decided to seek legal opinion from Legal Affair Division on the matter.**

Case No.25: DIFFERENCE IN PRODUCT LICENSE HOLDER /MANUFACTURER OF APPROVED PRODUCT IN 308TH MEETING OF REGISTRATION BOARD.

Registration Board in its M-308th meeting approve the following product of M/s Health Services Office 3A 3rd Floor Building No. 8, Civic Centre Bahria Town Phase 4, Islamabad as per decision mentioned alongside.

S. No	Name of Importer/Manufacturer	Product Name & Composition	Demanded Pack size & MRP
1.	M/s Health Services. Office A4, 3rd Floor, Building # 8, Civic Centre, Bahria Town, Phase IV, Islamabad **Product License Holder & Manufacturer:** M/s BiemHacSanayiVeTicaret A.S. Turgut Reis, Caddesi No. 21,0657 Tandogan-Anakara, Turkey"	Beastin 100mg IV Powder for Concentrate for Solution for Infusion Each Vial Contains: Bendamustine Hydrochloride…100mg" Alkylating Agent 36 months	Rs:17000/- 1's
Decision of 308: The Board was apprised that the firm had submitted original and legalized CoPP which was valid at the time of submission of registration dossier but the submitted CoPP was expired on 13/04/2020. Now the firm has submitted copy of valid CoPP. Keeping in view the above stated fact, the Board decided to approve the case with innovator's specification as per Policy for inspection of Manufacturer abroad and verification of local storage facility. The Board further decided that the applicant will submit original, legalized and valid CoPP before the issuance of registration letter			

The names/address of Marketing Authorization Holder & Manufacturer as per Minutes & CoPP seems like different as per following details: -

Names/address of Product License Holder & Manufacturer as per Minutes	Names/address of Product License Holder & Manufacturer as per CoPP
Product License Holder & Manufacturer: M/s BiemHacSanayiVeTicaret A.S. Turgut Reis, Caddesi No. 21,0657 Tandogan-Anakara, Turkey"	**Product License Holder.** M/s Biem Ilac San. Ve Tic. A.S Turgut Reis Cad. No: 21 06570 Tandogan-Ankara/ Turkey **Manufacturer.** M/s Onko Ilac San. Ve Tic. A.S. Gebze Organize Sanayi Bolgesi, 1700 Sokak, No.1703 Gebze/Kocaeli/ Turkey

Decision: Registration Board noted the information

Case No.26: PROPOSAL TO CONSIDER THE RELIANCE PATHWAY FOR THE REGISTRATION OF INNOVATOR PRODUCTS MANUFACTURED OUTSIDE THE UNTED STATES

Subject case was considered and defer in 316th meeting of Registration Board held on 15th, 16th, 17th & 18th March, 2022 as under: -

Pharma Bureau submit a letter on subject cited above which is reproduced as under:

Pharma Bureau member companies involved in the import of state-of-the-art drugs from the First World countries in general and the United States of America in particular.

As you are aware of, USFDA is usually the first authority to register any new drug or therapy for the use of its patients and at times, the difference between the initial approval-time from the USFDA to the next SRA (especially EU) can take anywhere from 6 months to 1 year. Due to this fundamental reason, most of the markets in the world relied on the USFDA approval, and proceeded with their local registrations accordingly with the US CPP.

There has, however, there is a policy change in within the USFDA regarding the Foreign Export (FE) CPP program for products not manufactured nor exported from the US, and eventually, they relinquished their foreign exported CPPs program due to lack of legal authority from the US Congress, which is notified as follows on their official website:

"The FDA Center for Drug Evaluation and Research (CDER) previously issued foreign exported CPPs for FDA-approved drugs and biologics that were exported from a country other than the United States. Now CDER does not issue foreign exported CPPs given the other resources available for stakeholders to verify whether a drug or biologic is FDA approved and to view FDA's classifications of its inspections of manufacturing facilities."
(Source link: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/human-drug-exports)

However, the US FDA has undertaken a number of transparency initiatives in recent years. These initiatives and associated documents below can serve as valid alternatives to an FE CPP, which are as follows:

1) USFDA approval letter present on FDA website.

2) The "90-Day Decisional e-mail" from FDA, which includes as an attachment a copy of the narrative portion of the Establishment Inspection Report (EIR), along with the FDA Market Authorization Letter which satisfies the intent of the FE CPP. Decisional email represents the manufacturing site along with its DUNS (Data Universal Numbering System). The DUNS can be traced on the official website for the full information about the manufacturing site on the following link:
   https://www.accessdata.fda.gov/scripts/cder/drls/default.cfm
   Hence, the manufacturing site of the product can also be verified from the FDA website.

3) National Drug Code (NDC) Directory of FDA is updated on a daily basis and is a key resource to verify the different attributes of products such as proprietary name, strength, dosage form, route of administration, marketing date, etc. It serves as a universal product identifier for the drugs approved by FDA. FDA publishes the listed NDC numbers with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by it for commercial distribution. Following is the website link for the NDC Directory:
   https://www.accessdata.fda.gov/scripts/cder/ndc/index.cfm

4) Further resources of information to verify miscellaneous attributes of the product along with its marketing status are the ORANGE BOOK for small molecules/chemical drugs and the PURPLE BOOK for biologicals. Following are the links for the said databases:
   ORANGE BOOK: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
   PURPLE BOOK: https://purplebooksearch.fda.gov/

In the light of above facts and information, we are confident that we have enough alternate resources to validate the necessary information, which is included in a CPP.

Considering the said details, we request you to exercise flexibility by accepting this alternate pathway for the new drugs manufactured outside the US, and make the registration of innovator drugs top priority in order to meet the unmet needs of the patients of Pakistan.

Decision 317:
Registration Board considered and deferred for further confirmation of CoPP requirement as per law. The Board further directed to send an email to USFDA for clarification on CoPP issuance in above scenario.

As per form-5F guidance documents:
"An importer shall provide Certificate of Pharmaceutical Product (CoPP) / Free Sale certificate and GMP certificate of the Manufacturer issued by relevant regulatory authority in the country of origin and name of exporting country"

Very similar case applied by M/s Roche pharma in which they informed that EMA will not issue CoPP anymore and they submit EMA online document which stated that:

"EMA is only issuing certificates electronically, as of March 2020. They are in PDF format, using an electronic signature that complies with Regulation (EU) No 910/2014 on the electronic identification and trust services for electronic transactions in the internal market (eIDAS Regulation)"

Decision: **Registration Board after deliberation decided to accept the CoPP copy if it is confirmed from the official website of the concerned issuing authority of a country of origin. Furthermore, the firm shall submit a notorized copy of CoPP of electronically issued CoPP for the record.**

Case No: 1 Renewal application of Hair Max Plus Topical Solution of M/s Elko Organization (Private) Ltd. Karachi.

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
027592	**Hair Max Plus Topical Solution** Each ml contains: Minoxidil……50mg Denatured Spirit….0.6ml	26.06.2002	Rs.10000/- dated 16.06.2017 and Dy No.14167 Dated 10.06.2022 Rs. 15000/-	As per Licensing Division No, F.2-256/84-Lic (vol-I), the firm didn't possess manufacturing facility for external preparations.

Decision: Deferred for clarification from firm regarding approval status of relevant manufacturing facility from Licensing Division.

Case No: 2 Renewal application of Ivomec Injection (009579) M/s Saadat International, Lahore.

Assistant Director (I& V) has referred below mentioned product for confirmation of renewal for change of name of manufacturer. Details are as under:

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
009597	**Ivomec 1% Injectable solution** Each ml contains; Ivermectin…...10gm **Manufacturer:** M/s Merial Saude Animal Paulinia Brazil.	31.03.1987 Transfer of Reg: **27.03.2010** Change of Mfg. site: 27.07.2011	Dy. No. 14087 dated 18.06.2020 Rs. 60000/-	Renewal application is submitted within one year

Decision: Registration Board regularized the renewal w.e.f 27.03.2020 to 26.03.2025 under SRO 1005(I)/2017. However, renewal letter shall be issued after approval of change of name of manufacturer as applied in I&V section.

Case No: 3 Renewal applications M/s. Xenon Pharmaceuticals (Pvt) Ltd. Lahore

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
020546	**Dexamethasone Tablets** Each tablet contains: Dexamethasone….0.5mg	12.11.1997	Rs.10, 000/- dated 09.03.2017 & Dy no.12766 Dated 24.05.2022	As per panel inspection report for renewal of DML dated 11.02.2022, the firm didn't possess Tablet steroid section.

			Rs.15000/-	

Decision: Deferred for clarification from firm regarding the approval status of relevant manufacturing facility from Licensing Division.

Case No: 4 Renewal applications M/s. Tec-Man International, Rawalpindi

M/s. Tech-Man International, Rawalpindi has informed that the renewal of below mentioned product was submitted on 06.07.2020 due to bank holiday and not able to submit renewal on due date i.e. 5th July, 2020 because 4th July 2020 was Saturday and 5th july,2020 was Sunday.

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Decision
009616	Colisol Powder Each 100gm contains:- Colistin Sulphate… 500,000,000IU **Manufacturer: -** M/s. Dopharma B.V. Zalmweg 24,4941 VX Raamsdonksveer The Netherlands. **Product License Holder:-** M/s. Dopharma Research B.V. Zalmweg 24,4941 VX Raamsdonksveer The Netherlands.	29-03-1987 Transfer of Reg: **05-07-2010**	Dy. No.16023 dated 06-07-2020 Rs.10,000/-	Registration Board granted renewal w.e.f. 05.07.2020 to 04.07.2025. However renewal letter shall be issued after approval of change of name of manufacturer as applied in I&V section.
011124	TSO Liquid Each 1000ml contains:- Trimethoprim … 20.000mg Sulfamethoxazole… 80.000mg **Manufacturer:** M/s. Dopharma B.V. Zalmweg 24,4941 VX Raamsdonksveer The Netherlands. **Product License Holder:-** M/s. Dopharma Research B.V. Zalmweg 24,4941 VX Raamsdonksveer The Netherlands.	23-05-1990 Transfer of Reg: **05-07-2010**	Dy. No.16023 dated 06-07-2020 Rs.10,000/-	Registration Board granted renewal w.e.f. 05.07.2020 to 04.07.2025. However, renewal letter shall be issued after approval of change of name of manufacturer as applied in I&V section.

Case No. 5 Renewal application of M/s Medisure Laboratories Pakistan Pvt Limited Karachi.

The below mentioned products were deferred in 317th meeting of Registration Board for submission of differential fee. The firm has now submitted differential fee. Details are recorded against each:

Sr. No.	Reg. No.	Brand Name & Composition	Date of Reg.	Renewal application submission details	Decision in 317th RB	Fee submission details
1.	048525	Synsma Tablet Each tablet contains: Doxofylline ….400mg	06.03.2008	Rs. 10000/- dated: 14.03.2013 Rs. 10000 dated: 12.4.2018 **Rs. 20,000/-** **Dy No.12763** **Date:24.05.2022**	Deferred for submission of differential fee (Rs. 20000/-) as renewal application for the year 2013 and 2018 was submitted late but within sixty days	Renewal is granted w.e.f. 06.03.2018 to 05.03.2023.
2.	055600	Xopra Plus Capsules Each Capsule contains: Omeprazole (as pellets) …...40mg (USP Specifications) **Source:** M/s EuroAsia Trans Continental India.	01.04.2009	Rs. 10000/- dated 25.04.2019 **Rs. 20,000/-** **Dy No.12763** **Date:24.05.2022**	Deferred for submission of differential fee (Rs. 30000/-) for following reasons: i. Renewal application for the year 2019 was submitted after due date but within sixty days. ii. Imported source of pellets	Renewal is granted w.e.f. 01.04.2019 to 31.03.2024
3.	058247	Albuterol Syrup Each 5ml contains: Salbutamol as sulphate…...2 mg (BP Specifications)	12.08.2009	Rs:10000/- dated 19.08.2019 **Rs. 10,000/-** **Dy No.12763** **Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 12.08.2009 to 11.08.2024.
4.	058248	Chewron Syrup Each 5ml contains: Iron (III) Hydroxide Polymaltose Complex eq.	12.08.2009	Rs:10000/- dated 19.08.2019 **Rs. 10,000/-** **Dy No.12763** **Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 12.08.2009 to 11.08.2024.

		to Elemental Iron…50mg (USP Specifications)				
5.	058249	Pinsure 10mg Tablet Each film coated tablet contains: Olanzapine…. 10mg	12.08.2009	Rs:10000/- dated 19.08.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 12.08.2009 to 11.08.2024.
6.	058250	Lactusure Syrup 120ml Lactulose ……3.35gm **Source of Bulk:** M/s Fresenius Kabi Austria	12-08-2009	Rs:10000/- dated 19.08.2019 **Rs. 30,000/- Dy No.12763 Date:124.05.2022**	Deferred for submission of differential fee (Rs. 30000/-) for following reasons: i. Renewal application for the year 2019 was submitted after due date but within sixty days. ii. Imported source of bulk	Renewal is granted w.e.f. 12.08.2009 to 11.08.2024.
Remarks: Product applied under SRO1005(I)/2017 in 278th meeting of Registration Board. Hence cancellation letter was not issued. Further renewal application for the year 2019 was submitted on 19.08.2019 with 10000/- fee which is also after due date but within sixty days. The firm may be advised to submit pending differential fee and case may be placed in forthcoming Registration Board meeting. **Decision in 316th meeting:** Keeping in view above facts, Registration Board revoked its earlier decision of cancellation of registration in its 312th meeting and further advised the firm to submit the differential fee for imported source of bulk and differential fee of late renewal submission (within sixty days) for the year 2019.						
7.	032639	Diabetal-2 Tablets Each tablet contains: Glimepiride ……2mg	13.08.2004	Rs.10000/- dated 26.09.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 13.08.2009 to 12.08.2024.
8.	032640	Miosil 5mg Tablet Each tablet contains: Amlodipine besylate eq. to Amlodipine…..5mg	13.08.2004	Rs.10000/- dated 26.09.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 13.08.2009 to 12.08.2024.
9.	032641	Miosil 10mg Tablet	13.08.2004	Rs.10000/- dated 26.09.2019	Deferred for submission of differential fee (Rs.	Renewal is granted w.e.f. 13.08.2009 to 12.08.2024.

		Each tablet contains: Amlodipine besylate eq. to Amlodipine…..10mg		**Rs. 10,000/- Dy No.12763 Date:24.05.2022**	10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	
10.	032469	Onyfine tablets 125mg Each tablet contains: Terbinafine HCl eq.to Terbinafine…..125mg	07.08.2004	Rs.10000/- dated 27.09.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 07.08.2019 to 06.08.2024
11.	032740	Arthosure Gel Each 100gm Contains: Diclofenac Diethyl Ammonium salt 1.6gm eq.tp Diclofenac Sodium…….. 1.00gm	07.08.2004	Rs.10000/- dated 26.09.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 07.08.2019 to 06.08.2024
12.	032462	Abgenix 20mg tablet Each tablet contains: Citalopram (as Hydrobromide) …….20mg	06.08.2004	Rs.10000/- dated 27.09.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 06.08.2019 to 05.08.2024
13.	032463	Kovence 60mg Capsule Each capsule contains Fexofenadine HCl…60mg	06.08.2004	Rs.10000/- dated 27.09.2019 **Rs. 10,000/- Dy No.12763 Date:24.05.2022**	Deferred for submission of differential fee (Rs. 10000/-) as renewal application for the year 2019 was submitted late but within sixty days.	Renewal is granted w.e.f. 06.08.2019 to 05.08.2024

Case No:6 Renewal applications M/s. Zafa Pharmaceutical Laboratories, Private Ltd. Karachi

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
028064	**Insulin NPH Suspension** Each ml contains Crystalline insulin purified (Beef Sourced) 100IU	19.07.2002	Rs.10, 000/- dated 19.04.2017 & Dy no.12436 Dated 21.05.2022 Rs.15000/-	Confirmation of manufacturing facility for biological drugs.

	Protamine Sulphate ….0.450mg			

Decision: Referred to Biological Evaluation & Research Division with the request to take up the matter for verification of the manufacturing facility from Licensing Division and proceed in accordance with law.

Case No: 7 Renewal applications M/s. Gulf Pharmaceuticals, Islamabad.

The firm has submitted copy of clearance certificate vide No. E-640308953476 dated 28.03.2022 for import of Levofloxacin hemihydrate (USP) for manufacturing of below mentioned products. The Assistant Director (I&E) has issued the aforementioned clearance with utilization restriction subject to the confirmation of renewal of below products. Details are tabulated as under:

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Decision
075170	Luvox-250 Tablet Each tablet contains: Levofloxacin as hemihydrate.250mg (Gulf's Specifications)	28.01.2013	Rs. 20000 dated 27.03.2018	Renewal is granted w.e.f. 28.01.2018 to 27.01.2023. The formulation shall be corrected as film coated tablet. Further the firm shall submit reference of finished product specifications as per decision of 295th meeting of Registration Board.
075170	Luvox-500 Tablet Each tablet contains: Levofloxacin as hemihydrate.500mg (Gulf's Specifications)	28.01.2013	Rs. 20000 dated 27.03.2018	Renewal is granted w.e.f. 28.01.2018 to 27.01.2023. The formulation shall be corrected as film coated tablet. Further the firm shall submit reference of finished product specifications as per decision of 295th meeting of Registration Board.

The aforementioned renewal applications have been submitted by the firm after the due date of expiry of registration but within sixty days with prescribed fee.

Case No: 08 Renewal applications M/s. Wise Pharmaceuticals, Rawalpindi

Sr. No.	Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Decision
1.	047848	Ultech 40mg Capsules Each capsule contains: Esomeprazole (as enteric coated pellets) …….40mg (wise Spec**)**	05-12-2007	Last Renewal was done with double fee Rs. 40,000/- on 2-2-2018 (copy Attached) Spec change fee challan#1984221	Renewal is granted w.e.f. 05.12.2017 to 04.12.2022

		Source of Pellets:- M/s. Lee Pharma Ltd, Ameepet, Hyderabad 500037 India then local encapsulation.		Dated 13-08-2020 (copy attached)	
2.	047849	Ultech 20mg Capsules Each capsule contains: Esomeprazole (as enteric coated pellets)……20mg (wise Spec) **Source of Pellets: -** M/s. Lee Pharma Ltd, Ameepet, Hyderabad 500037 India then local encapsulation.	05-12-2007	Last Renewal was done with double fee Rs. 40,000/- on 2-2-2018 (copy Attached) Spec change fee challan#1984221 Dated 13-08-2020 (copy attached)	Renewal is granted w.e.f. 05.12.2017 to 04.12.2022

The case was deferred in 316th meeting of Reg. Board for submission of differential fee

Case No: 09 Renewal applications M/s. Paramedic Laboratories (Pvt) Ltd.16 Km Multan Road, Lahore

Assistant Director (PR-II) has requested as informed that below mentioned product registered in name of M/s. Pharmedic Labs (Pvt) Ltd, Lahore were considered in 73rd meeting of PRVC and deferred for confirmation of renewal status. details are as under:

Reg. No.	**Brand Name & Composition**	**Initial date of Registration** **PRV (If any)**	**Date of application (R&I)** **Fee submitted**	**Decision**
040692	Letrozone Tablet Each tablet contains Letrozole……..2.5mg	07.07.2005	Rs.10000/- Dy No.16288 Dated: 07.07.2020 Dy No.18248 Rs.15000/- Dated:22.06.2022	Renewal is granted w.e.f. 07.07.2020 to 06.07.2025. The formulation shall be corrected as film coated tablet. Further the firm shall submit reference of finished product specifications as per decision of 295th meeting of Registration Board.
027850	Bleocin injection Each vail contains: Bleomycin Sulphate……15mg	04.05.2002	Rs.15000/- Dy No.8857 Dated: 04.06.2022 Dy No.18248 Rs.15000/- Dated:22.06.2022	Deferred for status of manufacturing facility form Licensing Disvion.
025801	Benda Tablet Each tablet contains: Albendazole…200mg	17.05.2000	Rs.10000/- Dy No.11213	Renewal is granted w.e.f. 17.05.2020 to 16.05.2025

			Dated: 18.05.2020 Dy No.18248 Rs.15000/- Dated:22.06.2022	The formulation shall be corrected as film coated tablet. Further the firm shall submit reference of finished product specifications as per decision of 295th meeting of Registration Board.

Case No: 10 Contract Manufacturing of Registered Products of M/s. Novartis Pharma (Pakistan) Ltd., 15-West Wharf Dockyard Road, Karachi at M/s GlaxoSmithKline Consumer Healthcare Pakistan Ltd., Petaro Road Jamshoro.

M/s. Novartis Pharma (Pakistan) Ltd., 15-West Wharf Dockyard Road, Karachi has submitted request for extension in contact manufacturing of below mentioned products registered in their name manufactured at M/s GlaxoSmithKline Consumer Healthcare Pakistan Ltd., Petaro Road Jamshoro. The firm has submitted following documents:

i. Fee deposit slip of 75000/- each product.
ii. Copies of DML
iii. Copies of registration letter
iv. GMP certificate of M/s GlaxoSmithKline Consumer Healthcare Pakistan Ltd., Petaro Road Jamshoro.
v. Contract agreement.

The permission was valid for the period of 30months from the date of issuance of registration. The case was discussed in 317th meeting of Registration Board and deferred for following:

i. Clarification for non-compliance of timelines granted by Registration Board i.e. 30months
ii. Status of products not applied for extension in contact manufacturing in registration letter dated: 22.01.2020 and 13.02.2020

Details of the products are as under:

Sr. No.	Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
1.	007823	Mepresor 100mg tablets Each tablet contains: Metoprolol……100mg (Manufacturer Specification)	22.01.2020	75000/- dated 21.02.2022	
2.	006144	Mosegor sugar coated tablet Each tablet contains: Pizotifen……..0.5mg (Manufacturer Specification)	22.01.2020	75000/- dated 21.02.2022	
3.	021529	Tegral 200mg tablets Each tablet contains: Carbamazepine……200 mg (Manufacturer Specification)	22.01.2020	75000/- dated 21.02.2022	

4.	041184	Trioptal 300mg tablet Each film coated tablet contains: Oxcarbazepin……300mg (Manufacturer Specification)	22.01.2020	75000/- dated 21.02.2022	
5.	041185	Trioptal 600mg tablet Each film coated tablet contains: Oxcarbazepin……600mg (Manufacturer Specification)	22.01.2020	75000/- dated 21.02.2022	
6.	006282	Mosegor Syrup Each 5ml contains: Pizotifen…….0.25 mg (Manufacturers Specification)	22.01.2020	75000/- dated 21.02.2022	
7.	021528	Caflam 50mg Tablets Each tablet contains: Diclofenac Potassium……..…50 mg (Manufacturer's Specification)*	13.02.2020	75000/- dated 21.02.2022	
8.	021525	Voltral 50 Tablets Each enteric coated tablet contains: Diclofenac sodium…..50mg (Manufacturer's Specification)*	13.02.2020	75000/- dated 21.02.2022	
9.	021524	Voltral 25 Tablets Each enteric coated tablet contains: Diclofenac sodium….25mg (Manufacturer's Specification)*	13.02.2020	75000/- dated 21.02.2022	
10.	021526	Voltral SR 100mg Tablets Each tablet contains: Diclofenac Sodium…….100mg (Manufacturer's Specification)*	13.02.2020	75000/- dated 21.02.2022	
11.	036125	Mepresor SR 200mg Tablets Each sustained release tablet contains: Metoprolol	13.02.2020	75000/- dated 21.02.2022	

		Tartrate…….200 mg (Manufacturer's Specification) *			
12.	070803	Tegral Suspension Each 5ml contains: Carbamazepine……100 mg (BP Specification)	13.02.2020	75000/- dated 21.02.2022	

The firm addressed the above queries as under:

Clarification for non-compliance of timelines given by the company and approved by Registration Board i.e., 30months:

With reference to earlier approval granted, we would like to share summary of progress in compliance of said decision as follows:

- Novartis has acquired a manufacturing plant, Drug Manufacturing License 000003, the approval letter of same was issued by DRAP in October 2020 (Attached Annexure 1).
- As per commitment, we have applied products for transfer of manufacturing site, to our newly acquired site, which we shared as "Wave 1" products in our undertaking. Approval of transfer is awaited.
- Further to our commitment, we have already started validation process and stability of Wave 2 products. Application of transfer will be applied as soon as all documentation are available mandatory to secure approval.
- We acknowledge that timelines of overall project have been delayed due to challenging situations of COVID in year 2020 and 2021. We have communicated same in our first quarterly report submitted to your kind office after approval granted by Drug Registration Board, however, it will not lead to any non-compliance to prevailing contract manufacturing when approval was granted nor with new contract manufacturing policy.

Status of products not applied for extension in contact manufacturing in registration letter dated: 22.01.2020 and 13.02.2020:

With reference to above query, we would like to update authorities' status of remaining products as follows which has not been applied for contract manufacturing:

- Products applied for transfer of registration as "Wave 1", in our undertaking, i-e Lamisil 250mg Tablet, Lamisil 125mg Tablet and Annuva Dispersible Tablet doesn't require said approval.
- Attached (Annexure 2), list of products, which we have divested to local pharmaceutical company "AGP Pharma", transfer of same has been submitted and many given approvals in registration board, therefore, approval of contract manufacturing is no longer relevant for Novartis to apply.
- Other products in the list, applied for contract manufacturing as per contract manufacturing policy.

Decision: **Registration Board discussed that initially M/s. Novartis Pharma (Pakistan) Ltd., 15-West Wharf Dockyard Road, Karachi was given contract manufacturing approval for thirty-nine products for a period of thirty months in 2017 and 2018 under Rule of 20A of Drug (LR&A) Rules 1976. The firm was again granted an extension for a period of 30 months vide DRAP letter dated 13.02.2020 with the condition to comply the aforesaid timelines, however same was not complied by the firm as per stance narrated above.**

Hence the Board directed the firm to provide timelines regarding the transfer of registration of above products to their own facility.

Case No: 11 Renewal applications M/s. Biogen Pharma 260/A- Industrial Triangle Kahuta Road, Islamabad

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
070175	Esotek Gel Contains: Erythromycin….20mg Isotretinoin….0.5mg (Biogen's Specification)	05.05.2011	**10000/- dated 09.05.2016** 20000/- dated 04.05.2021	Renewal is granted w.e.f. 05.05.2021 to 04.05.2026. The firm shall submit reference of finished product specifications as per decision of 295th meeting of Registration Board.

Case No: 12 Renewal applications M/s. Hoffmann Human Health Limited Lahore

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of renewal application	Remarks
028481	Sorbid Injection Each 10ml ampoule contains: Isosorbide Dinitrate... 10mg Sodium Chloride... 90mg.	22-08-2003 **Transfer of Reg: 31.08.2004**	20000 dated 27.06.2014	The product was cancelled in 317th meeting of Registration Board however before issuance of cancellation of registration the firm submitted a post registration variation approval regarding transfer of registration vide letter No. F.1-21/98-Reg-I dated 31.08.2004. Hence renewal application of firm is within time.

Decision: Keeping in view approval of transfer of registration vide letter No. F.1-21/98-Reg-I dated 31.08.2004, the renewal application for year 2014 is within time hence Registration Board revoked its earlier decision of cancellation of registration in its 317th meeting on above mentioned product.

Case No: 13 Renewal applications M/s. Noa Hemis Pharmaceuticals, Plot No. 154 Sector 23 Korangi Industrial Area Karachi.

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
042136	Artek 20 Tablet Each tablet contains: Esomeprazole Magnesium Trihydrate eq. to Esomeprazole (Pellets)…. 20mg	21-01-2006	10000/- dated 28.06.2016	The product was cancelled in 317th meeting of Registration Board however before issuance of cancellation of registration the firm submitted a copy of renewal letter issued vide letter No. F. 9-20/2008-RRR (Vol-I) dated 14.06.2011 wherein renewal was granted till 20.07.2016. Accordingly renewal was submitted on 28.06.2016 and is within time.
042137	Artek 40 Tablet Each tablet contains: Esomeprazole Magnesium Trihydrate eq. to Esomeprazole (Pellets)… 40mg	21-01-2006	10000/- dated 28.06.2016	-do-

Decision: **Keeping in view renewal letter issued vide letter No. F. 9-20/2008-RRR (Vol-I) dated 14.06.2011 wherein renewal was granted till 20.07.2016, the renewal application for year 2016 is within time hence Registration Board revoked its earlier decision of cancellation of registration in its 317th meeting on above mentioned products.**

Case No: 14 **Renewal applications M/s. Helix Pharma (Pvt) Ltd., A/56 SITE Mangopir Karachi.**

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Decision
002669	Cerelium Tablet 5mg Each tablet contains: Diazepam… 5mg	14-06-1977 PRV: **21.05.2005**	20-05-2015	The product was cancelled in 317th meeting of Registration Board and accordingly cancellation letter was issued on 05.07.2022 The firm has now submitted a copy of renewal letter issued vide letter No. F. 9-33/2006-RRR (Vol-I) dated 18.10.2010 wherein renewal was

				granted till **18.08.2015**. Hence renewal is within time.
024440	Oflocin Ear Drops 0.6% Each tablet contains: Ofloxacin …. 6mg (Inadvertently written as eye drops in 317 RB)	14-03-2002 PRV: **21.05.2005**	20-05-2015	-do-
024644	Zavir 600mg Tablet Each tablet contains: Ribavirin … 600mg	14-03-2002 PRV: **21.05.2005**	20-05-2015	-do-
015108	Limera Injection 600mg Each 2ml contains: Lincomycin as HCl… 600mg (Reg. No. Inadvertently written as 022542 in 317 RB)	26-11-1998 PRV: **18.08.2005**	20-05-2015	-do-
011361	Ulcerate Tablet Each tablet contains: Sucralfate (Basic Aluminum Sucrose Sulfate)… 1000mg (Reg. No. Inadvertently written as 024441 in 317 RB)	14-03-2002 PRV: **18.08.2005**	20-05-2015	

Decision: **Keeping in view renewal letter issued vide letter No. F. 9-33/2006-RRR (Vol-I) dated 18.10.2010 wherein renewal was granted till 18.08.2015, the renewal applications for year 2015 are within time hence Registration Board withdraw cancellation of registration issued vide letter No. F. No. 3-8/2022-RRR (M-317) dated 05.07.2022 as *void ab initio.***

Case No: 15 Renewal applications M/s. Rock Pharmaceutical Laboratories (Pvt) Ltd., Plot No. 134-B 135-B Nowshera Industrial Estate Risalpur

Reg. No.	Brand Name & Composition	Initial date of Registration	Due date	Renewal applied	Evidence provided by the firm
064256	Ranso 30mg Capsule Each capsule contains: Lansoprazole enteric coated pellets eq. to Lansoprazole… 30mg	10-08-2010	09-08-2015	22-11-2017	Rs. 10000/- dated 04.08.2015

064258	Dissium 50mg Capsules Each capsule contains: Diclofenac Sodium pellets eq. to Diclofenac sodium) …. 50mg	10-08-2010	09-08-2015	22-11-2017	Rs. 10000/- dated 04.08.2015
070367	Dissium 100mg Capsule Each capsule contains: Diclofenac Sodium (as sustained release pellets) … 100mg	05-05-2011	04-05-2016	22-11-2017	Rs. 10000/- dated 12.04.2016
The above products were cancelled in 317th meeting of Registration Board and accordingly cancellation letter was issued on 04.07.2022.The firm has now submitted evidence of submission of renewal of submission of above products which is recorded in last column above.					

Decision: **Keeping in view the submission of evidence of renewal by the firm which is recorded in last column above. The renewal applications of the above products are within time; hence Registration Board withdraws cancellation of registration issued vide F. No. 3-8/2022-RRR (M-317) dated 04.07.2022 as *void ab initio.***

Case No: 16 Application for renewal/ extension in contact manufacturing of M/s Tread Pharmaceuticals (Pvt) Limited Lahore from M/s Harman Pharmaceutical Laboratories (Pvt) Limited Lahore.

Reg. No.	Brand Name & Composition	Date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks
015773	Pentafen Injection Each ml contains: Pentazocine lactate…30mg	Transfer of reg. from Imp to local dated: 15.06.2002 Approval of extension in contract manufacturing dated: 21.10.2020	Dy. No: 13894 dated 08.06.2022 Rs. 75000/-	As per contact manufacturing policy contact manufacturing of psychotropic/ narcotics is not allowed.

Decision: **Registration Board did not accede the request of contract manufacturing extension of Pentafen Injection of the firm as the contract manufacturing of controlled drugs (narcotic drug or psychotropic substances or precursor chemicals) is not allowed under prevailing Contract Manufacturing Policy notified vide SRO 1374(I)/2021 dated 15.10.2021.**

Case No: 17 Renewal application of Cafol Injection 100mg applied by M/s Graton Pharma Karachi.

Reg. No.	Brand Name & Composition	Date of Registration PRV (If any)	Date of application (R&I) Fee submitted	Remarks

083163	Cafol 100mg/10ml Injection Each vial contains: 100mg Calcium Folinate Lyophilized Powder (B.P Specifications) Manufacturer: Yangtze River Pharmaceuticals Group Guanzhou Hairui Pharmaceutical Co., Ltd. No. Xiangshan Road Guangzhou Science City, High and New Technology Industrial Development Zone, Guangzhou China	**18.01.2017** Correction in formulation: 21.08.2017	Dy. No. 20787 dated 22.07.2022 Rs: 180000/-	The firm has requested for regularization of registration of product. Requisite fee is submitted under SRO 1005(I)/2017. The firm has submitted copy of CoPP issued by Medical Product Administration of Guangdong Province P.R. China.

Decision: **Registration Board regularized the renewal of registration of Cafol 100mg/10ml Injection (083163) under SRO 1005(I)/2017 and granted renewal w.e.f. 18.01.2022 to 17.01.2027. However, renewal letter shall be issued after submission of legalized CoPP and as per prevailing Import Policy for Finished Drugs.**

Case No: 18 Renewal application of M/s. Galaxy Pharma Pvt Ltd, Karachi for Aromek 2.5mg Tablet

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Renewal application submission details	Decision
052258	Aromek 10's Tabs Film Coated Tablets Each tablet contains: Letrozole……2.5mg **Product License Holder:** M/s Celon Pharma S.A, Ogrodowa 2A, Kielpin, 05-092 Lomianki, Poland **Manufacturer:** M/s Celon Pharma S.A. Marymoncka 15, 05-152 Kazun Nowy,Poland	11-06-2009	Dy. No. 1613 dated 25-03-2019 Rs. 20000/-	Renewal is granted w.e.f. 11.06.2019 to 10.06.2024 as per prevailing Import Policy for Finished Drugs.
Remarks: The case was discussed in the 317th meeting of Registration Board and deferred for clarification as manufacturer address mentioned on GMP certificate is different from the submitted CoPP. **As per**				

decision of the Board the firm has now submitted following documents vide Dy. No. 22030 dated 03.08.2022.

Original legalized CoPP vide No. 534/22 dated 14.06.2022 issued by Chief Pharmaceutical Inspector, Warsaw Poland indicating the product is registered and on market in Poland. Further details of product license holder and manufacturer are as under:

Product License Holder:

Celon Pharma S.A, Ogrodowa 2A, Kielpin, 05-092 Lomianki, Poland

Manufacturer:

Celon Pharma S.A. Marymoncka 15, 05-152 Kazun Norway, Poland

Original Legalized GMP certificate No. IWSF.405.60.2022.MP.1/WTC/0062_02_01/98 indicating inspection conducted on 22-25 Feb,2022 in compliance with GMP for the manufacturing site address: Celon Pharma S.A. Marymoncka 15, 05-152 Kazun Norway,Poland.

Case No: 19 Renewal application of Duofilm (005032) M/s. GlaxoSmithKline Pakistan Limited, Karachi

Assistant Director (I&V), DRAP, Islamabad has requested for confirmation of renewal status of below mentioned product registered in name of M/s GSK Pakistan Limited Karachi. Details are as under:

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Renewal application submission details	Decision
005032	Duofilm, application fluid (Cutaneous Solution) Contains: Lactic acid…15% w/w Salicylic acid….16.7%w/w	29.12.1979 Transfer of Reg: 23.10.1993 Transfer of Reg: 23.08.2011 Change of mfg. site: **20.05.2016**	Rs. 30000/- dated 20.05.2021 Dy. No. 30979 dated 11.11.2021 Rs. 60000/-	Renewal is granted w.e.f 20.05.2021 to 19.05.2026.

Case No: 20 Renewal application of M/s. Evergreen Pharmaceuticals 69-70/B Main Glazo Town Industrial Estate Anam Road, 20th KM-F/Pur Road Lahore

M/s. Evergreen Pharmaceuticals, Lahore has requested that for regularization of renewal of 2017 application of below mentioned registered product details as under:

Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Renewal application submission details	Decision
072687	Colif Solution Each ml contains: Flumequine sodium….200mg Colistin Sulphate…..252000IU	06-09-2012	Rs.10,000/- dated 09.10.2017 & Differential fee of 2017 Rs. 15000/- Dy.No.22925 Dated:15.08.2022	Deferred for evidence of submission of renewal for the year 2022.

072688	Flomax Solution Each ml contains: Florfenicol USP…..230mg	06-09-2012	Rs.10,000/- dated 09.10.2017 & Differential fee of 2017 Rs. 15000/- Dy.No.22925 Dated:15.08.2022	Deferred for evidence of submission of renewal for the year 2022.
072689	Heptic solution Each ml heptic contains: L. Carnitine…….50mg Betain Hcl……20mg Inositol……7mg Choline chloride.100mg Sorbitol……..200mg Magnesium Sulphate….10mg	06-09-2012	Rs.10,000/- dated 09.10.2017 & Differential fee of 2017 Rs. 15000/- Dy.No.22925 Dated:15.08.2022	Deferred for evidence of submission of renewal for the year 2022.
072690	Prokil Solution Each ml contains:- Amprolium as HCl….200mg	06-09-2012	Rs.10,000/- dated 09.10.2017 & Differential fee of 2017 Rs. 15000/- Dy.No.22925 Dated:15.08.2022	Deferred for evidence of submission of renewal for the year 2022.
072691	Ever-X Suspension Each ml contains:- Sulfadiazine…35.500mg Sulfadimidine.28.400mg Neomycin Sulfate..1.800mg Hyoscine Methyl Bromide……..0.040mg Pectin……7.100mg Kaolin……..103.300mg Vitamin B-1…..0.150mg Vitamin B- 2……0.220mg	06-09-2012	Rs.10,000/- dated 09.10.2017 & Differential fee of 2017 Rs. 15000/- Dy.No.22925 Dated:15.08.2022	Deferred for evidence of submission of renewal for the year 2022.

Case No: 21 Cancellation of Registration in 317th meeting of Registration Board of M/s. Jawa Pharmaceuticals (Pvt) Ltd.,112/10 Quaid-e-Azam Industrial Estate Kot Lakhpat Lahore. (DML No.000150).

Sr. No.	Reg. No.	Product Name & Composition	Date of Reg/ PRV	Renewal Due Date	Renewal Application Submission Date	Renewal Status
1.	004713	Ammonium Chloride Cough Syrup Each 5ml contains: Ammonium chloride …100mg	27-03-1979	26-03-2014	17-02-2016	

		Sodium Citrate….60mg Chlorpheniramine Maleate….2mg Ephedrine HCl….5mg Menthol….5ml				
2.	007873	Aminophylline 100mg Tablet Each tablet contains: Aminophylline…100mg	03-02-1985	02-02-2015	13-04-2015	
3.	007875	Chlorpheniramine Maleate 4mg Tablet Each tablet contains: Chlorpheniramine. 4mg	03-02-1985	02-02-2015	13-04-2015	
4.	007874	M.Broplex Tablet Each tablet contains: Thiamine HCl….1mg, Riboflavin…..1mg Nicotinamide...15 mg	03-02-1985	02-02-2015	13-04-2015	
5.	004712	Calamine Lotion Calamine…..15% Zinc Oxide……15%	27-03-1979	26-03-2014	13-04-2015	
6.	004954	Carminative Mixture Soda Bicarb……5% Spt Ammon.Arom….6.5%, TR Zingib. Forte….0.4%, TR, Card Co……..6.5%, SPT.Chloroform... 4% Aqua Menthpip	05-08-1979	04-08-2014	13-04-2015	
7.	004486	Chloroquine Phosphate Syrup Each ml contains: Chloroquine Base…..40mg	20-11-1978	19-11-2013	13-04-2015	
8.	004955	Ferrous Gluconate Syrup	08-09-1979	07-09-2014	13-04-2015	

		Ferrous Gluconae….300mg				
9.	007794	M.Brozine Elixir Promethazine Hcl…..5mg Vitamin C…..10mg Citric Acid……..50mg	28-01-1985	27-01-2015	13-04-2015	
10.	004953	Mephen Syrup Diphenhydramine HCl…..13.5mg Ammonium Chloride….131.5mg Sodium Citrate Citrate….55mg Chloroform……22 mg Menthol……1mg	05-08-1979	04-08-2014	13-04-2015	
11.	007877	M.Brovit Syrup Vitamin A 25000Iu Vitamin D 250IU Thiamine HCl…..0.55mg Nicotinamide…..5.5mg Riboflavin….065mg Ascorbic Acid….15mg	03-02-1985	02-02-2015	13-04-2015	
12.	004432	Diatrin Suspension Kaolin……2.92mg Pectin…..0.26mg Aluminum Hydroxide…..0.39 mg	30-09-1985	29-09-2015	13-04-2015	
13.	004433	Tr. Benzoine Co Benzoin….10% Aloes……2% Tolu Balsam….2.5% Prepared Storate…..7.5% Methyl SPT…..90% TR.Male…….100 ml	22-11-1978	21-11-2013	13-04-2015	
14.	006603	Mandls Paint	23-11-1982	22-11-2012	13-04-2015	
15.	006710	Gum Paint	21-02-1983	20-02-2013	13-04-2015	
16.	007876	Scabicid Lotion Benzyle Benzoate…..25%	03-02-1985	02-02-2015	13-04-2015	
Decision of 317th meeting:						

Registration Board cancelled the registration of above products as renewal applications were submitted after prescribed time period under rule 27 of Drug (LR&A) Rules 1976. Accordingly, cancellation letter was issued on 04 & 05th July 2022.

Reply of the firm:

Sr. No.	Reg. No	Name of product	Transfer of Reg /Issuance of renewal	Date of submission of renewal
1.	004713	Amrid Syrup (Ammonium Chloride Cough Syrup)	23.12.2006	17-02-2016
2.	007873	Aminophylline 100mg Tablet	Renewal granted till **28.04.2015** vide letter No. 11-17/2006-RRR dated 11.06.2009	13-04-2015
3.	007875	Chlorpheniramine Maleate 4mg Tablet	-do-	13-04-2015
4.	007874	M.Broplex Tablet	-do-	13-04-2015
5.	004712	Calamine Lotion	-do-	13-04-2015
6.	004954	Carminative Mixture	-do-	13-04-2015
7.	004486	Chloroquine Phosphate Syrup	-do-	13-04-2015
8.	004955	Ferrous Gluconate Syrup	-do-	13-04-2015
9.	007794	M.Brozine Elixir	-do-	13-04-2015
10.	004953	Mephen Syrup	-do-	13-04-2015
11.	007877	M.Brovit Syrup	-do-	13-04-2015
12.	004432	Diatrin Suspension	-do-	13-04-2015
13.	004433	Tr. Benzoine Co	-do-	13-04-2015
14.	006603	Mandls Paint	-do-	13-04-2015
15.	006710	Gum Paint	-do-	13-04-2015
16.	007876	Scabicid Lotion	-do-	13-04-2015

Firm has requested to review the above decision.

Decision: **Registration Board advised RRR section to come up with renewal submission details of above products for the year 2021 at Sr. No. 1 and for year 2020 at Sr. No. 2-16.**

Case No. 22 Cancellation of Registration in 317th meeting of Registration Board M/s. Biolabs (Pvt) Ltd., Plot No.145 Kahuta Triangle Industrial Estate Islamabad.

Sr. No.	Reg. No.	Brand Name & composition	Date of Reg	Due date	Renewal application date	Change of BN approval
1.	043169	Bio-Coccinil Water Soluble Powder	20-05-2006	19-05-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
2.	043174	Spelinamox Water Soluble Powder	27-04-2006	26-04-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
3.	043175	Bio-Tylodox Liquid	27-04-2006	26-04-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007

4.	043176	Bio-Reyl Water Soluble Powder	27-04-2006	26-04-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
5.	043177	Bio-Cox Water Soluble Powder	27-04-2006	26-04-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
6.	043178	Bio-Leva CS Oral Powder	20-05-2006	19-05-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
7.	043179	Bio-Fursebell Water Soluble Powder	20-05-2006	19-05-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
8.	043180	Trisulpham Suspension	20-05-2006	19-05-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
9.	043181	Albende CS Suspension	20-05-2006	19-05-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
10.	043182	Bio-Multibiotic Powder	27-04-2006	26-04-2016	24-02-2017	F.1-1/03-Reg-I (vet) dated: 13.03.2007
11.	023410	Panta Prol 50 Powder Each gm contains: Amprolium HCl… 500mg	17-05-1999	16-05-2014	11-06-2015	F.1-1/03-Reg-I (vet) dated: 22.06.2005
12.	025799	Kerry TS Suspension Each 100ml contains: Sulfadiazine … 40mg Trimethoprim… 8mg	07-10-2000	06-10-2015	30-05-2016	F.1-4/90-Reg-I (vet) dated: 28.12.2002

Remarks:
Registration Board cancelled the registration of above products as renewal applications were submitted after prescribed time period under rule 27 of Drug (LR&A) Rules 1976 and accordingly cancellation letters were issued vide letter dated: 04.07.2022, 05.07.2022 and 06.07.2022. The firm has now submitted that brand name of above products were changed vide erstwhile MOH approvals as recorded in last column above. As these approvals the renewal applications for the years recorded above are within time. The requested the Board to review the decision regarding cancellation of registrations.

Decision: **Keeping in view the approval of change of brand name recorded in last column above granted at the time of erstwhile MoH to the firm, renewal applications submitted above are within time, hence Registration Board withdraws cancellation of registration issued vide letter F. No. 3-8/2022-RRR (M-317) dated 04.07.2022, 05.07.2022 and 06.07.2022 as *void ab initio*.**

Case No: 23 Renewal Applications submitted after prescribed time period

Sr. No.	Reg. No.	Product Name & Composition	Date of Reg/ PRV	Renewal Due Date	Renewal Application Submission Date	Renewal Status
M/s. Otsuka Pakistan Ltd, No. F/4-9, Hub Industrial Estate, Distt Lasbella Balochistan, Pakistan						

13.	042288	Plasaline Irrigation Solution Each 1000ml contains:- Sodium chloride…0.9% Water for injection…q.s To make 1000ml	22-03-2006	21-03-2021	Dy. No. 21754 dated 01.08.2022 Rs. 15000/- Rs. 30000/- dated 29.11.2017	

Decision: Registration Board cancelled the registration of Plasaline Irrigation Solution (042288) as renewal application for year 2016 and 2021 was submitted after prescribed time period as required under Drug (LR&A) Rules 1976.

Case No. 24 M/s. Lachman Pharmaceuticals Lahore

Below mentioned product registered in name of M/s Lachman Pharmaceuticals Lahore was cancelled in 317th meeting of registration Board as renewal application was submitted after prescribed time period under rule 27 of Drug (LR&A) Rules 1976. Accordingly, cancellation letter was issued on 04.07.2022. The firm has now submitted evidence of submission of renewal which indicates the submission of 25.06.2016 rather 27.06.2016 and renewal application is within 60 days after the due date. The firm had submitted 40000/- at that time. The section has verified the date of submission of renewal from the record and it is found that submission date was 25.06.2016 instead 27.06.2016 but still application was filed on 61st day and is after the prescribed time period.

Sr. No.	Reg. No.	Brand Name & composition	Date of Reg	Due date	Renewal application date
1.	043111	Mycogal 105 Injection Each 100ml contains: Spiramycin Adipate…. 105MIU	26-04-2006	25-04-2016	25.06.2016

Decision: As the submission of renewal application is after the prescribed time period i.e. on 25.06.2016 (on 61st day after the due date). Hence Registration Board upheld its decision in its 317th meeting for cancellation of registration of Mycogal 105 Injection (043111).

Case No. 25 Renewal application of Batamine Injection (078954) of M/s Bajwa Pharmaceuticals Pvt Limited Lahore.

Sr. No.	Reg. No.	Brand Name & composition	Date of Reg	Renewal application date	Remarks
2.	078954	Batamine Injection Each ml contains: Ketamine HCl eq. to Ketamine….50mg	06.05.2015	Dy. No. 10967 dated 15.05.2020 Rs. 10000 Rs. 10000/- dated 24.05.2022	The renewal application is submitted within sixty days after due date. The firm has submitted differential fee.

Decision: Registration Board granted renewal to Batamine Injection (078954) w.e.f. 06.05.2020 to 05.05.2025

Case No. 26 Renewal applications of M/s. Berlex Labs. International Multan.

The registration of below mentioned products in name of M/s. Berlex Labs. International Multan were cancelled in 317th meeting of Registration Board and accordingly cancellation letter was issued on 04.07.2022. The firm has now informed that these products were granted renewal in 291st meeting of Registration Board as recorded in last column below and submitted copy of minutes of aforesaid meeting. Perusal of record revealed that stance of the firm is correct. Details are as under:

Sr. No.	Reg. No.	Brand Name & composition	Date of Reg	Due date	Renewal application date	Decision in M-291
1.	062592	Acio Tablets 40mg Each tablet contains: Famotidine……. 40mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
2.	062600	Azelab 250mg Capsules Each Capsule contains: Azithromycin (as Dihydrate) …250mg	24-02-2010	23-02-2015	12-05-2017	w.e.f. 06-06-2016 to 05-06-2021
3.	062599	Azelab 250mg Tablets Each tablet contains: Azithromycin (as Dihydrate)…250mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
4.	062598	Beridal 10mg Tablets Each tablet contains:- Cetirizine 2HCl….. 10mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
5.	060608	Bs Zole 20 mg Each Capsule contains: Esomeprazole Coated pellets of Magnesium trihydrate equivalent to Esomeprazole …...20mg	24-02-2010	23-02-2015	12-05-2017	Deferred for confirmation of Minutes of 291st of Meeting of Registration Board, DRAP (2-4th September, 2019) 1279 source fixation letter
6.	062606	BS-Zole Capsules 40mg Each Capsule contains: Esomeprazole Coated pellets of Magnesium trihydrate equivalent to	24-02-2010	23-02-2015	12-05-2017	Deferred for confirmation of source fixation letter

		Esomeprazole …...40mg				
7.	062594	Byrex 20mg Capsules Each Capsule contains: Piroxicam …..20mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
8.	062607	Diclotal 50mg Capsules Each Capsule contains: Diclofenac Sodium…. 50mg	24-02-2010	23-02-2015	12-05-2017	Deferred for confirmation of source fixation letter
9.	062609	Diclotal 100mg SR Capsules Each Capsule contains: Diclofenac Sodium…. 100mg	24-02-2010	23-02-2015	12-05-2017	Deferred for confirmation of source fixation letter
10.	062604	Diclotal SR100mg Tablets Each sustained release tablet contains: Diclofenac Sodium…. 100mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
11.	062591	Diclotal-K Tablets 75mg Each tablet contains: Diclofenac Potassium….75mg	24-02-2010	23-02-2015	12-05-2017	Deregistered vide letter dated: 18-08-2011
12.	062605	Lamizol Capsules 20mg Each Capsule contains: Omeprazole (Pellets) …… 20mg	24-02-2010	23-02-2015	12-05-2017	Deferred for confirmation of source fixation letter
13.	062602	Levobex 250mg Tablets Each tablet contains: Levofloxacin (as hemihydrate) …250mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
14.	062601	Levobex 500mg Tablets Each tablet contains: Levofloxacin (as hemihydrate)...500 mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
15.	062597	Mosther Forte Tablets Each tablet	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020

		contains: Artemether……80 mg Lumefantrine ..480mg				
16.	062589	Mosther Tablets Each tablet contains:- Artemether…40mg Lumefantrine ..240mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
17.	062603	Qubid 200mg Tablets Each tablet contains:- Ofloxacin……200 mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
18.	062590	Veoxy 250mg Tablets Each tablet contains:- Ciprofloxacin (as HCl)…. 250mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
19.	062595	Veoxy 500mg Tablets Each tablet contains:- Ciprofloxacin (as HCl) …500mg	24-02-2010	23-02-2015	12-05-2017	w.e.f 24-02-2015 to 23-02-2020
20.	065979	Bexelex 30mg Tablet Each tablet contains: Ephedrine HCL.30mg	18-10-2010	17-10-2015	31-07-2017	w.e.f 18-10-2015 to 17-10-2020
21.	071444	BS Pram Tablet Each tablet contains: Escitalopram as Oxalate…. 10mg	18-08-2011	17-08-2016	31-07-2017	w.e.f 18-08-2016 to 17-08-2021
22.	065981	Bercavir 0.5mg Tablet Each tablet contains: Entecavir….0.5mg	18-10-2010	17-10-2015	31-07-2017	w.e.f 18-10-2015 to 17-10-2020
23.	071443	Para Tablet Each tablet contains: Paracetamol… 450mg Orphenadrine Citrate… 35mg	18-08-2011	17-08-2016	31-07-2017	w.e.f 18-08-2016 to 17-08-2021
24.	065983	Diclotal 50mg Tablet Each tablet	18-10-2010	17-10-2015	31-07-2017	w.e.f 18-10-2015 to 17-10-2020

		contains: Diclofenac sodium….50mg				
25.	065984	Belex 5mg Tablet Each tablet contains: Levocetirizine 2HCL….5mg	18-10-2010	17-10-2015	31-07-2017	w.e.f 18-10-2015 to 17-10-2020

Decision: Keeping in view the decision of 291st meeting of Registration Board, the cancellation letter issued vide letter F. No. 3-8/2022-RRR (M-317) dated is hereby withdrawn up to the extent on the products granted renewal in 291st meeting.

Case No. 27 Renewal applications of M/s. Orient Animal Health (Pvt) Ltd, Karachi.

Below mentioned renewal application of M/s. Orient Animal Health, (Pvt) Ltd, Karachi was considered in 297th meeting of Registration Board and decided as follows:

Sr. No	Reg. No.	Brand Name and Composition	Initial date of Registration	Date of application (R&I) Fee submitted	Decision
1.	048127	Aivlosin Soluble (Granules for use in drinking water) Contains: - Tylosin Tartrate (Acetyl Isovaleryl) ……85.0% **Product License Holder:** M/s. ECO Animal Health 78 Coombe Road new malden Surrey, KT3 4QS, United Kingdom **Manufacturer:** Cod Beck Blenders Ltd., Cod beck Estate, Dalton Thirsk, north Yorkshire Y07 3HR, United Kingdom	03-03-2008	Dy. No. 30454 dated 15-01-2020 Rs. 20000/-	Renewal is granted w.e.f.03.03.2018 to 02.03.2023 as per Import Policy for Finished Drugs.

Remarks:

The product was deferred in 297th meeting of Registration Board for submission of COPP for Aivlosin Soluble Powder 85% as the submitted COPP is of Aivlosin 62.5% granules. Hence the firm submitted the statement on behalf of manufacturer that ***"The product Aivlosin Soluble is same in all markets. Although the pharmaceutical form is listed as an oral granule on some product labels the generic term oral powder is used. Despite this difference the product in question is the same".***

Further as per CoPP submitted by the firm Tylvalosin as Tartrate 62% is equivalent to Tylvalosin tartrate 85% (Acetyl Isovaleryl Tylosin Tartrate) as per registration letter.

Sr. No.	Details of application	No. of Cases
A	Imported Human Biologicals from Reference Countries/WHO PQ	04
B	Imported Human Biologicals from Non-Reference Countries	08
C	Imported Veterinary Biologicals from Reference Countries	03
D	Imported Veterinary Biologicals from Non-Reference Countries	09
E	Miscellaneous/ Deferred Cases	29
Additional Agenda		19
Total		72

Sr. No.	Assistant Director	Designated No.	No. of Cases
1.	Mr. M. Zubair Masood	AD-I	23
2.	Mr. Saadat Ali Khan	AD-II	28
3.	Ms. Haleema Shareef	AD-III	17
4.	Mr. M. Kashif	AD_IV	04

Cases of AD-I (M. Zubair Masood)

A: Imported Human Biologicals from Reference countries/WHO PQ

1.	**Name, address of Applicant / Importer**	M/s Roche Pakistan Limited, 1st floor, 37-B, Block 6, PECHS, Karachi.
	Details of Drug Sale License of importer	**License No:** 0171 **Address:** Roche Pakistan Limited, 1st floor, 37-B Block 6 PECHS, Karachi. **Address of Godown:** • R-PI, plot no. 56, sector 15, K.I.A, Karachi **Validity:** 13-09-2022. **Status:** Drug License by way of wholesale **Renewal:** N/A
	Name and address of marketing authorization holder (abroad)	M/s Roche Pharma (Schweiz) AG, Gartenstrasse 9, 4052 Basel, Switzerland
	Name, address of manufacturer(s)	M/s F. Hoffmann-La Roche AG, Wurmisweg, Kaiseraugst, 4303, Switzerland
	Name of exporting country	Switzerland
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	Firm has submitted original, legalized copy of CoPP certificate (21006031) dated 15-06-2021 issued by Swissmedic. CoPP indicates that the applied product is on free sale in the market in exporting country free sale and manufacturer conforms GMP.

	Details of letter of authorization / sole agency agreement	• Pakistan Notarized copy of Authorization letter from M/s F. Hoffmann-La Roche Ltd., Basel Switzerland in name of M/s Roche Pakistan Limited, Karachi dated 16-12-2020. • Pakistan notarized copy of letter indicating relationship between product license holder and M/s F. Hoffmann-La Roche Ltd., Basel. Switzerland.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) Generic Drug Product (GDP)
	Intended use of pharmaceutical product	Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 16131 & 6925 (R&I) Dated 10-06-2021 & 11-03-2022
	Details of fee submitted	PKR 75,000/-: 11-03-2022
	The proposed proprietary name / brand name	Polivy 30mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Polatuzumab Vedotin ……30mg
	Dosage form of applied drug	Powder for Concentrate for Solution for Injection
	Pharmacotherapeutic Group of (API)	Monoclonal Antibody
	Reference to Finished product specifications	Innovator.
	Proposed Pack size	1's Vial
	Proposed unit price	Not Provided.
	Shelf Life	30 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	The product is itself approved in SwissMedic.
	For generic drugs (me-too status)	Not Available

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Lonza Ltd., Lonzastrasse, CH-3930 Visp, Switzerland
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at -20^0C is for 24 months. The accelerated stability data conducted at $5^0C \pm 3^0$C is for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the validation of Analytical procedures including verification of compendial methods and validated of product-specific methods for their suitability of intended use to support polatuzumab vedotin lyophilized drug product testing.
	Container closure system of the drug product	• 6 mL, USP/Ph. Eur./JP Type I glass, borosilicate, colorless • 20 mm D777-1, fluororesin laminate, latex-free (lyophilization type) • 20 mm aluminum seal with plastic flip-off cap.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 Process Performance Qualification Batches. The accelerated stability study data is conducted at 25^0C /60RH for 6 months. The real time stability study data is conducted at 5 ± 3^0C for 9 months.
	Module-IV Non-Clinical	Pharmacology: • Comparing Efficacy of DCDS4501A and DCDS5017A against Human Burkitt's Lymphoma BJAB-PD.cyCD79b.E3 Xenograft in C.B-17 Fox Chase SCID Mice

		• The Effect of MCDS4409A and DCDS4501A against Human Diffuse Large B-Cell Lymphoma WSU-DLCL2 Xenograft in C.B-17 Fox Chase SCID Mice. • The Effect of MCDS4409A and DCDS4501A against Human Burkitt's Lymphoma BJAB-luc Xenograft in C.B-17 Fox Chase SCID Mice. • Measurement of Cell-Based Binding Affinities of Anti-CD79b Clinical Candidate Antibodies DCDS4501A and MCDS4409A and Anti-CD79b Cynomolgus Monkey Surrogate Antibodies DCDS5017A and MCDS1358A. • Effects of MCDS4409A and MCDS1358A on the Induction of Cytokine Release by Peripheral Blood Mononuclear Cells. • Effects of Monomethyl Auristatin E (MMAE) on Cloned hERG Potassium Channels Expressed in Human Embryonic Kidney Cells. Pharmacokinetics: • Full Validation of a Method for the Determination of MMAE in Cynomolgus Monkey Plasma by HPLC with MS/MS Detection. • Quantitative Determination of MMAE in Cynomologus Monkey Plasma by LCIMSIMS. • Quantitative Determination of MMAE in Cynomolgus Monkey Plasma by LC/MS/MS. • Quantitative Determination of MMAE in Rat (Sprague-Dawley) Plasma by LC/MS/MS. • CD79.005 Total Anti-huCD79 (DCDS4501A) Antigen ELISA. • CD79.006 Anti-huCD79b-vc-MMAE (DCDS4501A) Antibody ELISA. • A 6-Week Single Dose Intravenous Pharmacokinetic and Pharmacodynamic Study of MCDS1358A and DCDS5017A in Male Cynomolgus Monkeys. • Characterization of the Pharmacokinetics of Naked SN8 (MCDS4409A), SN8-vc-MMAE (DCDS4501A), Naked 10D10 (MCDS1358A), and 10D10-vc-MMAE(DCDS5017A) in Female SCID Mice. • Determination of Metabolism, Tissue Distribution, and Route of Excretion Following IV Administration of [3H]-MMAE and Unlabeled MMAE in Female Sprague-Dawley RatsEvaluation of In Vitro MMAE Red Blood Cell • Partitioning Potential in Mouse, Rat, Cynomolgus Monkey, and Human. • In Vitro Plasma Protein Binding Determination of G00060245 (MMAE) in Human, Rat, and Monkey. • Determination of Tissue Distribution of DCD4501A (Anti-CD79b-vc-MMAE) Following IV Administration of [125I]/[111In]-Anti-CD79b-vc-MMAE in Female Sprague-Dawley Rats. Toxicology:

		• Safety Evaluation of Herceptin-Auristatin (AS) Immunoconjugates in Female Sprague- Dawley Rats. • Multiple Dose Intravenous Toxicity, Toxicokinetic, and Cardiovascular Safety Pharmacology Study of DCDS4501A and DCDS5017A Administered Intravenously to Cynomolgus Monkeys Once Every 3 Weeks for Four Doses, Followed by at Least a 9-Week Recovery Period. • L5178Y TK+/- Mouse Lymphoma Forward Mutation Assay with a Confirmatory Assay. • In Vivo Rat Bone Marrow Micronucleus Assay. • Intravenous Injection Study for Effects on Embryofetal Developmental and Toxicokinetics with SGN-35 and SGD-1010 in Rats. • Tissue Cross-Reactivity of DCDS4501A with Human Tissues Ex Vivo. SGD-1006, SGD-1427 and SGD-1010 photosafety evaluation.
	Module-V Clinical	• Selectivity in the Presence of Co-Administered Drugs on Bendamustine in Human Plasma by HPLC with MS/MS Detection. • Validation of a Method for the Determination of Cyclophosphamide in Human Plasma by HPLC with MS/MS Detection. • Selectivity in the Presence of Co-Administered Drugs on Doxorubicin in Human Plasma by HPLC with MS/MS Detection. • Validation of a Method for the Determination of Bendamustine and M3 in Human Plasma by HPLC with MS/MS Detection. • An Open-Label, Multicenter, Phase I Trial of the Safety and Pharmacokinetics of Escalating Doses of DCDS4501A in Patients with Relapsed or Refractory B-Cell Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia and DCDS4501A in Combination with Rituximab in Patients With Relapsed or Refractory B-Cell Non-Hodgkin's Lymphoma. • Evaluation of Concentration-QTc Relationship of Polatuzumab Vedotin in Patients with B-Cell Hematologic Malignancies.
	Remarks of Evaluator	**The firm has submitted real time stability data of 09 months only and requested shelf life of 30 months.**
Decision: **Keeping in view legalized CoPP and approval of Swissmedic (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs. Firm will submit real time stability data of 3 commercial batches up to the demanded shelf life before issuance of registration letter.**		
2.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novo Nordisk Pharma (Private) Limited,** **113, Shahra-e-Iran, Clifton, Karachi.**
	Name, address of Manufacturing site.	113, Shahra-e-Iran, Clifton, Karachi. **Address of go-down:** 208/1, Sector 23, KIA, Karachi

		Validity: 09-04-2023 Status: License to sell drugs by way of Wholesale.
	Name and address of marketing authorization holder (abroad)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
	Name, address of manufacturer(s)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
	Name of exporting country	Denmark
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: • Firm has submitted legalized copy of CoPP (No. 2021110493) dated 03-11-2021 issued by Danish Medicine Agency valid for two years. The CoPP specifies free sale status of the product in Exporting country with its availability. The CoPP also confirms the GMP status of the firm.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Corporate Vice President (Global Regulatory Affairs) of Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark authorizes "M/s Novo Nordisk Pharma (Private) Limited" to be their wholly owned subsidiary and sole importer in Pakistan and to import, distribute & sale the product. The letter was issued on 21-10-2021 and valid till 31-12-2024.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 31966 dated 22-11-2021
	Details of fee submitted	PKR 75,000/-: dated 22/10/2021 Deposit Slip No. 6686005328
	The proposed proprietary name / brand name	NovoEight® 250 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Powder Vial:** Each Vial contains: Human Coagulation Factor VIII, Turoctocog alfa…..250IU **Diluent PFS:**

		Each Pre-filled syringe contains: 0.9% Sodium chloride……4mL
	Dosage form of applied drug	Powder and solvent for solution for Injection
	Pharmacotherapeutic Group of (API)	Antihemorrhagics, blood coagulation factor VIII, ATC code: B02BD02
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's (Powder + Solvent)
	Proposed unit price	Not Provided/As per SRO
	Shelf Life	30 months
	Storage Conditions	Store in refrigerator (2°C – 8°C).
	The status in reference regulatory authorities	The product is itself registered in Danish Medicine Agency & EMA.
	For generic drugs (me-too status)	Not Applicable
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	Novo Nordisk US Bio Production Inc. 9 Technology Drive Lebanon, NH 03784 USA Novo Nordisk A/S Brennum Park 25K, DK-3400, Hillerød, Denmark Novo Nordisk A/S Novo Allé, DK-2880 Bagsværd, Denmark Bioreliance Ltd Todd Campus West of Scotland Science Park, Glasgow G20 OXA, Scotland, UK.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated and real time conditions. The real time stability data is conducted at -80°C±10°C for 60 months for 3 batches with the approved shelf life of 48 months.

	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted analytical methods as per Pharmacopeia. The methods are validated as per SOPs. The Analytical methods are listed below • Water content-Karl Fischer Coulorimetric titration (USP/JP) • Visual evaluation of clarity (Ph.Eur) • Color (Ph.Eur) • Particulate contamination/Foreign insoluble matter (Ph.Eur/JP) • pH (Ph.Eur/USP/JP) • Potency-chromogenic substrate assay (Ph.Eur/) • Particulate matter (Ph.Eur/USP/JP) • Osmalality (Ph.Eur/USP/JP) • Endotoxin (Ph.Eur/USP/JP) • Sterility (Ph.Eur/USP/JP)
	Container closure system of the drug product	Powder in Vial: The primary packaging of vial for turoctocog alfa drug product is a 5 mL vial made of type I glass, high hydrolytic resistance, in compliance with Ph Eur, USP and JP. The lyophilisation rubber stopper for the turoctocog alfa drug product is made of a grey chlorobutyl rubber. The rubber meets the requirements of Ph Eur (Rubber closures for aqueous preparations for parenteral use, Type I) and USP (Elastomeric Closures for Injections). The stopper is sealed with a snap-off cap made of aluminium and plastic.
		Diluent in PFS: The container closure system consists of a siliconised glass barrel made of borosilicate glass type 1 (Ph. Eur., USP and JP), a siliconised rubber plunger made of bromobutyl rubber (Ph. Eur., USP), and a syringe closure system (V-OVS 10.6®) composed of a tip cap with a luer lock and a tamperevident seal. Only the tip cap of the syringe closure system is in contact to the 0.9 % Sodium Chloride Solution. This tip cap is also made of bromobutyl rubber (Ph. Eur., USP).
	Stability study data of drug product, shelf life and storage conditions	Powder in Vial: Firm has submitted Primary stability study data of 3 batches. The accelerated stability study data is conducted at 30°C±2°C/75%±5RH for 12 months. The real time stability study data is conducted at 5°C±3°C/75%±5RH for 30 months. Firm has also submitted 6 months data at 40°C±2°C/75%±5RH
		Diluent in PFS: Firm has submitted Primary stability study data of 3 batches respectively. The accelerated stability study data is conducted at 30°C±2°C/65%±5RH for 60 months. The real time stability study data is conducted at 5°C for 60 months.

	Module-IV Non-Clinical	The Firm has submitted following non-clinical studies: Pharmacology: Primary Pharmacodynamics • Species crossreactivity (Turoctocog alfa enhanced thrombin generation in rat, cynomolgus monkey and human plasma in a dose dependent manner. This demonstrates species cross-reactivity of turoctocog alfa to rat and cynomolgus) • Thrombin generation assay (Dose dependent increase in thrombin generation. Similar thrombin generation capacity by turoctocog alfa and Advate®, ReFacto® and Haemate®). • vWF interaction (Turoctocog alfa and ReFacto® bind vWF with very similar affinities.) • vWF interaction (Turoctocog alfa, Advate® and ReFacto® bind vWF with very similar affinities). • SDS-PAGE and Western blot (FVIII related peptides, detected by Western Blot using different FVIII antibodies, are similar for turoctocog alfa and different commercially available FVIII products). • Kinetics mAb by SPR (Binding constants of different FVIII • mAbs are similar for turoctocog alfa, Advate® and ReFacto®). • Tail bleeding in F8 knock-out mice (Bleeding time and blood loss were significantly longer in vehicle treated F8 knock-out mice compared to normal CB57. The bleeding time and blood loss after administration of 200 IU/kg Advate® or turoctocog alfa was not significantly different from normal controls. No difference in potency was observed between Advate® and turoctocog alfa). • Knee injury model in F8 knock-out mice (F8 knock-out mice had a visual bleeding score (VBS) of 2.04 (SD1.30). Treatment with turoctocog alfa and Advate® significantly reduced the bleeding with a mean of 0.58 (SD 0.93) and 0.50 (SD 1.06) respectively. The mean change in joint diameter for F8 knock-out, untreated, and treated with turoctocog alfa and Advate® respectively was: 1.23 mm (SD 0.94); 0.32 mm (SD 0.39) and 0.25 mm (SD 0.39). • PK/PD study in haemophilia A dogs (Turoctocog alfa and Advate® were equally capable of normalising whole blood clotting time and showed similar activity profile over time). Secondary Pharmacodynamics • Not applicable as all studies done are related to desired therapeutic target. Safety Pharmacology • Safety Pharmacology is done on Male Cynomolgus and monkeys and observed following functions • Central Nervous System • Respiratory Function • Kindey Funcation • Cardiovascular system Pharmacodynamic Drug Interactions • Not Performed Pharmacokinetic:

		Absorption is studied with Test System • F8 Knock-out mice, single dose (PK of turoctocog alfa, Advate® and ReFacto® in F8 knock-out mice) • Haemophilia A dog, single dose (PK in heamophila A dogs) • Cynomolgus monkey, single dose (Toxicokinetics) • Sprague Dawley rat, multiple dose (Toxicokinetics) • Cynomolgus monkey, multiple dose (Toxicokinetics) Distribution is studies with Test System (C57Bl mice) Toxicology: • Single Dose Escalation Toxicity in Male cynomolgus monkey • Repeat Dose Toxicity in Rat and Male cynomolgus monkey • Genotoxicity • Carcinogenicity • Reproductive and Developmental Toxicity • Local Tolerance in Male New Zealand White Rabbits and Male cynomolgus monkey and Rats. • Other Toxicity Studies • Immunogenicity Study in rats
	Module-V Clinical	The Firm has submitted following clinical studies: • NN7008-3522 First human dose trial A multi-centre, multi-national, open-label, first human dose, PK, safety, single dose trial using a sequential design in patients with haemophilia A. • NN7008-3600 PK in Japanese patients. A multi-centre, open-label, single dose trial investigating the PK of turoctocog alfa in Japanese patients with haemophilia A. • NN7008-3893 PK trial (two lots). A multi-centre, open-label, trial investigating the PK of a single dose of turoctocog alfa in patients with haemophilia A. • NN7008-4015 PK trial (four lots). A multi-centre, open-label trial investigating the PK of four lots of turoctocog alfa in patients with haemophilia A. • NN7008-4239 PK trial. A multicentre, open-label trial evaluating the PK of turoctocog alfa in relation to BMI in patients with haemophilia A. • NN7008-3543 Pivotal trial. A multi-centre, multi-national, • open-label, safety, efficacy, single arm trial in patients with severe haemophilia A investigating turoctocog alfa when used for prevention and treatment of bleeds. The trial included a sub-trial designed to evaluate the safety and efficacy of turoctocog alfa when used for prevention and treatment of bleeding during surgical procedures and in the surgery period • NN7008-3545 Paediatric trial. A multi-centre, open-label, noncontrolled safety and efficacy trial of turoctocog alfa in previously treated paediatric patients with haemophilia A. • NN7008-3568 Extension trial. A multi-centre, multi-national, open-label, non-randomised, single treatment arm safety and efficacy extension trial in patients with haemophilia A investigating turoctocog alfa when used in a preventative or on-demand treatment regimen. The trial

		• includes a sub-trial designed to evaluate safety and efficacy of turoctocog alfa during surgery. • NN7008-4028 Previously treated Chinese patients. Efficacy and safety of turoctocog alfa for prevention and treatment of bleeding episodes in previously treated Chinese patients with haemophilia A. • NN7008-3553 Non-interventional post autorisation safety study (PASS). A multi-centre non-interventional study of safety and efficacy of turoctocog alfa during long-term prevention and treatment of bleeds in previously FVIII treated patients with severe and moderately severe haemophilia A (FVIII ≤2%). • NN7008-4105 Non-interventional study. A multicentre, non-interventional post marketing study of safety and efficacy of turoctocog alfa (rFVIII) during long-term treatment of haemophilia A in Japan. • NN7008-4253 Non-interventional study. Multicentre, post-authorisation safety study with turoctocog alfa in Mexican haemophilia A patients. • NN7008-4304 Non-interventional study. A prospective multicentre observational study of safety and efficacy outcomes with turoctocog alfa for prevention and control of bleeds in mild, moderate and severe Haemophilia A in India. • NN7008-3809 Trial in previously untreated patients. Safety and efficacy of turoctocog alfa in prevention and treatment of bleeds in paediatric previously untreated patients with haemophilia A (<6 years of age).
Decision: **Keeping in view legalized CoPP and approval of Dansih Medicine Agency (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs.**		
3.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novo Nordisk Pharma (Private) Limited,** **113, Shahra-e-Iran, Clifton, Karachi.**
	Name, address of Manufacturing site.	113, Shahra-e-Iran, Clifton, Karachi. **Address of go-down:** 208/1, Sector 23, KIA, Karachi Validity: 09-04-2023 Status: License to sell drugs by way of Wholesale.
	Name and address of marketing authorization holder (abroad)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
	Name, address of manufacturer(s)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
	Name of exporting country	Denmark
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: • Firm has submitted legalized copy of CoPP (No. 2021110493) dated 03-11-2021 issued by Danish Medicine Agency valid for two years. The

		CoPP specifies free sale status of the product in Exporting country with its availability. The CoPP also confirms the GMP status of the firm.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Corporate Vice President (Global Regulatory Affairs) of Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark authorizes "M/s Novo Nordisk Pharma (Private) Limited" to be their wholly owned subsidiary and sole importer in Pakistan and to import, distribute & sale the product. The letter was issued on 21-10-2021 and valid till 31-12-2024.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 31967 dated 22-11-2021
	Details of fee submitted	PKR 75,000/-: dated 22/10/2021 Deposit Slip No. 96507294753
	The proposed proprietary name / brand name	NovoEight® 500 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Powder Vial:** Each Vial contains: Human Coagulation Factor VIII, Turoctocog alfa…..500IU **Diluent PFS:** Each Pre-filled syringe contains: 0.9% Sodium chloride……4mL
	Dosage form of applied drug	Powder and solvent for solution for Injection
	Pharmacotherapeutic Group of (API)	Antihemorrhagics, blood coagulation factor VIII, ATC code: B02BD02
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's (Powder + Solvent)

	Proposed unit price	Not Provided/As per SRO
	Shelf Life	30 months
	Storage Conditions	Store in refrigerator (2°C – 8°C).
	The status in reference regulatory authorities	The product is itself registered in Danish Medicine Agency & EMA
	For generic drugs (me-too status)	Not Applicable
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	Novo Nordisk US Bio Production Inc. 9 Technology Drive Lebanon, NH 03784 USA Novo Nordisk A/S Brennum Park 25K, DK-3400, Hillerød, Denmark Novo Nordisk A/S Novo Allé, DK-2880 Bagsværd, Denmark Bioreliance Ltd Todd Campus West of Scotland Science Park, Glasgow G20 OXA, Scotland, UK.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated and real time conditions. The real time stability data is conducted at -80°C±10°C for 60 months for 3 batches with the approved shelf life of 48 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Analytical method validation/verification of product	Firm has submitted analytical methods as per Pharmacopeia. The methods are validated as per SOPs. The Analytical methods are listed below • Water content-Karl Fischer Coulorimetric titration (USP/JP) • Visual evaluation of clarity (Ph.Eur) • Color (Ph.Eur) • Particulate contamination/Foreign insoluble matter (Ph.Eur/JP) • pH (Ph.Eur/USP/JP) • Potency-chromogenic substrate assay (Ph.Eur/) • Particulate matter (Ph.Eur/USP/JP) • Osmalality (Ph.Eur/USP/JP) • Endotoxin (Ph.Eur/USP/JP) • Sterility (Ph.Eur/USP/JP)
	Container closure system of the drug product	Powder in Vial: The primary packaging of vial for turoctocog alfa drug product is a 5 mL vial made of type I glass, high hydrolytic resistance, in compliance with Ph Eur, USP and JP. The lyophilisation rubber stopper for the turoctocog alfa drug product is made of a grey chlorobutyl rubber. The rubber meets the requirements of Ph Eur (Rubber closures for aqueous preparations for parenteral use, Type I) and USP (Elastomeric Closures for Injections). The stopper is sealed with a snap-off cap made of aluminium and plastic.
		Diluent in PFS: The container closure system consists of a siliconised glass barrel made of borosilicate glass type 1 (Ph. Eur., USP and JP), a siliconised rubber plunger made of bromobutyl rubber (Ph. Eur., USP), and a syringe closure system (V-OVS 10.6®) composed of a tip cap with a luer lock and a tamperevident seal. Only the tip cap of the syringe closure system is in contact to the 0.9 % Sodium Chloride Solution. This tip cap is also made of bromobutyl rubber (Ph. Eur., USP).
	Stability study data of drug product, shelf life and storage conditions	Powder in Vial: Firm has submitted Primary stability study data of 3 batches for lowest strength (250IU) & higher strength (3000IU). The accelerated stability study data is conducted at 30°C±2°C/75%±5RH for 12 months. The real time stability study data is conducted at 5°C±3°C/75%±5RH for 30 months. Firm has also submitted 6 months data at 40°C±2°C/75%±5RH
		Diluent in PFS: Firm has submitted Primary stability study data of 3 batches respectively. The accelerated stability study data is conducted at 30°C±2°C/65%±5RH for 60 months. The real time stability study data is conducted at 5°C for 60 months.
	Module-IV Non-Clinical	The Firm has submitted following non-clinical studies: Pharmacology: Primary Pharmacodynamics • Species crossreactivity (Turoctocog alfa enhanced thrombin generation in rat, cynomolgus monkey and human plasma in a dose dependent manner.

		This demonstrates species cross-reactivity of turoctocog alfa to rat and cynomolgus) • Thrombin generation assay (Dose dependent increase in thrombin generation. Similar thrombin generation capacity by turoctocog alfa and Advate®, ReFacto® and Haemate®). • vWF interaction (Turoctocog alfa and ReFacto® bind vWF with very similar affinities.) • vWF interaction (Turoctocog alfa, Advate® and ReFacto® bind vWF with very similar affinities). • SDS-PAGE and Western blot (FVIII related peptides, detected by Western Blot using different FVIII antibodies, are similar for turoctocog alfa and different commercially available FVIII products). • Kinetics mAb by SPR (Binding constants of different FVIII • mAbs are similar for turoctocog alfa, Advate® and ReFacto®). • Tail bleeding in F8 knock-out mice (Bleeding time and blood loss were significantly longer in vehicle treated F8 knock-out mice compared to normal CB57. The bleeding time and blood loss after administration of 200 IU/kg Advate® or turoctocog alfa was not significantly different from normal controls. No difference in potency was observed between Advate® and turoctocog alfa). • Knee injury model in F8 knock-out mice (F8 knock-out mice had a visual bleeding score (VBS) of 2.04 (SD1.30). Treatment with turoctocog alfa and Advate® significantly reduced the bleeding with a mean of 0.58 (SD 0.93) and 0.50 (SD 1.06) respectively. The mean change in joint diameter for F8 knock-out, untreated, and treated with turoctocog alfa and Advate® respectively was: 1.23 mm (SD 0.94); 0.32 mm (SD 0.39) and 0.25 mm (SD 0.39). • PK/PD study in haemophilia A dogs (Turoctocog alfa and Advate® were equally capable of normalising whole blood clotting time and showed similar activity profile over time). Secondary Pharmacodynamics • Not applicable as all studies done are related to desired therapeutic target. Safety Pharmacology • Safety Pharmacology is done on Male Cynomolgus and monkeys and observed following functions • Central Nervous System • Respiratory Function • Kindey Funcation • Cardiovascualar system Pharmacodynamic Drug Interactions • Not Performed Pharmacokinetic: Absorption is studied with Test System • F8 Knock-out mice, single dose (PK of turoctocog alfa, Advate® and ReFacto® in F8 knock-out mice) • Haemophilia A dog, single dose (PK in heamophila A dogs)

		• Cynomolgus monkey, single dose (Toxicokinetics) • Sprague Dawley rat, multiple dose (Toxicokinetics) • Cynomolgus monkey, multiple dose (Toxicokinetics) Distribution is studies with Test System (C57Bl mice) Toxicology: • Single Dose Escalation Toxicity in Male cynomolgus monkey • Repeat Dose Toxicity in Rat and Male cynomolgus monkey • Genotoxicity • Carcinogenicity • Reproductive and Developmental Toxicity • Local Tolerance in Male New Zealand White Rabbits and Male cynomolgus monkey and Rats. • Other Toxicity Studies • Immunogenicity Study in rats
	Module-V Clinical	The Firm has submitted following clinical studies: • NN7008-3522 First human dose trial A multi-centre, multi-national, open-label, first human dose, PK, safety, single dose trial using a sequential design in patients with haemophilia A. • NN7008-3600 PK in Japanese patients. A multi-centre, open-label, single dose trial investigating the PK of turoctocog alfa in Japanese patients with haemophilia A. • NN7008-3893 PK trial (two lots). A multi-centre, open-label, trial investigating the PK of a single dose of turoctocog alfa in patients with haemophilia A. • NN7008-4015 PK trial (four lots). A multi-centre, open-label trial investigating the PK of four lots of turoctocog alfa in patients with haemophilia A. • NN7008-4239 PK trial. A multicentre, open-label trial evaluating the PK of turoctocog alfa in relation to BMI in patients with haemophilia A. • NN7008-3543 Pivotal trial. A multi-centre, multi-national, • open-label, safety, efficacy, single arm trial in patients with severe haemophilia A investigating turoctocog alfa when used for prevention and treatment of bleeds. The trial included a sub-trial designed to evaluate the safety and efficacy of turoctocog alfa when used for prevention and treatment of bleeding during surgical procedures and in the surgery period • NN7008-3545 Paediatric trial. A multi-centre, open-label, noncontrolled safety and efficacy trial of turoctocog alfa in previously treated paediatric patients with haemophilia A. • NN7008-3568 Extension trial. A multi-centre, multi-national, open-label, non-randomised, single treatment arm safety and efficacy extension trial in patients with haemophilia A investigating turoctocog alfa when used in a preventative or on-demand treatment regimen. The trial • includes a sub-trial designed to evaluate safety and efficacy of turoctocog alfa during surgery.

		• NN7008-4028 Previously treated Chinese patients. Efficacy and safety of turoctocog alfa for prevention and treatment of bleeding episodes in previously treated Chinese patients with haemophilia A. • NN7008-3553 Non-interventional post autorisation safety study (PASS). A multi-centre non-interventional study of safety and efficacy of turoctocog alfa during long-term prevention and treatment of bleeds in previously FVIII treated patients with severe and moderately severe haemophilia A (FVIII ≤2%). • NN7008-4105 Non-interventional study. A multicentre, non-interventional post marketing study of safety and efficacy of turoctocog alfa (rFVIII) during long-term treatment of haemophilia A in Japan. • NN7008-4253 Non-interventional study. Multicentre, post-authorisation safety study with turoctocog alfa in Mexican haemophilia A patients. • NN7008-4304 Non-interventional study. A prospective multicentre observational study of safety and efficacy outcomes with turoctocog alfa for prevention and control of bleeds in mild, moderate and severe Haemophilia A in India. • NN7008-3809 Trial in previously untreated patients. Safety and efficacy of turoctocog alfa in prevention and treatment of bleeds in paediatric previously untreated patients with haemophilia A (<6 years of age).
Decision: Keeping in view legalized CoPP and approval of Dansih Medicine Agency (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs.		
4.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Novo Nordisk Pharma (Private) Limited, 113, Shahra-e-Iran, Clifton, Karachi.**
	Name, address of Manufacturing site.	113, Shahra-e-Iran, Clifton, Karachi. **Address of go-down:** 208/1, Sector 23, KIA, Karachi Validity: 09-04-2023 Status: License to sell drugs by way of Wholesale.
	Name and address of marketing authorization holder (abroad)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
	Name, address of manufacturer(s)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
	Name of exporting country	Denmark
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: • Firm has submitted legalized copy of CoPP (No. 2021110493) dated 03-11-2021 issued by Danish Medicine Agency valid for two years. The CoPP specifies free sale status of the product in Exporting country with its availability. The CoPP also confirms the GMP status of the firm.

	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Corporate Vice President (Global Regulatory Affairs) of Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark authorizes "M/s Novo Nordisk Pharma (Private) Limited" to be their wholly owned subsidiary and sole importer in Pakistan and to import, distribute & sale the product. The letter was issued on 21-10-2021 and valid till 31-12-2024.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 31965 dated 22-11-2021
	Details of fee submitted	PKR 75,000/-: dated 22/10/2021 Deposit Slip No. 262346819428
	The proposed proprietary name / brand name	NovoEight® 1000 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Powder Vial:** Each Vial contains: Human Coagulation Factor VIII, Turoctocog alfa…..1000IU **Diluent PFS:** Each Pre-filled syringe contains: 0.9% Sodium chloride……4mL
	Dosage form of applied drug	Powder and solvent for solution for Injection
	Pharmacotherapeutic Group of (API)	Antihemorrhagics, blood coagulation factor VIII, ATC code: B02BD02
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's (Powder + Solvent)
	Proposed unit price	Not Provided/As per SRO
	Shelf Life	30 months

	Storage Conditions	Store in refrigerator (2°C – 8°C).
	The status in reference regulatory authorities	The product is itself registered in Danish Medicine Agency & EMA
	For generic drugs (me-too status)	Not Applicable
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	Novo Nordisk US Bio Production Inc. 9 Technology Drive Lebanon, NH 03784 USA Novo Nordisk A/S Brennum Park 25K, DK-3400, Hillerød, Denmark Novo Nordisk A/S Novo Allé, DK-2880 Bagsværd, Denmark Bioreliance Ltd Todd Campus West of Scotland Science Park, Glasgow G20 OXA, Scotland, UK.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated and real time conditions. The real time stability data is conducted at -80°C±10°C for 60 months for 3 batches with the approved shelf life of 48 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted analytical methods as per Pharmacopeia. The methods are validated as per SOPs. The Analytical methods are listed below • Water content-Karl Fischer Coulorimetric titration (USP/JP) • Visual evaluation of clarity (Ph.Eur) • Color (Ph.Eur)

		• Particulate contamination/Foreign insoluble matter (Ph.Eur/JP) • pH (Ph.Eur/USP/JP) • Potency-chromogenic substrate assay (Ph.Eur/) • Particulate matter (Ph.Eur/USP/JP) • Osmalality (Ph.Eur/USP/JP) • Endotoxin (Ph.Eur/USP/JP) • Sterility (Ph.Eur/USP/JP)
	Container closure system of the drug product	Powder in Vial: The primary packaging of vial for turoctocog alfa drug product is a 5 mL vial made of type I glass, high hydrolytic resistance, in compliance with Ph Eur, USP and JP. The lyophilisation rubber stopper for the turoctocog alfa drug product is made of a grey chlorobutyl rubber. The rubber meets the requirements of Ph Eur (Rubber closures for aqueous preparations for parenteral use, Type I) and USP (Elastomeric Closures for Injections). The stopper is sealed with a snap-off cap made of aluminium and plastic.
		Diluent in PFS: The container closure system consists of a siliconised glass barrel made of borosilicate glass type 1 (Ph. Eur., USP and JP), a siliconised rubber plunger made of bromobutyl rubber (Ph. Eur., USP), and a syringe closure system (V-OVS 10.6®) composed of a tip cap with a luer lock and a tamperevident seal. Only the tip cap of the syringe closure system is in contact to the 0.9 % Sodium Chloride Solution. This tip cap is also made of bromobutyl rubber (Ph. Eur., USP).
	Stability study data of drug product, shelf life and storage conditions	Powder in Vial: Firm has submitted Primary stability study data of 3 batches for lowest strength (250IU) & higher strength (3000IU). The accelerated stability study data is conducted at 30°C±2°C/75%±5RH for 12 months. The real time stability study data is conducted at 5°C±3°C/75%±5RH for 30 months. Firm has also submitted 6 months data at 40°C±2°C/75%±5RH
		Diluent in PFS: Firm has submitted Primary stability study data of 3 batches respectively. The accelerated stability study data is conducted at 30°C±2°C/65%±5RH for 60 months. The real time stability study data is conducted at 5°C for 60 months.
	Module-IV Non-Clinical	The Firm has submitted following non-clinical studies: Pharmacology: Primary Pharmacodynamics • Species crossreactivity (Turoctocog alfa enhanced thrombin generation in rat, cynomolgus monkey and human plasma in a dose dependent manner. This demonstrates species cross-reactivity of turoctocog alfa to rat and cynomolgus) • Thrombin generation assay (Dose dependent increase in thrombin generation. Similar thrombin generation capacity by turoctocog alfa and Advate®, ReFacto® and Haemate®).

		• vWF interaction (Turoctocog alfa and ReFacto® bind vWF with very similar affinities.) • vWF interaction (Turoctocog alfa, Advate® and ReFacto® bind vWF with very similar affinities). • SDS-PAGE and Western blot (FVIII related peptides, detected by Western Blot using different FVIII antibodies, are similar for turoctocog alfa and different commercially available FVIII products). • Kinetics mAb by SPR (Binding constants of different FVIII • mAbs are similar for turoctocog alfa, Advate® and ReFacto®). • Tail bleeding in F8 knock-out mice (Bleeding time and blood loss were significantly longer in vehicle treated F8 knock-out mice compared to normal CB57. The bleeding time and blood loss after administration of 200 IU/kg Advate® or turoctocog alfa was not significantly different from normal controls. No difference in potency was observed between Advate® and turoctocog alfa). • Knee injury model in F8 knock-out mice (F8 knock-out mice had a visual bleeding score (VBS) of 2.04 (SD1.30). Treatment with turoctocog alfa and Advate® significantly reduced the bleeding with a mean of 0.58 (SD 0.93) and 0.50 (SD 1.06) respectively. The mean change in joint diameter for F8 knock-out, untreated, and treated with turoctocog alfa and Advate® respectively was: 1.23 mm (SD 0.94); 0.32 mm (SD 0.39) and 0.25 mm (SD 0.39). • PK/PD study in haemophilia A dogs (Turoctocog alfa and Advate® were equally capable of normalising whole blood clotting time and showed similar activity profile over time). Secondary Pharmacodynamics • Not applicable as all studies done are related to desired therapeutic target. Safety Pharmacology • Safety Pharmacology is done on Male Cynomolgus and monkeys and observed following functions • Central Nervous System • Respiratory Function • Kindey Funcation • Cardiovascular system Pharmacodynamic Drug Interactions • Not Performed Pharmacokinetic: Absorption is studied with Test System • F8 Knock-out mice, single dose (PK of turoctocog alfa, Advate® and ReFacto® in F8 knock-out mice) • Haemophilia A dog, single dose (PK in heamophila A dogs) • Cynomolgus monkey, single dose (Toxicokinetics) • Sprague Dawley rat, multiple dose (Toxicokinetics) • Cynomolgus monkey, multiple dose (Toxicokinetics) Distribution is studies with Test System (C57Bl mice) Toxicology:

		• Single Dose Escalation Toxicity in Male cynomolgus monkey • Repeat Dose Toxicity in Rat and Male cynomolgus monkey • Genotoxicity • Carcinogenicity • Reproductive and Developmental Toxicity • Local Tolerance in Male New Zealand White Rabbits and Male cynomolgus monkey and Rats. • Other Toxicity Studies • Immunogenicity Study in rats
	Module-V Clinical	The Firm has submitted following clinical studies: • NN7008-3522 First human dose trial A multi-centre, multi-national, open-label, first human dose, PK, safety, single dose trial using a sequential design in patients with haemophilia A. • NN7008-3600 PK in Japanese patients. A multi-centre, open-label, single dose trial investigating the PK of turoctocog alfa in Japanese patients with haemophilia A. • NN7008-3893 PK trial (two lots). A multi-centre, open-label, trial investigating the PK of a single dose of turoctocog alfa in patients with haemophilia A. • NN7008-4015 PK trial (four lots). A multi-centre, open-label trial investigating the PK of four lots of turoctocog alfa in patients with haemophilia A. • NN7008-4239 PK trial. A multicentre, open-label trial evaluating the PK of turoctocog alfa in relation to BMI in patients with haemophilia A. • NN7008-3543 Pivotal trial. A multi-centre, multi-national, • open-label, safety, efficacy, single arm trial in patients with severe haemophilia A investigating turoctocog alfa when used for prevention and treatment of bleeds. The trial included a sub-trial designed to evaluate the safety and efficacy of turoctocog alfa when used for prevention and treatment of bleeding during surgical procedures and in the surgery period • NN7008-3545 Paediatric trial. A multi-centre, open-label, noncontrolled safety and efficacy trial of turoctocog alfa in previously treated paediatric patients with haemophilia A. • NN7008-3568 Extension trial. A multi-centre, multi-national, open-label, non-randomised, single treatment arm safety and efficacy extension trial in patients with haemophilia A investigating turoctocog alfa when used in a preventative or on-demand treatment regimen. The trial • includes a sub-trial designed to evaluate safety and efficacy of turoctocog alfa during surgery. • NN7008-4028 Previously treated Chinese patients. Efficacy and safety of turoctocog alfa for prevention and treatment of bleeding episodes in previously treated Chinese patients with haemophilia A. • NN7008-3553 Non-interventional post autorisation safety study (PASS). A multi-centre non-interventional study of safety and efficacy of turoctocog alfa during long-term prevention and treatment of bleeds in

		previously FVIII treated patients with severe and moderately severe haemophilia A (FVIII ≤2%). • NN7008-4105 Non-interventional study. A multicentre, non-interventional post marketing study of safety and efficacy of turoctocog alfa (rFVIII) during long-term treatment of haemophilia A in Japan. • NN7008-4253 Non-interventional study. Multicentre, post-authorisation safety study with turoctocog alfa in Mexican haemophilia A patients. • NN7008-4304 Non-interventional study. A prospective multicentre observational study of safety and efficacy outcomes with turoctocog alfa for prevention and control of bleeds in mild, moderate and severe Haemophilia A in India. • NN7008-3809 Trial in previously untreated patients. Safety and efficacy of turoctocog alfa in prevention and treatment of bleeds in paediatric previously untreated patients with haemophilia A (<6 years of age).
Decision: Keeping in view legalized CoPP and approval of Dansih Medicine Agency (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs.		

B: Imported Human Biologicals from Non-reference countries

1.	**Name, address of Applicant / Importer**	**M/s Uniplan Trade International (Pvt.) Ltd., 132/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-352-0070-034348D **Address:** 132/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore. **Validity: 07-07-2022** **Status:** License to sell drugs as a distributor.
	Name and address of marketing authorization holder (abroad)	M/s Allmed Middle East, 2nd Industrial Zone, Parts No. 72, 70, 87, 6th of October City, Egypt.
	Name, address of manufacturer(s)	M/s Global Pharmaceutical Industries (2), 5th Industrial Zone, Parts No. 2A, 6th of October City, Egypt.
	Name of exporting country	Egypt
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized GMP Certificate (No. 5/2022) dated 13-01-2022 valid till 13-01-2023 issued by Egyptian Drug Authority. The certificate specifies the GMP status of the manufacturer. • Firm has submitted legalized FSC (No. 00185/2020/H) dated 19-05-2020 issued by Egyptian Drug Authority. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from Managing Director of Allmed Middle East. According to the letter, the firm *M/s Allmed Middle East* authorizes "Uniplan Trade International (Pvt.) Limited" to distribute and sale the product. The letter was issued on 21-10-2020 and valid till 31-12-2022.
	Status of the applicant	☐ Manufacturer

		☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 12486, 9062 & 12486 (R&I) Dated 27-04-2021, 11-02-2022 & 06-04-2022
	Details of fee submitted	Rs. 100,000/- dated 22-04-2021
	The proposed proprietary name / brand name	**BoviParin**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Heparin Sodium……5000IU
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	USP
	Proposed Pack size	1's Vial (5mL)
	Proposed unit price	Not Provided.
	Shelf Life	02 Years
	Storage Conditions	$\leq 30^0$C
	The status in reference regulatory authorities	Heparin Panpharma of M/s Panpharma, France.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.

	Name, address of drug substance manufacturer	M/s Kin Master Products Quimicos LTDA, Brazil
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of Drug Substance at real time conditions. The real time stability data conducted at $5^0C \pm 3^0C$ is for 18 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical method of Heparin Sodium Assay.
	Container closure system of the drug product	Amber Type I Glass vial. Chlorobutyl rubber stopper, Aluminum cap & seal.
	Stability study data of drug product	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at $40 \pm 2^0C/75\%RH \pm 5\%$ for 6 months. The real time stability study data is conducted at 30 ± 2^oC for 24 months.
	Remarks of Evaluator	The firm has submitted the Biosimilarity & Bioequivalence report for Heparin Sodium Injection. Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product, hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin.
Decision: Keeping in view the availability of product in country of origin as per submitted FSC and Heparin injection being non-rDNA pharmacopoeial product; Registration Board approved the product as per current Import Policy for finished drugs.		
2.	**Name, address of Applicant / Importer**	**M/s Altimi Biosciences (Pvt.) Ltd., Office No. 201, Plot No. 43-C, Bukhari Commercial, Lane-10, Pase-VI DHA, Karachi.**
	Details of Drug Sale License of importer	License No: 2988 Address: Office No. 201, Plot No. 43-C, Bukhari Commercial, Lane-10, Pase-VI DHA, Karachi. Address of go-down: B-40, S.I.T.E., Karachi. Validity: 18-08-2021 Status: License to sell drugs by way of Whole sale.

	Name and address of marketing authorization holder (abroad)	M/s Hetero Biopharma Limited, Sy. No. 458(Part), TSIIC-Formulation SEZ, Polepally (Village), Jadcherla (Mandal), Mahaboobnagar (District)- 509301, Telangana State, India.
	Name, address of manufacturer(s)	M/s Hetero Biopharma Limited, Sy. No. 458(Part), TSIIC-Formulation SEZ, Polepally (Village), Jadcherla (Mandal), Mahaboobnagar (District)- 509301, Telangana State, India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. 8963/E1/2018-24) dated 19-01-2019 valid till 23-11-2021 issued by DCA Telangana India. The CoPP specifies free sale status of the product in country of origin along with its availability. The certificate also specifies the GMP status of the manufacturer. • Firm has submitted the copy of valid CoPP (No. 3049930/TS/2022) dated 27-06-2022 valid till 11-06-2025 issued by DCA Telangana India. The CoPP specifies free sale status of the product in country of origin along with its availability. The certificate also specifies the GMP status of the manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Sole Agent Authorization from Global Head- Biologics Business of M/s Hetero Biopharma Limited, Sy. No. 458(Part), TSIIC-Formulation SEZ, Polepally (Village), Jadcherla (Mandal), Mahaboobnagar (District)- 509301, Telangana State, India. According to the letter, the firm M/s Hetero Biopharma authorizes "Altimi Biosciences (Pvt.) Ltd.," to register, sale and quote the products within Pakistan. The letter was issued on 30-01-2020 and valid for 24 months.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)/ Biosimilar
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 28447, 33278, 5394 & 22784 (R&I) Dated 29-10-2020, 21-12-2021, 25-02-2022 & 11-08-2022
	Details of fee submitted	Rs. 100,000/- dated 26-10-2020
	The proposed proprietary name / brand name	Pamera 40 (Adalimumab 40mg/0.8mL)
	Strength / concentration of drug of Active	Each Pre-filled glass syringe (0.8 mL) contains: Adalimumab (r-DNA Origin)……..40mg

	Pharmaceutical ingredient (API) per unit	
	Dosage form of applied drug	Solution for sub-cutaneous Injection in single use pre-filled syringe
	Pharmacotherapeutic Group of (API)	TNF Blocker
	Reference to Finished product specifications	As per Innovator.
	Proposed Pack size	1's Vial
	Proposed unit price	Not Provided.
	Shelf Life	18 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Idacio 40mg of M/s Fresenius Kabi Ltd., UK.
	For generic drugs (me-too status)	Not Registered.
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Hetero Biopharma Limited, Sy. No. 458(Part), TSIIC-Formulation SEZ, Polepally (Village), Jadcherla (Mandal), Mahaboobnagar (District)- 509301, Telangana State, India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 Commercial batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at -20^0C±5^0C is for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Analytical method validation/verification of product	Firm has submitted Validation of Analytical Procedures: Protein content by UV SDS-PAGE with CP-B staining Weak Cation Exchange Chromatography Size Exclusion Chromatography Relative Potency by VEGF Neutralization Bacterial Endotoxin Text Sterility Test
	Container closure system of the drug product	• Transparent glass Prefilled Syringe Barrel with stainless steel Hypodermic needle covering with rigid needle shield. • Plunger stopper packaged in sealed double polypropylene bag. • Polypropylene plunger rod.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 commercial batches. The accelerated stability study data is conducted at 25 ± 2^0C for 6 months. The real time stability study data is conducted at 5 ± 3^0C for 18 months.
	Module-IV Non-Clinical	Summarized in Biosimilarity data.
	Module-V Clinical	Summarized in Biosimilarity data.

Biosimilarity data as per WHO guidelines submitted by the firm is as follows:

WHO Biosimilarity Guidelines	**Data Submitted by the firm**
Quality Comparison • Physicochemical Characterization	• Protein Content **a.** UV absorbance at 280nm • General Properties **a.** pH **b.** Osmolality **c.** Physical Appearnce **d.** Immunogenic Specificity by Western Blot **e.** Isoelectric point of adalimumab **6** • Primary Structure a. Amino Acid Sequencing by LC-MS/MS b. Molecular weight of intact adalimumab by Intact Mass spectrometry c. Molecular weight for light & heavy chain of adalimumab by Reduced Mass spectrometry d. Peptide Mapping • **Higher order structure** a. Secondary structure by Far UV CD Spectroscopy b. Tertiary structure by Near UV CD Spectroscopy c. Tertiary structure by Intrinsic fluorescence Spectroscopy d. Tertiary structure by Extrinsic fluorescence Spectroscopy e. Confirmation of disulphide integrity by Free Thiol estimation **7** • Purity

	a. High & Low Molecular weight impurities by SE-UPLC b. Quantification of non-glycosylated variants by CE-SDS (Reducing) c. Determination of low molecular weight impurities by CE-SDS (Non-Reducing) d. Determination of charge related impurities by CEX • **Glycan Analysis** a. Qualitative Glycosylation pattern by N-linked glycosylation
Biological Activity & Immunochemical properties	a. Neutralization of soluble TNF-alpha induced cell death in L929 cells b. Ability to induce Antibody Dependent Cell mediated Cytotoxicity (ADCC) using tmCHOK1 cells. c. Ability to induce Complement Dependent Cytotoxicity using tmTNF-alpha d. C1q Binding Assay e. Soluble TNF-alpha binding assay (ELISA)/SPR/tmTNF-alpha binding assay f. Inhibition of soluble TNF-alpha induced IL-8 in HUVEC g. Specificity against TNF-β
Impurities	• <u>Product Purity & related Impurities</u> a. HMW & Monomers by Size Exclusion Chromatography b. LMW Impurities by Capillary SDS-PAGE (Non-reducing) c. Non-Glycosylated Heavy Chain by Capillary SDS-PAGE (Reducing) d. Charge Related variants by cation exchange chromatography • **Process-Related Impurities** a. Host Cell derived proteins b. Quantification of host cell DNA content by qPCR c. Protein A leachate d. Bacterial Endotoxin (BET) test e. Microbial enumeration test (TAMC) f. Microbial enumeration test (TYMC)
Stability Studies	Detailed Above.
Non-clinical Comparison	**In vitro functional assays** Already detailed in Biological Activity. **Toxicology Studies** a. Single dose Toxicity studies in Swiss Albino Mice (sub-cutaneous) b. Single dose Toxicity studies in Swiss Albino Mice (Intravenous) c. Single dose Toxicity studies in Wistar Rats (sub-cutaneous) d. Single dose Toxicity studies in Wistar Rats (Intravenous) e. 28 days repeated dose Toxicity Study in Wistar Rats with 14 days recovery period following weekly subcutaneous administration f. 28 days repeated dose Toxicity Study in New Zealand White Rabbits with 14 days recovery period following weekly subcutaneous administration g. Skin Sensitization study of Adalimumab in Guinea Pigs)
Clinical Comparison	1. A prospective, Randomized, Multiple-Dose, Multi-Center, Comparative, Parallel Clinical Study to evaluate safety, efficacy, immunogenicity and Pharmacokinetics of subcutaneous injection of Adalimumab (Hetero) with RMP concomitantly administered with Rheumatoid Arthritis. (n=168)
Remarks of Evaluator	The initially submitted legalized CoPP was valid till 23-11-2021 which is now expired. Now, the firm has submitted copy of CoPP valid till 11-06-2025 and submitted an undertaking that the said CoPP is in-process of legalization and will

	be submitted as soon as receive. Moreover, the firm has also applied for inspection exemption of manufacturer abroad as the products of same type Bevaas 100 & Bevaas 400 (Bevacizumab) are registered in Indonesia. Both the above products have already been granted inspection exemption on the basis of registration in Indonesia and the instant product is also a monoclonal antibody. The current Import Policy for finished drugs states the following: *"……..products fulfilling below mentioned criteria are exempted from dosage form specific inspection of manufacturer abroad:* *Any product approved by Pharmaceutical Inspection Co-operation Scheme (PIC/S) Participating Authority and manufacturing facility (section) of such product. (https://picscheme.org/en/members)."*

Decision: Keeping in view legalized CoPP indicating product availability in country of origin and biosimilarity data submitted in light of decision of 297th meeting of Registration Board; Registration Board approved the product subject to compliance of current Import Policy for finished drugs.

~~**The application for inspection exemption shall be processed after confirmation of minutes as per practice.**~~

3.	**Name, address of Applicant / Importer**	**M/s Sindh Medical Store,** **Sector 13B/B-10, Block-6, PECHS, Karachi.**
	Details of Drug Sale License of importer	**License No:** 0257 **Address:** Sector 13B/B-10, Block-6, PECHS, Karachi **Address of go-down: N/A** **Validity: 01-07-2024** **Status:** License to sell drugs by way of Wholesale
	Name and address of marketing authorization holder/ Product License Holde (abroad)	M/s SK Plasma Co., Ltd., 157 Saneopdanji-gil, Pungsan-eup, Andong-si Gyeongsangbuk-do, Republic of Korea.
	Name, address of manufacturer(s)	M/s SK Plasma Co., Ltd., 157 Saneopdanji-gil, Pungsan-eup, Andong-si Gyeongsangbuk-do, Republic of Korea.
	Name of exporting country	Korea
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** • Firm has submitted original, legalized CoPP (No.2018-A1-1396) dated 07-09-2018 issued by Ministry of Food and Drug Safety, Korea. The CoPP specifies free sale status of the product in country of export along with its availability. The CoPP also confirms the GMP status of the firm. (Periodicity of routine inspection:3years)
	Details of letter of authorization / sole agency agreement	Legalized Product Specific Sole Agency Agreement dated 10-04-2019 valid for 03 years is submitted.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 8787, 7049 (R&I) Dated 23-04-2020, 03-03-2021
	Details of fee submitted	Rs. 100000/- Dated 21-04-2020
	The proposed proprietary name / brand name	**Liv-Gamma SN Inj.**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Human Normal Immunoglobulin-G……50mg
	Dosage form of applied drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Human Normal Immunoglobulin
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's Vial (50mL)
	Proposed unit price	As per DPC
	Shelf Life	24 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Intratect 50g/L of M/s Biotest Pharma GmbH, Germany.
	For generic drugs (me-too status)	Bioven Mono of M/s SMS Corporation (Reg. No. 111087)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, Characterization (Elucidation of Structure and Other Characteristics), impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	M/s SK Plasma Co., Ltd., 157 Saneopdanji-gil, Pungsan-eup, Andong-si Gyeongsangbuk-do, Republic of Korea.

	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	The firm has submitted stability data of drug substance/ bulk at accelerated and real time conditions. The real time stability data conducted at 2^0C-8^0C is for 12 months for 3 batches.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted Validation & verification of Analytical Procedures.
	Container closure system of the drug product	Glass vial Colorless Type II glass 30mm Chlorobutyl rubber type I stopper 12.5mm, flip-off seal; Polypropylen (PP), Aluminum
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 25±2^{O}C/RH 60±5% for 6 months. The real time stability study data is conducted at 2^OC-8^0C for 24 months.
	Module-IV	No non-clinical studies are performed.
	Module-V	• A multicenter, Open-Label, Phase III Study to evaluate the efficacy and safety of Liv-Gamma SN Inj. in primary Immune Thrombocytopenia (ITP) • Observational study to evaluate the efficacy and safety of Liv-Gamma SN Injection in primary immunodeficiency disease (PID).
4.	**Name, address of Applicant / Importer**	**M/s Sindh Medical Store,** **Sector 13B/B-10, Block-6, PECHS, Karachi.**
	Details of Drug Sale License of importer	**License No:** 0257 **Address:** Sector 13B/B-10, Block-6, PECHS, Karachi **Address of go-down: N/A** **Validity: 01-07-2024** **Status:** License to sell drugs by way of Wholesale
	Name and address of marketing authorization holder/ Product License Holde (abroad)	M/s SK Plasma Co., Ltd., 157 Saneopdanji-gil, Pungsan-eup, Andong-si Gyeongsangbuk-do, Republic of Korea.
	Name, address of manufacturer(s)	M/s SK Plasma Co., Ltd., 157 Saneopdanji-gil, Pungsan-eup, Andong-si Gyeongsangbuk-do, Republic of Korea.

	Name of exporting country	Korea
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** • Firm has submitted original, legalized CoPP (No.2018-A1-1396) dated 07-09-2018 issued by Ministry of Food and Drug Safety, Korea. The CoPP specifies free sale status of the product in country of export along with its availability. The CoPP also confirms the GMP status of the firm.
	Details of letter of authorization / sole agency agreement	Legalized Product Specific Sole Agency Agreement dated 10-04-2019 valid for 03 years is submitted.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 8790, 7049 (R&I) Dated 23-04-2020, 03-03-2021
	Details of fee submitted	Rs. 100000/- Dated 21-04-2020
	The proposed proprietary name / brand name	**Liv-Gamma SN Inj.**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Human Normal Immunoglobulin-G……50mg
	Dosage form of applied drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Human Normal Immunoglobulin
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's Vial (100mL)
	Proposed unit price	As per DPC

	Shelf Life	24 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Intratect 50g/L of M/s Biotest Pharma GmbH, Germany.
	For generic drugs (me-too status)	Bioven Mono of M/s SMS Corporation (Reg. No. 111087)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, Characterization (Elucidation of Structure and Other Characteristics), impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	M/s SK Plasma Co., Ltd., 157 Saneopdanji-gil, Pungsan-eup, Andong-si Gyeongsangbuk-do, Republic of Korea.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	The firm has submitted stability data of drug substance/ bulk at accelerated and real time conditions. The real time stability data conducted at 2^0C-8^0C is for 12 months for 3 batches.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted Validation & verification of Analytical Procedures.
	Container closure system of the drug product	Glass vial Colorless Type II glass 30mm Chlorobutyl rubber type I stopper 12.5mm, flip-off seal; Polypropylen (PP), Aluminum
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 25±2^{O}C/RH 60±5% for 6 months. The real time stability study data is conducted at 2^OC-8^0C for 24 months.
	Module-IV	No non-clinical studies are performed.
	Module-V	• A multicenter, Open-Label, Phase III Study to evaluate the efficacy and safety of Liv-Gamma SN Inj. in primary Immune Thrombocytopenia (ITP)

		• Observational study to evaluate the efficacy and safety of Liv-Gamma SN Injection in primary immunodeficiency disease (PID).

Remarks of the evaluator:

The firm has submitted single CoPP for both strengths and submitted that as per Regulation on Pharmaceuticals Approval standard unit of raw material is 1ml for liquid injections which is mentioned in authorization certificate and CoPP is also issued with the same contents.

Decision: Registration Board deferred the case for submission of following by the firm:

i. No non-clinical studies

ii. Submission of screenshots of available packs in country of origin.

C: Miscellaneous/ Deferred Cases

1. Imported Human Biological applied by M/s Pfizer Pakistan Limited, Karachi deferred in 316th meeting of RB.

Following product of M/s Pfizer Pakistan Limited, Karachi was deferred in 316th meeting of Registration Board:

Name, address of Applicant / Importer	**M/s Pfizer Pakistan Limited,** **B-2, S.I.T.E., Karachi.**
Details of Drug Sale License of importer	**License No:** 1258 **Address:** B-2, S.I.T.E., Karachi. **Address of go-down:** 12 Dockyard Road West Wharf, Karachi. **Validity: 21-04-2022** Status: License to sell drugs by way of Whole sale.
Name and address of marketing authorization holder (abroad)	M/s Pfizer AG, Scharenmoosstrasse 99, 8052 Zurich, Switzerland.
Name, address of manufacturer(s)	M/s Catalent Indiana, LLC 1300 South Patterson Dr. Bloomington, Indiana (IN) 47403, USA
Name of exporting country	Switzerland
Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted original, legalized CoPP (No. 20005811) dated 22-12-2020 issued by Swissmedic. The CoPP specifies that the product is licensed for sale in country of origin but actually not available. • Firm has submitted copy of Eudra GMP certificate No. NL/H 17/1013621a dated 07-06-2017 of said manufacturer.
Details of letter of authorization / sole agency agreement	Firm has submitted notarized copy of Letter of product specific authorization from Head Regulatory Affairs Switzerland of *M/s Pfizer AG, Scharenmoosstrasse 99, 8052 Zurich, Switzerland*. According to the letter, the firm *M/s Pfizer AG* authorizes "Pfizer Pakistan Limited" to be Market Authorization Holder in Pakistan and to be responsible for all matters pertaining to the regulation of this product in Pakistan. The letter was issued on 25-01-2021.

Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	Domestic and Export sales
For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
Dy. No. and date of submission	Dy. No. 9811 (R&I) Dated 29-03-2021
Details of fee submitted	PKR 100,000/-: 29-03-2021
The proposed proprietary name / brand name	Abrilada 40mg/0.8mL
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each PFS (0.8mL) contains: Adalimumab ……40mg
Dosage form of applied drug	Solution for Injection in Pre-filled Syringe
Pharmacotherapeutic Group of (API)	TNF Blocker
Reference to Finished product specifications	As per Innovator.
Proposed Pack size	1's PFS
Proposed unit price	Not Provided.
Shelf Life	36 months
Storage Conditions	2^0C-8^0C
The status in reference regulatory authorities	Abrilada 40mg/0.8mL PFS, USFDA
For generic drugs (me-too status)	Not Available
Module-II (Quality Overall Summary)	Firm has submitted QOS on WHO Template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and

	clinical overviews and summaries.
Name, address of drug substance manufacturer	M/s Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC. One Burtt Road, Andover, MA 01810, USA
Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 7 batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at --20^0C±5^0C is for 60 months for 4 batches and for 36 months for 03 batches. The accelerated stability data conducted at 5^0C±3^0C is for 6 months for 4 batches and for 9 months for 03 batches.
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Analytical method validation/verification of product	Firm has submitted that Validation of test methods performed to ensure the quality, identity, potency, purity, and safety of PF-06410293 drug product have been performed. The suitability of methods for their intended use was performed by assessment of all relevant validation elements described in International Conference on Harmonization (ICH) Guidelines on Validation of Analytical Procedures: Text and Methodology Q2 and the current USP <1225> Validation of Compendial Methods.
Container closure system of the drug product	• 1 mL BD Hypak Type I Borosilicate glass with 29 gauge, ½ inch, thin-walled stainless steel staked needle, and thermoplastic elastomer (TPE) elastomeric needle shield that is not manufactured from natural rubber (latex) within a non-product contact rigid polypropylene cover. • 1mL West Pharmaceutical chlorobutyl elastomeric closure Plunger stopper
Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 process validation batches. The accelerated stability study data is conducted at 25±2^0C /60±5%RH for 6 months. The real time stability study data is conducted at 5±3^0C for 36 months. The batches are not stable at accelerated conditions.
Module-IV Non-Clinical	Summarized in Biosimilarity data.
Module-V Clinical	Summarized in Biosimilarity data.

Bio similarity data as per WHO guidelines submitted by the firm is as follows:

WHO Biosimilarity Guidelines	Data Submitted by the firm
Quality Comparison • Physicochemical Characterization	• Primary Structure and Posttranslational Modifications a. Establishment and Verification of Adalimumab Amino Acid Sequence b. Characterization of Molecular Mass, Primary Structure and Posttranslational Modifications c. HILIC/MS - N-Linked Glycan Mapping d. N-LINKED GLYCAN STRUCTURE - SIALIC ACID ANALYSIS • Charge Heterogeneity a. Heightened Characterization of Charge Isoforms b. LC/MS Characterization of Charge Isoforms c. Characterization by Carboxypeptidase B Treatment d. Biological Activity of Charge Isoforms • **Disulfide Bonds** a. Characterization of Disulfide Bonds b. Sulfhydryl Analysis • **Higher order structure** a. Secondary Structure Characterization – Far-UV CD Spectroscopy b. Secondary Structure Characterization – FTIR Spectroscopy c. Tertiary Structure by Near-UV CD Spectroscopy d. Tertiary Structure Characterization – Intrinsic Fluorescence Emission Spectroscopy e. Thermal Stability Characterization – DSC f. Higher Order Structure - X-ray crystallography
Biological Activity & Immunochemical properties	• **Functional Characterization of the Fc domain** i. Characterization of Antibody-Dependent Cellular Cytotoxicity (ADCC) Function a. Primary NK Cell ADCC Assay b. PBMC ADCC Assay (FcɣRIIIa 158 V/F donor genotype) c. PBMC ADCC Assay (Fc□RIIIa 158 F/F donor genotype) d. FcγRIIIa Reporter Gene Assay (FcγRIIIa RGA) e. Binding to FcɣRIIIa by SPR Analysis ii. Characterization of Complement Dependent Cytotoxicity (CDC) Function a. CDC Assay b. C1q Binding ELISA c. CDC Effector Function Conclusion d. Mixed Lymphocyte Reaction (MLR) Assay e. Additional Fcɣ Receptor Binding SPR Assays f. FcRn Binding SPR Assay • **Functional Characterization of The Fab Domain** i. Functional Assays Demonstrating Blockade of sTNF a. Inhibition of Apoptosis Assay b. Inhibition of ELAM-1 Expression Assay c. Binding to sTNF Target Antigen by ELISA ii. Functional Assays Demonstrating mTNF Binding Activity a. Binding to mTNF Target Antigen on NS0 Cells b. Reverse Signaling

	iii. Lymphotoxin alpha (LT-a) Binding Activity
Impurities	• Product Purity a. HMMS and Monomer – Size Exclusion HPLC b. Fragments and Heavy Chain + Light Chain - Capillary Gel Electrophoresis (Reducing) c. Intact IgG - Capillary Gel Electrophoresis (Non-Reducing)
Stability Studies	**Forced Degradation** Confirmation of similar degradation profiles forced degradation conditions of Elevated temperature, Light exposure, Forced deamidation and Forced oxidation with peracetic acid.
Non-clinical Comparison	**Primary Pharmacodynamic Studies** Already recorded in Biological Activity **Pharmacokinetic Studies** a. Quantitation of PF-06410293 and Adalimumab-EU in Cynomolgus Monkey Serum. b. Detection of Anti-PF-06410293 and Adalimumab-EU Antibodies in Cynomolgus Monkey Serum. c. Repeat-Dose Toxicokinetics
Clinical Comparison	i. A double-blind (Sponsor-open), randomized (1:1:1), parallel-group, 3-arm, single-dose, PK similarity study of PF-06410293 and adalimumab sourced from the US and EU administered SC in the lower abdomen by a PFS to healthy adult. ii. A double-blind (Sponsor-open), randomized (1:1:1), parallel-group, 3-arm, single-dose, definitive PK similarity study of PF-06410293 and adalimumab sourced from the US and EU administered SC in the lower abdomen by a PFS to healthy adult subjects. iii. An open-label, randomized (1:1), parallel-group, 2-arm, single-dose PK comparability study to assess the PK of PF-06410293 following SC administration in the lower abdomen or upper anterior thigh (alternative assignment in each device weight group) using a PFS or a PFP in healthy adult subjects iv. A multi-national, 2-arm, randomised (1:1), double-blind, parallel-group study designed to evaluate the safety, efficacy, population PK, and immunogenicity of PF-06410293 versus adalimumab-EU administered SC in the abdomen or thigh by a PFS, both in combination with methotrexate (MTX) to treat subjects with moderately to severely active RA who had an inadequate response to MTX therapy.
Decision of RB in 316th Meeting: *Registration Board deferred the product for submission of following by the firm:* *i. Valid legalized CoPP indicating product availability in country of origin.* *ii. Regulatory Guidelines from country of origin confirming that product stability at accelerated conditions is not necessary.*	

The firm has now submitted the valid legalized CoPP No. 22001795 dated 06-05-2022 issued by Swissmedic indicating product availability in country of origin. Moreover, the firm has submitted the following reference of ICH Q1A (R2):
"if significant change occurs between 3 and 6 months' testing at the accelerated storage condition, the proposed shelf life should be based on the real time data available from the long term storage condition."

Decision: Keeping in view legalized CoPP and approval of Swissmedic (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs.

2. Imported Human Biologicals applied by M/s BF Biosciences Limited, Lahore deferred in 317th meeting of Registration Board.

Following products of M/s BF Biosciences Limited, Lahore were deferred in 317th meeting of Registration Board:

1.	**Name, address of Applicant / Importer**	**M/s BF Biosciences Limited,** **5-KM Sunder Raiwind Road, Raiwind, Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-352-0066-034461D **Address:** 5-KM Sunder Raiwind Road, Raiwind, Lahore. **Address of go-down:** 5-KM Sunder Raiwind Road, Raiwind, Lahore. **Validity: 29-06-2022** **Status:** License to sell drugs as a distributor.
	Name and address of marketing authorization holder (abroad)	M/s Sinergium Biotech S.A., Route 9 Km 38.7, of the City of Garin, Province of Buenos Aires, Argentine Republic
	Name, address of manufacturer(s)	M/s Sinergium Biotech S.A., Route 9 Km 38.7, of the City of Garin, Province of Buenos Aires, Argentine Republic
	Name of exporting country	Argentina
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. CE-2021-13181178-APN-DECBR#ANMAT) dated 15-02-2021 valid for two years issued by Argentina. The CoPP specifies free sale status of the product in country of origin along with its availability. The certificate also specifies the GMP status of the manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Sole Agent Authorization from Attorney of Sinergium Biotech. According to the letter, the firm *M/s Sinergium Biotech* authorizes "BF Biosciences Limited" to apply for registration. The letter was issued on 04-03-2021 and valid for one year.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 18230 & 9560 (R&I) Dated 29-06-2021 & 14-04-2022
	Details of fee submitted	Rs. 75,000/- dated 09-06-2021

	The proposed proprietary name / brand name	**Viraflu**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose (0.5ml) contains: A/Victoria/2570/2019 (H1N1)-(like strain: A/Victoria/2570/2019, IVR-215)……..15 micrograms HA* A/Hong Kong/2671/2019 (H3N2) - (like strain: A/Hong Kong/2671/2019, IVR-208)…….15 micrograms HA* B/Washington/02/2019 - (B/ Victoria lineage) (like strain: B/Victoria/705/2018, BVR-11)…….15 micrograms HA* *viral haemagglutinin
	Dosage form of applied drug	Suspension for Injection
	Pharmacotherapeutic Group of (API)	Seasonal Influenza Vaccine
	Reference to Finished product specifications	As per Innovator.
	Proposed Pack size	1's PFS, 10's PFS
	Proposed unit price	Rs. 870/PFS
	Shelf Life	12 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Agriflu of M/s Seqirus Inc., FDA.
	For generic drugs (me-too status)	Agrippal S1 vaccine M/s Novartis Pharma.
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Seqirus Vaccines Ltd., Gaskill Road, Speke Liverpool, L24 9GR, UK.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 9 batches of Drug Substance at accelerated (25 ± 2^0C) and real time conditions. The real time stability data conducted at $5^0C\pm2^0$C is for 6 months.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted Validation of Analytical Procedures.
	Container closure system of the drug product	• Syringe barrel Neutral clear glass, type I, colorless, single dose with a total volume of 1 ml. Syringe barrels are ethylene oxide sterilized. • Silicone Oil The Silicone oil covers the inside barrel surface, to provide easy and smooth plunger stopper motion and the needle, to reduce needle penetration drag force. • Needle Metal needle of 25G 5/8". Metal needle is ethylene oxide sterilized. • Needle shield (component not in contact with the product) The needle shield is a grey colour silicone-butyl protection which function is to protect the needle tip, to seal the cannula opening and maintain sterility. • Stopper The rubber stopper for plunger used with the Nuova Ompi and BD syringes, is made of grey colour butyl. It seals the flange end of the barrel and functions as a piston to deliver the drug and maintain sterility. □□Plunger Rod (component not in contact with the product) Plunger rod is made of plastic material and its function is to impart the movement to the plunger
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 25±2°C for 6 months. The real time stability study data is conducted at 5±3°C for 36 months.
	Module-IV Non-Clinical	**Primary Pharmacodynamics** • Immunogenicity testing of influenza antigens in mice (Study No. KOE 050601). • Study of antibody response with influenza vaccines in young and old mice (Study No. 94-0184). • Study of lymphoproliferative response with influenza vaccines in young and old mice (Study No. 94-0184). • Study of the antibody response in young and old seropositive mice (Study No. 93-847). • Studies of antibody response to various doses of influenza vaccine in mice (Study Nos. 94-0307, 94-0214, and 94-0215).

		• Dose-response Study of Agrippal in 8-week-old and 18-month-old female BALB/c mice (Study No. MF-1/MF-2 2003/04). • Study of the relative post-exposure viral load in the lungs of immunized mice (Study Nos. 94-0307, 94-0214 and 94-0215). • Mouse exposure model • Immunogenicity in rabbits • Intramuscular toxicity study of two doses of influenza vaccine formulation in New Zealand White rabbits (Study No. 191-44). • Reproductive and developmental intramuscular toxicity study of Agrippal vaccine in rabbits, including a post-natal evaluation (Study No. UBA00040). • Reproductive and developmental intramuscular toxicity study of Agrippal vaccine in rabbits, including a post-natal evaluation (Study No. UBA00043). • Immunogenicity and exposure in ferrets • Determination of the efficacy of an influenza vaccine in the experimental exposure model in ferrets (Study No. CBI-PCS-007) **Repeat Dose Toxicity Studies** • 30-Day subacute toxicity study in rabbits by intramuscular route (Study No. 940292).
	Module-V Clinical	• Safety and immunogenicity study of two influenza vaccines in healthy subjects aged 3 to 64 years • Safety and immunogenicity of three commercial lots of influenza vaccines in children aged 6-36 months • Safety and immunogenicity of three lots of cell-derived subunit influenza vaccines compared with 1 lot of egg-derived subunit influenza vaccine in healthy adults • Safety and immunogenicity of influenza vaccine in healthy adults and > older adults • Comparison of the safety, tolerability and immunogenicity of influenza vaccines in adults and the elderly • To evaluate the safety and immunogenicity of Agrippal without thimerosal and Agrippal authorized without preservatives, when administered to subjects aged 3-60 years, stratified into four age groups (3-5 years, 6-11 years, 12-17 years, 18-60 years) • To test the non-inferiority of the immune response to Agrippal with traces of thimerosal (no preservatives) compared to the conventional formulation (i.e. formulation with preservatives, or full formulation with thimerosal) • To test the non-inferiority of the immune response after complete removal of residual thimerosal (Agrippal without thimerosal) to Agrippal with traces of thimerosal. The study was conducted in elderly patients. • To evaluate the safety and immunogenicity of Fluad and other vaccine formulations with MF59 adjuvant when administered to adult patients aged 50-64 years

		• To evaluate the safety and immunogenicity of Fluad and other vaccine formulations with MF59 adjuvant when administered to adult patients aged 18-64 years with renal transplantation • To evaluate the immunogenicity and safety of Agrippal in adults aged 18-60 and elderly > 60 years. • Open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of trivalent influenza virus vaccine (surface antigen, inactivated) AGRIPPAL S1®, formulation 2005-2006, when administered to adults and older adults. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1® surface antigen, inactivated, influenza vaccine, Formulation 2006-2007, when administered to adults and the elderly. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1® surface antigen, inactivated, influenza vaccine, Formulation 2007-2008, administered to adults and the elderly. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1, inactivated surface antigen influenza vaccine, 2008-2009 formulation, when administered to adult and elderly adult subjects. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL® S1 inactivated surface antigen influenza vaccine, Formulation 2009-2010, when administered to adults and older adults. • Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1®, trivalent influenza virus vaccine (surface antigen, inactivated), 2010-2011 formulation, when administered to adults and older adults.
	Remarks of Evaluator	• The firm has not analyzed all the parameters as per monograph of the product in accelerated stability studies for which the firm submitted that accelerated stability data is conducted to test if accidental exposures to conditions other than proposed can affect stability of product, leading to loss of potency, hence, only potency test is performed. • The product gets out of specifications at 1st and 2nd month of accelerated stability studies for which the firm submitted that accelerated stability studies are conducted only for information purpose, hence, an "out of specification" does not require analysis of it.
2.	**Name, address of Applicant / Importer**	**M/s BF Biosciences Limited,** **5-KM Sunder Raiwind Road, Raiwind, Lahore.**
	Details of Drug Sale License of importer	License No: 05-352-0066-034461D Address: 5-KM Sunder Raiwind Road, Raiwind, Lahore. Address of go-down:

		5-KM Sunder Raiwind Road, Raiwind, Lahore. Validity: 29-06-2022 Status: License to sell drugs as a distributor.
	Name and address of marketing authorization holder (abroad)	M/s Sinergium Biotech S.A., Route 9 Km 38.7, of the City of Garin, Province of Buenos Aires, Argentine Republic
	Name, address of manufacturer(s)	M/s Sinergium Biotech S.A., Route 9 Km 38.7, of the City of Garin, Province of Buenos Aires, Argentine Republic
	Name of exporting country	Argentina
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. CE-2021-13184701-APN-DECBR#ANMAT) dated 15-02-2021 valid for two years issued by Argentina. The CoPP specifies free sale status of the product in country of origin along with its availability. The certificate also specifies the GMP status of the manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Sole Agent Authorization from Attorney of Sinergium Biotech. According to the letter, the firm M/s Sinergium Biotech authorizes "BF Biosciences Limited" to apply for registration. The letter was issued on 04-03-2021 and valid for one year.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 18229 & 9560 (R&I) Dated 29-06-2021 & 14-04-2022
	Details of fee submitted	Rs. 75,000/- dated 09-06-2021
	The proposed proprietary name / brand name	Pediatric Viraflu
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose (0.25ml) contains: A/Victoria/2570/2019 (H1N1)-(like strain: A/Victoria/2570/2019, IVR-215)……..7.5 micrograms HA* A/Hong Kong/2671/2019 (H3N2) - (like strain: A/Hong Kong/2671/2019, IVR-208)…….7.5 micrograms HA* B/Washington/02/2019 - (B/ Victoria lineage) (like strain: B/Victoria/705/2018, BVR-11)…….7.5 micrograms HA* *viral haemagglutinin

	Dosage form of applied drug	Suspension for Injection
	Pharmacotherapeutic Group of (API)	Seasonal Influenza Vaccine
	Reference to Finished product specifications	As per Innovator.
	Proposed Pack size	1's PFS, 10's PFS
	Proposed unit price	Rs. 870/PFS
	Shelf Life	12 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Agriflu of M/s Seqirus Inc., FDA.
	For generic drugs (me-too status)	Agrippal S1 vaccine M/s Novartis Pharma.
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Seqirus Vaccines Ltd., Gaskill Road, Speke Liverpool, L24 9GR, UK.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 9 batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at 50C±20C is for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted Validation of Analytical Procedures.

	Container closure system of the drug product	• Syringe barrel Neutral clear glass, type I, colorless, single dose with a total volume of 1 ml. Syringe barrels are ethylene oxide sterilized. • Silicone Oil The Silicone oil covers the inside barrel surface, to provide easy and smooth plunger stopper motion and the needle, to reduce needle penetration drag force. • Needle Metal needle of 25G 5/8". Metal needle is ethylene oxide sterilized. • Needle shield (component not in contact with the product) The needle shield is a grey colour silicone-butyl protection which function is to protect the needle tip, to seal the cannula opening and maintain sterility. • Stopper The rubber stopper for plunger used with the Nuova Ompi and BD syringes, is made of grey colour butyl. It seals the flange end of the barrel and functions as a piston to deliver the drug and maintain sterility. • Plunger Rod (component not in contact with the product) Plunger rod is made of plastic material and its function is to impart the movement to the plunger.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 25±2oC for 6 months. The real time stability study data is conducted at 5±3oC for 36 months.
	Module-IV Non-Clinical	Primary Pharmacodynamics • Immunogenicity testing of influenza antigens in mice (Study No. KOE 050601). • Study of antibody response with influenza vaccines in young and old mice (Study No. 94-0184). • Study of lymphoproliferative response with influenza vaccines in young and old mice (Study No. 94-0184). • Study of the antibody response in young and old seropositive mice (Study No. 93-847). • Studies of antibody response to various doses of influenza vaccine in mice (Study Nos. 94-0307, 94-0214, and 94-0215). • Dose-response Study of Agrippal in 8-week-old and 18-month-old female BALB/c mice (Study No. MF-1/MF-2 2003/04). • Study of the relative post-exposure viral load in the lungs of immunized mice (Study Nos. 94-0307, 94-0214 and 94-0215). • Mouse exposure model • Immunogenicity in rabbits • Intramuscular toxicity study of two doses of influenza vaccine formulation in New Zealand White rabbits (Study No. 191-44).

		• Reproductive and developmental intramuscular toxicity study of Agrippal vaccine in rabbits, including a post-natal evaluation (Study No. UBA00040). • Reproductive and developmental intramuscular toxicity study of Agrippal vaccine in rabbits, including a post-natal evaluation (Study No. UBA00043). • Immunogenicity and exposure in ferrets • Determination of the efficacy of an influenza vaccine in the experimental exposure model in ferrets (Study No. CBI-PCS-007) Repeat Dose Toxicity Studies • 30-Day subacute toxicity study in rabbits by intramuscular route (Study No. 940292).
	Module-V Clinical	• Safety and immunogenicity study of two influenza vaccines in healthy subjects aged 3 to 64 years • Safety and immunogenicity of three commercial lots of influenza vaccines in children aged 6-36 months • Safety and immunogenicity of three lots of cell-derived subunit influenza vaccines compared with 1 lot of egg-derived subunit influenza vaccine in healthy adults • Safety and immunogenicity of influenza vaccine in healthy adults and > older adults • Comparison of the safety, tolerability and immunogenicity of influenza vaccines in adults and the elderly • To evaluate the safety and immunogenicity of Agrippal without thimerosal and Agrippal authorized without preservatives, when administered to subjects aged 3-60 years, stratified into four age groups (3-5 years, 6-11 years, 12-17 years, 18-60 years) • To test the non-inferiority of the immune response to Agrippal with traces of thimerosal (no preservatives) compared to the conventional formulation (i.e. formulation with preservatives, or full formulation with thimerosal) • To test the non-inferiority of the immune response after complete removal of residual thimerosal (Agrippal without thimerosal) to Agrippal with traces of thimerosal. The study was conducted in elderly patients. • To evaluate the safety and immunogenicity of Fluad and other vaccine formulations with MF59 adjuvant when administered to adult patients aged 50-64 years • To evaluate the safety and immunogenicity of Fluad and other vaccine formulations with MF59 adjuvant when administered to adult patients aged 18-64 years with renal transplantation • To evaluate the immunogenicity and safety of Agrippal in adults aged 18-60 and elderly > 60 years. • Open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of trivalent influenza virus vaccine (surface antigen,

		inactivated) AGRIPPAL S1®, formulation 2005-2006, when administered to adults and older adults. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1® surface antigen, inactivated, influenza vaccine, Formulation 2006-2007, when administered to adults and the elderly. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1® surface antigen, inactivated, influenza vaccine, Formulation 2007-2008, administered to adults and the elderly. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1, inactivated surface antigen influenza vaccine, 2008-2009 formulation, when administered to adult and elderly adult subjects. • A Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL® S1 inactivated surface antigen influenza vaccine, Formulation 2009-2010, when administered to adults and older adults. • Phase II, open-label, uncontrolled, multi-site study to evaluate the safety and immunogenicity of AGRIPPAL S1®, trivalent influenza virus vaccine (surface antigen, inactivated), 2010-2011 formulation, when administered to adults and older adults.
	Remarks of Evaluator	• The firm has not analyzed all the parameters as per monograph of the product in accelerated stability studies for which the firm submitted that accelerated stability data is conducted to test if accidental exposures to conditions other than proposed can affect stability of product, leading to loss of potency, hence, only potency test is performed. • The product gets out of specifications at 1st and 2nd month of accelerated stability studies for which the firm submitted that accelerated stability studies are conducted only for information purpose, hence, an "out of specification" does not require analysis of it.

Decision of RB in 317th meeting:

"Registration Board deferred the product for submission of details of WHO recommended strains of

seasonal Influenza vaccines for Northern Hemisphere for year 2021-2022."

Now the firm has submitted the WHO recommended composition of influenza virus vaccines for use in the 2021-2022 northern hemisphere influenza season which indicates the following strains for trivalent vaccine:

i. an A/Victoria/2570/2019 (H1N1) pdm09-like virus
ii. an A/Cambodia/e0826360/2020 (H3N2)-like virus
iii. a B/Washington/02/2019 (B/Victoria lineage)-like virus

Decision: Keeping in view legalized CoPPs indicating products availability in country of origin; Registration Board approved the products subject to compliance of current Import Policy for finished drugs.

3. Emergency Use Authorizations granted in name of M/s AGP Limited, Karachi for Sputnik Vaccine.

Following Emergency Use Authorizations (EUAs) were granted to M/s AGP Limited, Karachi for COVID-19 vaccines imported from Russia:

Sr. No.	Reg. No.	Name of Product	Name of Manufacturer	Pack Size
1.	107881	Gam-COVID-Vac Combined vector vaccine for the prevention of coronavirus infection caused by the SARS-CoV-2 virus Solution for Intramuscular Injection	M/s Medgamal Branch, FSBI N.F. Gamaleya"National Research Center for Epidemiology and Microbiology"of the Ministry of Health of the Russian Federation, 18 Gamalei Street, Moscow 123098, Russia.	1's (1 Vial of Component I + 1 Vial (3.0ml) of Component II)
2.	107888		**Product License Holder & Quality Control Site:** M/s Medgamal Branch, FSBI N.F. Gamaleya"National Research Center for Epidemiology and Microbiology"of the Ministry of Health of the Russian Federation, 18 Gamalei Street, Moscow 123098, Russia. **Manufacturer:** M/s Generium Joint-Stock Company (Generium JSC), 601125, Vladimir Oblast, Petushky District, Volginsky, ul. Zavodskaya, bld. 263, Russia	1's (1 Vial (3.0ml) of Component I + 1 Vial (3.0ml) of Component II)
3.	107889		**Product License Holder & Quality Control Site:** M/s Medgamal Branch, FSBI N.F. Gamaleya "National Research Center for Epidemiology and Microbiology" of the Ministry of Health of the Russian Federation, 18 Gamalei Street, Moscow 123098, Russia. **Drug Substance Manufacturer:** M/s Generium Joint-Stock Company (Generium JSC), 601125, Vladimir Oblast, Petushky District, Volginsky, ul. Zavodskaya, bld. 263, Russia. **Finished Product Manufacturer:** M/s Closed Joint Stock Company "Pharmaceutical Company" LEKKO, 601125, Vladimir Oblast, Petushky District, Volginsky, ul. Zavodskaya, bld 277, 279, Russia.	1's (1 Vial (3.0ml) of Component I + 1 Vial (3.0ml) of Component II)
4.	107890		**Product License Holder & Quality Control Site:** M/s Medgamal Branch, FSBI N.F. Gamaleya "National Research Center for Epidemiology and Microbiology" of the Ministry of Health of the Russian	1's (1 Vial (3.0ml) of Component I +

			Federation, 18 Gamalei Street, Moscow 123098, Russia. **Drug Substance Manufacturer:**	1 Vial (3.0ml) of Component II)
5.	107891		M/s Generium Joint-Stock Company (Generium JSC), 601125, Vladimir Oblast, Petushky District, Volginsky, ul. Zavodskaya, bld. 263, Russia. **Finished Product Manufacturer:** M/s Open Joint Stock Company Pharmastandard-UfaVITA Plant, Republic of Bashkortostan, Ufa, Khudayberdina, Street 28, Russia.	5's (5 Ampoules (0.5ml) of Component I + 5 Ampoules (0.5ml) of Component II)

It is pertinent to mention that all the above EUAs were valid till 01-04-2022 as agency authorization of M/s AGP issued by Russian Direct Investment Fund was valid till 01-04-2022. Accordingly, the firm was asked to submit the updated Letter of Authorization. The firm submitted the following:

"We would like to inform you that Emergency Use Authorization (EUA) for Gam-Covid-Vac (Sputnik V) granted by RDIF to AGP has lapsed/ expired on April 1, 2022. Please note that no further authorization has been granted to AGP by RDIF"

Decision: Registration Board decided to give personal hearing to the firm to explain their position why not the Emergency use Authorizations of aforesaid products be revoked with immediate effect due to expiry of agency agreement which provokes the provisions of Section 7 (11) (b) and 42 of the Drug Act, 1976 and Rule 24 (17) of Drugs (Licensing, Registering & Advertising) Rules, 1976.

4. Likang 10µg/0.5ml PFS applied for export registration by M/s Nextar Pharma (Pvt.) Ltd., Karachi.

Name of Local Manufacturer	Bulk Concentrate Manufacturer	Brand Name & Composition	Local & International Availability	Dy. No., Date of Application & Fee Status
M/s Nextar Pharma (Pvt.) Ltd., Plot No. E-58, North Western Industrial Zone, Port Qasim, Karachi.	M/s Livzon Mabpharm Inc., No. 38 Chuangye north Road, Jinwan District, China.	Likang 10µg/0.5mL Each PFS (0.5ml) contains: Recombinant SARS-CoV-2 Fusion Protein (V-01)…… 10µg	No Available	Dy. No. 11705 (R&I) dated 14-05-2022 Rs. 75000/- dated 09-05-2022.

The firm has submitted the following documents as per SOPs of 283rd meeting of Registration Board**:**

Sr. No.	Documents as per SOPs	Documents Submitted by the firm
1.	Application with required fee as per relevant SRO	Application on Form-5D. Fee Challan of Rs. 75000/-
2.	Copy of approved section from CLB	Copy of Pre-filled Syringes (Biological) section renewal dated 22-09-2021.

3.	Copy of last inspection report conducted by DRAP within last 12 months	Copy of GMP Certificate dated 03-06-2021 issued by DRAP valid for two years.
4.	An undertaking that applied registration is exclusively for export purpose and will not be sold in Pakistan	Submitted
5.	Evidence of generic / approval status by Reference Regulatory Authorities for applied formulation. In cases where the formulations are neither generic nor approved by Reference Regulatory Authorities, applicant will provide evidence of approval status of applied formulation by regulatory authority of importing country.	Not Available locally & in reference authorities.
6.	Copy of DML along with its renewal status.	Copy of DML No. 000777 dated 15-03-2018.
7.	An undertaking that the proposed names/ label/ color do not resemble with already registered brands in importing country. In case of resemblance/similarity with already registered drug product in importing country, the applicant will be liable to change immediately.	Submitted.

The firm has also submitted the copy of GMP compliance letter dated 23-08-2021 issued by Guangdong Provincial Medical Products Administration. The firm has submitted export order of Myanmar. Moreover, the firm has the section approval of Biological r-DNA PFS while the instant product is recombinant vaccine.

Decision:

Registration Board deferred the case for submission of following clarifications by the firm:

iii. **The product is not registered in country of origin**
iv. **The formulation is not registered in any of the reference regulatory authorities.**
v. **The applied product is vaccine while the available section of the firm is Biological r-DNA PFS.**

5. Imported Human Biological applied by M/s Biotech Pakistan, Karachi approved in 308th meeting of Registration Board.

Following product of M/s Biotech Pakistan, Karahi was approved in 308th meeting of Registration Board:

5.	**Name, address of Applicant / Importer**	**M/s BIOTECH PAKISTAN** Suit No. 302 Third Floor Tahir Plaza KCHS Karachi
	Details of Drug Sale License of importer	**License No: 0049** **Address:** Suit No. 302 Third Floor Tahir Plaza KCHS Karachi **Validity:** 14-11-2022 **Status:** DSL by way of wholesale.
	Name and address of marketing authorization holder (abroad)	Baxter Medical Products GmbH Stella-Klein-Low-Weg 15, 1020 Wien Austria.

	Name, address of manufacturer(s)	Tisseel powder (component 1, lyophilized, with 91mg/ml human fibrinogen) Baxter AG., Lange Allee 24 B, 1221 Wien, Austria; Baxter AG., Lange Allee 24 A, 1221 Wien, Austria; Baxter AG. Uferstraβe 15, 2304 Orth/Donau, Austria Thrombin powder (component 2, lyophilized with 500 IU/ml human thrombin) Baxter AG., Lange Alee 24 B, 1221 Wien, Austria; Baxter AG., Lange Alee 24 A, 1221 Wien, Austria; Baxter AG., Uferstraβe 15, 2304 Orth/Donau, Austria Aprotinin solution (solvent for component 1 with 3000 KIU/ml aprotinin) Baxter AG., industriestraβe 72, 1221 Wien, Austria; Baxter AG., Lange Allee 51, 1221 Wien, Austria; Baxter AG., Lange Allee 51, 1221 Wien, Austria; Baxter AG., Uferstraβe 15, 2304 Orth/Donau, Austria
	Name of exporting country	Austria
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** • Firm has submitted legalized CoPP certificate No. 11120764 issued by Bundesamt für Sicherheit im Gesundheitswesen. The CoPP specifies that the product is licensed to be placed for use in the exporting country. The certificate was issued on 27.6.2018
		GMP: 1. Legalized certificate of GMP (No.INS-480001-0213-001(3/10) 2. Legalized certificate of GMP (No.INS-480777-0087-001(8/20)
	Details of letter of authorization / sole agency agreement	Firm has submitted a copy of letter of authorization from Baxter AG Thurgauerstrasse 130 8152 Glattpark/Opfikon, Switzerland. According to the letter, the firm Baxter AG authorizes Biotech Pakistan with Address: Suit# 302 Third Floor Tahir Plaza KCHS Karachi to perform the registration procedures, sales and other similar activities concerning medicinal products for territory of Pakistan. The letter is valid until 31st May 2022.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 15184, 29th June 2020
	Details of fee submitted	PKR 50,000/- Slip No. 1912301

<table>
<tr><td></td><td>The proposed proprietary name / brand name</td><td>Tisseel Lyo</td></tr>
<tr><td></td><td>Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit</td><td>Amount per unit dose:
<table>
<tr><th>Dose form</th><th>Name</th><th>Quantity operator</th><th>Amount from</th></tr>
<tr><td>Powder for solution</td><td>Human Clottable Protein containing mainly Fibrinogen and Fibronectin</td><td>Equal to</td><td>91 mg</td></tr>
<tr><td>Solvent</td><td>Aprotinin Acetate</td><td>Equal to</td><td>3000 kIU</td></tr>
<tr><td>Solvent</td><td>Water for Injection</td><td>Ad</td><td>1 ml</td></tr>
<tr><td>Powder for solution</td><td>Thrombin</td><td>Equal to</td><td>500 IU</td></tr>
<tr><td>Solvent</td><td>Calcium Chloride Dihydrate</td><td>Equal to</td><td>40 µmol</td></tr>
<tr><td>Solvent</td><td>Water for Injection</td><td>Ad</td><td>1 ml</td></tr>
</table></td></tr>
<tr><td></td><td>Pharmaceutical form of applied drug</td><td>Each component in separate vials with rubber stopper equipped with syringe for final use.</td></tr>
<tr><td></td><td>Pharmacotherapeutic Group of (API)</td><td>Fibrin Sealant</td></tr>
<tr><td></td><td>Reference to Finished product specifications</td><td>EU Pharmacopeia</td></tr>
<tr><td></td><td>Proposed Pack size</td><td>1x2ml (1ml+1ml) Vials
Content of Package:
- 1 vial containing Tisseel powder (component 1, lyophilized, with 91mg/ml human fibrinogen)
- 1 vial containing thrombin powder (component2, lyophilized, with 500IU/ml human thrombin)
- 1 vial containing aprotinin solution (solvent for component 1 with 3000 KIU/ml synthetic aprotinin)
- 1 vial containing calcium chloride solution (solvent for component 2 with 40 µmol/ml calcium chloride)
- 1 Duploject system device set for reconstitution and application.</td></tr>
<tr><td></td><td>Proposed unit price</td><td>Rs. 50,000.00</td></tr>
<tr><td></td><td>The status in reference regulatory authorities</td><td>Austria</td></tr>
<tr><td></td><td>For generic drugs (me-too status)</td><td>Not available</td></tr>
<tr><td></td><td>Module-II (Quality Overall Summary)</td><td>Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification</td></tr>
</table>

		of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Baxter AG Benatzkygasse 2-6 A–1221 Vienna Baxter AG Lange Allee 24 A A–1221 Vienna Baxter AG Lange Allee 24 A A–1221 Vienna Baxter AG Uferstrasse 15 A-2304 Orth/Donau, Austria.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of APIs real time and accelerated have been submitted.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not Applicable
	Analytical method validation/verification of product	Process validation, batch analysis and stability studies have been performed.
	Container closure system of the drug product	**Aprotinin Concentrate:** surface treated, sodalime silica glass vial, hydrolytic type II, manufactured by SGD Kipfenberg Stopper: 20 mm halogenobutyl rubber stopper, pink, manufactured by West Pharmaceuticals Services Crimp Cap: Silver 1676luminium cap, pink polypropylene disk, manufactured by Datwyler **Thrombin: Vial** Neutral glass 6R, hydrolytic type I, manufactured by ISO – Gesellschaft für Arzneiverpackungen mbH **Stopper:** 19 mm fluoro-resin laminated butyl rubber stopper, grey, manufactured by Daikyo Seiko Ltd. **Crimp Cap**: Black aluminum cap, white polypropylene disk, manufactured by Datwyler **Calcium Chloride Solution:** colorless glass vials, hydrolytic type I, with a nominal volume of 6 ml, ISO 8362-1. The pertinent stoppers are bromobutyl rubber stopper, 20 mm that are secured onto the vials with crimp caps.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability study data of 3 batches at 2-8^{o}C. The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 12 months.

	Module 4	**Pharmacodynamics** (Studies in Rat and Rabbits have been provided) **Toxicology** (Studies in Rat and Rabbits have been provided) **Genotoxicity** The assay was performed in two independent experiments, both with and without liver microsomal activation. The items were tested in triplicate at six predefined concentrations up to a maximum dose of 100 microliters **Pharmacokinetics** (FS VH S/D (frozen and lyophilized) is intended for local application only, therefore systemic exposure or distribution to other organs and tissues is not expected and Pharmacokinetic Studies were not conducted. Nevertheless, in order to demonstrate the bioequivalence of bovine and synthetic aprotinin, a pharmacokinetic study in mice was performed and bio-equivalence of bovine and synthetic aprotinin could be demonstrated
	Module 5	**Safety** of FS was demonstrated in 10 clinical studies including a total of 931 subjects in the IP treatment groups. Study **550904** is a randomized, controlled, subject-blinded multicenter Phase II study to evaluate the efficacy and safety of FS VH S/D 500 s apr for hemostasis in subjects undergoing hepatic resection. (Patients: 35) Study **550701** had a lower age limit of ≥3 years. Age ranged from 4 to 76 years in subjects in the FS VH S/D 500 s-apr group and a total of 14 pediatric subjects aged <18 years received FS VH S/D 500 s-apr, of which 11 were included in the ITT analysis. Study **550602** is a Phase II, prospective, randomized, controlled, subject-blinded, multicenter study that was designed to evaluate the efficacy and safety of FS VH S/D 500 s-apr for hemostasis. Study **125** was a Phase IIIb, prospective, open-label, non-controlled multi-center study to monitor the efficacy and safety of low FXIII (≤10 IU/mL) FS VH for hemostasis in cardiac patients undergoing re-operative cardiovascular surgery or resternotomy. (Patients: 27) Study **550003** is a pivotal, comparative, Phase III, prospective, parallel design, randomized (1:1), double-blind, multicenter clinical study to evaluate the efficacy of FS VH S/D in subjects undergoing cardiac surgery requiring CPB. (Patients: 288) Study **014/016**, a randomized, controlled multicenter Phase III study in subjects undergoing repeated cardiac surgery or emergency resternotomy, demonstrated the efficacy of FS VH in this patient population in comparison to conventional topical agents. (Patients: 490) Study **550801** is a pivotal, confirmatory, Phase III, prospective, controlled, randomized, subject-blinded, multicenter study in 2 parallel, equal-sized treatment arms. (Patients: 70) Study **550002** is a prospective, randomized, controlled, parallel group, single-blind, multinational, multicenter Phase III study investigating the

		safety of FS VH S/D and its efficacy in the reduction of lymphatic leakage by sealing axillary lymphatics in subjects with breast cancer undergoing lumpectomy and level I and II axillary lymph node dissection with two separate incisions. In the control group, conventional surgical procedures alone were applied to reduce lymphatic leakage. (Patients: 50) Comparison of comorbidity (hepatic disease, coagulopathy, renal disease, and other signs of morbidity) showed no difference between the FS HT and control groups. (Patients: 60)

As multiple manufacturing sites were mentioned for each component, hence, the firm was asked to confirm one site for each product. The firm then submitted a new CoPP wherein the name of manufacturing site of solvent of component II was changed from "Hamlen Pharmaceutical GmbH" to "Siegfried Hameln GmbH". Moreover, batch release site was also mentioned in new CoPP. Hence, the firm submitted the fee challan of Rs. 75000/- and confirmed the following sites for each component:

Sr. No.	**Component**	**Manufacturing Site**
1.	Human Fibrinogen (Component I)	M/s Baxter AG., Lange Allee 24 A, 1221 Wien, Austria
2.	Human Thrombin (Component II)	M/s Baxter AG. Uferstraβe 15, 2304 Orth/Donau, Austria
3.	Aprotinin Soln. Solvent for Component I	M/s Baxter AG., industriestraβe 72, 1221 Wien, Austria
4.	Calcium Chloride Soln. (Solvent for Component II)	M/s Siegfried Hameln GmbH, Langes Feld 13, 31789 Hameln, Germany
Batch Release Site		M/s Baxter AG., industriestraβe 67, 1221 Wien, Austria

Decision: Keeping in view legalized CoPP and approval of Austria (Reference Regulatory Authority); Registration Board approved above manufacturing & batch release sites for the product.

6. Change in nomenclature of Erythropoietin from "Recombinant Human Erythropoietin" to "Human Erythropoietin for approve products of M/s AJ Mirza Pharma (Pvt.) Ltd., Karachi.

Following products of M/s AJ Mirza Pharma (Pvt.) Ltd., Karachi were approved in 313th meeting of Registration Board:

Sr. No.	**Name of Manufacturer**	**Brand Name & Composition**	**Document Details**	**Decision of RB in 313th Meeting**
1.	M/s Shenyang Sunshine Pharmaceutical Co. Ltd., No. 3 A1, Road 10, Econ & Tech Development Zone, Shenyang 110027, China.	EPIAO 2000IU Injection Each 1ml vial contains: Recombinant Human Erythropoietin…2000IU BP Specifications	Legalized CoPP No. 2017.79 dated 26-12-2017	*Keeping in view legalized CoPPs indicating products availability in country of origin and NOC submitted by M/s AA Pharma, Karachi; Registration Board cancelled the registration of Epiao 2000IU (Reg. No. 047578), Epiao 4000IU (Reg. No.*
2.		EPIAO 4000IU Injection Each 1ml vial contains: Recombinant Human Erythropoietin…4000IU BP Specifications		

3.		EPIAO 10000IU Injection Each 1ml vial contains: Recombinant Human Erythropoietin…10000IU BP Specifications		*047579) & Epiao 10000IU (Reg. No. 047580) from M/s AA Pharma, Karachi and granted in name of M/s A.J. Mirza Pharma (Pvt.) Ltd., Karachi subject to the compliance of current Import Policy for Finished Drugs, confirmation of latest MRP of the products from Costing & Pricing Division and verification of cold storage facility.*

During processing the case for issuance of registration letter, the firm submitted that the generic name of Recombinant Human Erythropoietin has been changed in country of origin to Human Erythropoietin. The firm requested to issue registration letter with revised nomenclature. The firm submitted the following for this request:

i. Fee challan of Rs. 7500/- for each product
ii. Valid Legalized CoPPs for all the products indicating changed nomenclature
iii. Weblink of official website of NMPA indicating the following:
"ACCORDING TO THE 2020 EDITION OF THE CHINESE PHARMACOPOEIA, THE GENERIC NAME OF THE DRUG FOR RECOMBINANT HUMAN ERYTHROPOIETIN INJECTION (CHO CELLS) WAS CHANGED, AND THE GENERIC NAME OF THE VARIETY WAS CHANGED FROM "RECOMBINANT HUMAN ERYTHROPOIETIN INJECTION (CHO CELL)" TO "HUMAN ERYTHROPOIETIN INJECTION". THE APPROVAL NUMBER OF THE ORIGINAL DRUG REMAINS UNCHANGED, AND PLEASE MAKE CORRESPONDING MODIFICATIONS TO THE INSTRUCTIONS AND PACKAGING LABELS."

Decision: Keeping in view legalized CoPP and BP monograph of Erythropoietin Injection; Registration Board approved the change in nomenclature from "Recombinant Human Erythropoietin" to "Human Erythropoietin" for above products.

Cases of AD-II (Saadat Ali Khan)

Imported Human Biological from Non-reference countries

1.	**Name, address of Applicant / Importer**	**M/s Gene-Tech Laboratories** 246-B, Block-6, P.E.C.H.S, Karachi, 75400, Pakistan
	Details of Drug Sale License of importer	**License No:** 0002 **Address:** 246-B, Block-6, P.E.C.H.S, Karachi, 75400, Pakistan **Address of Godown: :** 246-B, Block-6, P.E.C.H.S, Karachi **Validity:** 15-08-2022. **Status:** Drug License by way of wholesale **Renewal: N/A**
	Name and address of marketing authorization holder (abroad)	**M/s Gene-Tech Laboratories** 246-B, Block-6, P.E.C.H.S, Karachi, 75400, Pakistan

	Name, address of manufacturer(s)	**Biocon Biologics India Limited** Block No. B1, B2, Q13 of Q1 and W20 & Unit S18, 1st Floor, Block B4, Special Economic Zone Plot No. 2, 3, 4 & 5 Phase-IV Bommasandra-Jigani Link Road Bommasandra Post, Bengaluru 560099, **India**
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted **legalized copy of CoPP certificate** (No. DCD/CR-1310/Spl.Cell–I/19-20) dated 26-06-2020 issued by Drugs Control Department, Government of Karnataka. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP was valid till 25-12-2022.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of authorization from Biocon Biologics UK Ltd. The letter shows that the manufacturer appoints M/s Gene-Tech Laboratories to register and market their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.9371 dated 24-03-2021, Dy. No.13918 dated 08-06-2022
	Details of fee submitted	PKR 100,000/-: 24-03-2021 and PKR 50,000/- on 27-07-2022 (total PKR 150,000/-)
	The proposed proprietary name / brand name	**KRABEVA 100** mg/4 mL single-dose vials
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Biocon's Bevacizumab is developed in 100 mg/4 mL single-dose vials.
	Pharmaceutical form of applied drug	Concentrate for solution for intravenous infusion
	Pharmacotherapeutic Group of (API)	ATC code: L01X C07 Anticancer MAB

	Reference to Finished product specifications	In house
	Shelf life & storage condition	24 months (2-8^{o}C)
	Proposed Pack size	100 mg/4 mL single-dose vials
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Avastin **(EU, USA,** Approved).
	For generic drugs (me-too status)	Avastin 100mg available in Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, verification studies of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability
	Name, address of drug substance manufacturer	Biocon Biologics India Limited, Block No. B1, B2, Q13 of Q1 and W20 & Unit S18, 1st Floor, Block B4, Special Economic Zone, Plot No. 2, 3, 4 & 5 Phase-IV, Bommasandra-Jigani Link Road, Bommasandra Post, Bengaluru 560099, India
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The accelerated stability study data is conducted at **5°C ± 3°C up to 6 months.** The real time stability data is conducted at-**20°C ± 5°C up to 48 months**
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	The Biocon's Bevacizumab DP is filled in 6R, Type-I clear glass vial (USP/Ph.Eur) for 100 mg presentation. 6R vial closed with 20mm flurotec coated, chlorobutyl serum stoppers. The rubber stoppers are sealed with an aluminium seal with plastic flip-off cap component. The seal and cap do not come into contact with the drug product.
	Stability study data of drug product, shelf life and storage conditions	The accelerated stability study data is conducted at 25°C ± 2°C / 60% RH ± 5% RH up to 6 Months. The real time stability study data is conducted at 5°C ± 3°C up to 24 months3 **commercial scale batches.** The real time stability study data is conducted at 5°C ± 3°C up to 36 months for three **developmental batches**. The real time stability study data is conducted at 5°C ± 3°C up to 36 months for three **consistency batches.**
2.	**Name, address of Applicant / Importer**	**M/s Gene-Tech Laboratories** **246-B, Block-6, P.E.C.H.S, Karachi, 75400, Pakistan**
	Details of Drug Sale License of importer	License No: 0002 Address: 246-B, Block-6, P.E.C.H.S, Karachi, 75400, Pakistan Address of Godown: : 246-B, Block-6, P.E.C.H.S, Karachi Validity: 15-08-2022. Status: Drug License by way of wholesale Renewal: N/A
	Name and address of marketing authorization holder (abroad)	M/s Gene-Tech Laboratories 246-B, Block-6, P.E.C.H.S, Karachi, 75400, Pakistan
	Name, address of manufacturer(s)	Biocon Biologics India Limited Block No. B1, B2, Q13 of Q1 and W20 & Unit S18, 1st Floor, Block B4, Special Economic Zone Plot No. 2, 3, 4 & 5 Phase-IV Bommasandra-Jigani Link Road Bommasandra Post, Bengaluru 560099, India
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted legalized copy of CoPP certificate (No. DCD/CR-1310/Spl.Cell–I/19-20) dated 26-06-2020 issued by Drugs Control Department, Government of Karnataka. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP was valid till 25-12-2022.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of authorization from Biocon Biologics UK Ltd. The letter shows that the manufacturer appoints M/s Gene-Tech Laboratories to register and market their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.9372 dated 24-03-2021, Dy. No.13918 dated 08-06-2022
	Details of fee submitted	PKR 100,000/-: 24-03-2021 and PKR 50,000/- on 27-07-2022 (total PKR 150,000/-)
	The proposed proprietary name / brand name	KRABEVA 400 mg/16 mL single-dose vials
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Biocon's Bevacizumab 400 mg/16 mL single-dose vials.
	Pharmaceutical form of applied drug	Concentrate for solution for intravenous infusion
	Pharmacotherapeutic Group of (API)	ATC code: L01X C07 Anticancer MAB
	Reference to Finished product specifications	In house
	Shelf life & storage condition	24 months (2-8^{o}C)
	Proposed Pack size	400 mg/16 mL single-dose vials
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Avastin (EU, USA, Approved).
	For generic drugs (me-too status)	Avastin 400mg available in Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

		The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, verification studies of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability
	Name, address of drug substance manufacturer	Biocon Biologics India Limited, Block No. B1, B2, Q13 of Q1 and W20 & Unit S18, 1st Floor, Block B4, Special Economic Zone, Plot No. 2, 3, 4 & 5 Phase-IV, Bommasandra-Jigani Link Road, Bommasandra Post, Bengaluru 560099, India
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The accelerated stability study data is conducted at 5°C ± 3°C up to 6 months. The real time stability data is conducted at-20°C ± 5°C up to 48 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	The Biocon's Bevacizumab DP is filled in 6R, Type-I clear glass vial (USP/Ph.Eur) for 100 mg presentation. 6R vial closed with 20mm flurotec coated, chlorobutyl serum stoppers. The rubber stoppers are sealed with an aluminium seal with plastic flip-off cap component. The seal and cap do not come into contact with the drug product.
	Stability study data of drug product, shelf life and storage conditions	The accelerated stability study data is conducted at 25°C ± 2°C / 60% RH ± 5% RH up to 6 Months. The real time stability study data is conducted at 5°C ± 3°C up to 24 months3 **commercial scale batches.** The real time stability study data is conducted at 5°C ± 3°C up to 36 months for three **developmental batches**. The real time stability study data is conducted at 5°C ± 3°C up to 36 months for three **consistency batches.**
Biosmilarity Data evaluation: Biocon's Bevacizumab, a proposed biosimilar to reference drug product Avastin is produced in a Chinese Hamster Ovary (CHO) mammalian cell expression system. The US-Licensed Avastin and EU-Approved Avastin are available in two single dose presentations, 100 mg/vial (4 mL of 25 mg/mL) and 400 mg/vial (16 mL of 25		

mg/mL). Proposed biosimilar Biocon's Bevacizumab has also been developed for both presentations with identical formulation buffer. The DS is manufactured as ready-to-fill bulk formulation at the required concentration of 25 mg/mL. Therefore, from a DP manufacturing perspective, the same DS batch can be used to prepare either of these presentations (100 mg or 400 mg).

WHO Bio-similarity guidelines	**Data submitted by the firm**
Quality Comparison Physicochemical characterization	**a)** Protein concentration by Ultra-violet 280 Absorption **b) Primary Structure-:** i. Amino acid sequence by Peptide Mass fingerprint ii. Amino acid sequence by Intact Mass iii. Amino acid sequence by Light Chain and Heavy Chain Mass iv. Amino acid sequence by cIEF (capillary isoelectric focusing) **c) Secondary Structure & high order Structure by** i. Far UV Circular Dichroism ii. Fourier transform infrared spectroscopy iii. Free Cysteine iv. Disulphide Bridging v. Near UV Circular Dichroism vi. Differential scanning calorimetry vii. Intrinsic Fluorescence viii. Hydrophobic Interaction Chromatography **d) Aggregates by:** i. Size Exclusion Chromatography -UV ii. Analytical Ultra Centrifugation (AUC) iii. Size Exclusion iv. Chromatography –MALS **e) Glycoform variants-** i. % Afucosylation with and without high mannose by Normal Phase HPLC ii. % High Mannose by Normal Phase HPLC iii. % Galactosylation mannose by Normal Phase HPLC iv. Sialic acid by reverse Phase HPLC
Biological Activity	**Biological activity was carried by:** • Fab mediated by VEGF165 Binding Assay ELISA • Fab mediated by Inhibition of VEGF165 induced HUVEC Proliferation • Fc mediated by FcγRIIIa-V158 binding kinetics assay (SPR) • Fc mediated by FcγRIIIa-F158 binding kinetics assay (SPR) • Fc mediated by FcRn binding kinetics assay (SPR) • Fab mediated by Inhibition of VEGF121 induced HUVEC Proliferation • Fab mediated by Inhibition of VEGF165 induced VEGFR-2 phosphorylation • Fab mediated by VEGF165 binding kinetics assay • Fab mediated by VEGF121 binding kinetics assay
Impurities	**Purity and impurities**: Size Variants/Aggregates by • Size Exclusion Chromatography (SEC) • Non-Reduced CE-SDS (nrCE-SDS) • Reduced CE-SDS (rCE-SDS)

Stability Studies		Stability studies are provided.
Non-clinical Studies		**Repeat dose toxicity study:** • Repeated Dose Four Week Intravenous Comparative Toxicity Study of Humanized Monoclonal Antibody – Bevacizumab (Biocon Ltd) and Avastin (Genentech) with Toxicokinetics in Swiss Albino Mice. • 28-day Repeat-Dose Toxicity study in the Cynomolgus monkey intravenously administered Biocon's Bevacizumab and Avastin
Clinical Studies		• A double-blind, single-dose, three-treatment, parallel group, pharmacokinetic comparability study of Biocon's Bevacizumab manufactured by Biocon compared to US-Avastin and EU-Avastin in healthy adult male volunteers. • A double blind, randomized, active controlled, parallel design, comparative PK, efficacy, safety and immunogenicity study of Bmab-100 and Avastin, both in combination with XELOX (oxaliplatin and capecitabine) chemotherapy in patients with metastatic colorectal cancer. • A multicenter, double-blind, randomized, parallel-group study to assess the efficacy and safety of Biocon's Bevacizumab compared with Avastin, in the first-line treatment of patients with Stage IV Non-Squamous Non-Small Cell Lung Cancer (NSCLC).
Decision: Keeping in view legalized CoPPs indicating products availability in country of origin and biosimilarity data submitted in light of decision of 297th meeting of Registration Board; Registration Board approved the products subject to compliance of current Import Policy for finished drugs.		
3.	**Name, address of Applicant / Importer**	**M/s Himmel Pharmaceuticals (Pvt.) Ltd, 793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan**
	Details of Drug Sale License of importer	**License No:** 05-352-0065-0016174D **Address:** 793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan **Address of go-down: N/A** **Validity: 06-02-2022** **Status:** License to sell drugs by way of Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited **Plant address**: Kathali Bhaluka Mymensingh **Bangladesh.** **Office Address**: 9/B/2 Toyenbee Circular Road Motijheel, Dhaka 1223 Bangladesh
	Name, address of manufacturer(s)	-do-
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized COPP (DA/6-110/2016/3355) issued on 4-June-2020 **by** Directorate General of Drug Administration Ministry of Health & Family welfare Government of the people's republic of Bangladesh. The CoPP specifies free sale status of the product in country of origin along with its availability. The CoPP also confirms the GMP status of the firm. (Periodicity of routine inspection:2years)
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific letter of authorization dated 02-06-2020 from Beacon Pharmaceuticals limited. The letter specifies that the

		manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register & sell their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No32920 Dated 10.12.2020, Dy. No.8733 Dated 05.04.2022, Dy. No.13612 Dated 06.06.2022
	Details of fee submitted	Rs. /- 50000 Dated 19.11.2020
	The proposed proprietary name / brand name	Nivolunix 40 Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose contains Formulated bulk of Nivolumab INN….40mg
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Antineoplastic agents (Anti-cancer), Monoclonal Antibodies
	Reference to Finished product specifications	In house
	Proposed Pack size	Pack Size: 1's
	Proposed unit price	Retail price As per SRO
	Shelf Life	24 months
	Storage Conditions	2 ^{O}C -8^{O}C
	The status in reference regulatory authorities	OPDIVO (NIVOLUMAB 40mg/4mL single dose vial) | BLA #125554 | BRISTOL MYERS SQUIBB in USFDA
	For generic drugs (me-too status)	Not available in Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, Characterization

		(Elucidation of Structure and Other Characteristics), impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Geneway Bio-Technology co., Ltd Address: No. 6 Anmin Road, Huangdai Town, Xiangcheng, Suzhou, Jiangsu China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at 25±2 °C for 10 days, at 5 ±3 °C for 6months & ≤-30 °C for 12 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted specification & in-house analytical method along with Analytical method validation studies for the applied product.
	Container closure system of the drug product	Nivolunix 40mg injection is provided in 5mL clear glass vial (USP type-I glass) 20 mm rubber stopper, type -1 and 20 mm Flip off seal with red color top.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 commercial batches. The accelerated stability study data is conducted at 40° C ± 2° C & 75% ± 5% RH for 6 months. The real time stability study data is conducted at 2 ^{O}C - 8^{O}C for 24 months.
	Module-IV	**Pharmacology studies:** The binding of product to human CD279 (programmed cell death 1, PD-1): • Effects on interaction between PD-1 and PD-1 ligands using the PD-1/CHO cell line and biotin-labeled recombinant human PD-L1- Fc and PD-L2-Fc fusion proteins. • Effect on immunoreactivity (on alloantigen-induced T-cell activation, antigen-specific T cell reactivity using Cynomolgus monkeys) • Activity against malignant tumors in mice with malignant melanoma B16F10 cells. • Secondary pharmacodynamics (antibody-dependent cell-mediated cytotoxicity)

		• Safety pharmacology (Effects on the central nervous system, Effects on the cardiovascular system, Effects on the respiratory system) **Pharmacokinetic studies:** (Analytical procedures-assay, antibody assay, Single-dose administration, Repeated-dose administration) **Toxicology studies:** Single-dose toxicity using cynomolgus monkeys, Repeated-dose toxicity in cynomolgus monkeys, Extended study of pre- and postnatal development in cynomolgus monkeys, Cross-reactivity studies, Four-week repeated intravenous dose toxicity study with ipilimumab coadministration in cynomolgus monkeys) **Note:** The submitted clinical trial data is from bulk manufacture not from the finish product manufacter.
	Module-V	**Phase I study:** • An open-label study to investigate the pharmacokinetics (PK) in 17 patients with advanced solid tumors resistant to conventional therapies. **Phase II study:** An open-label study to investigate the PK and other endpoints in 35 patients. **Phase III study:** A Phase III trial to compare the efficacy & safety of FX02 and Opidivo (Nivolumab) injection in patients with advance NSCLC who had received prior platinum-based chemotherapy. **Note:** The submitted clinical trial data is from bulk manufacture not from the finish product manufacturer.
4.	Name, address of Applicant / Importer	**M/s Himmel Pharmaceuticals (Pvt.) Ltd, 793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan**
	Details of Drug Sale License of importer	License No: 05-352-0065-0016174D Address: 793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan Address of go-down: N/A Validity: 06-02-2022 Status: License to sell drugs by way of Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited Plant address: Kathali Bhaluka Mymensingh Bangladesh. Office Address: 9/B/2 Toyenbee Circular Road Motijheel, Dhaka 1223 Bangladesh
	Name, address of manufacturer(s)	-do-
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: Firm has submitted original legalized COPP (DA/6-110/2016/3355) issued on 4-June-2020 by Directorate General of Drug Administration Ministry of Health & Family welfare Government of the people's republic of Bangladesh. The CoPP specifies free sale status of the product in country of origin along with its availability. The CoPP also confirms the GMP status of the firm. (Periodicity of routine inspection:2years)

	Details of letter of authorization / sole agency agreement	Firm has submitted product specific letter of authorization dated 02-06-2020 from Beacon Pharmaceuticals limited. The letter specifies that the manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register & sell their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No32921 Dated 10.12.2020, Dy. No.8733 Dated 05.04.2022, Dy. No.13612 Dated 06.06.2022
	Details of fee submitted	Rs. /- 50000 Dated 19.11.2020
	The proposed proprietary name / brand name	**Nivolunix 100 Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose contains Formulated bulk of Nivolumab INN….100mg
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Antineoplastic agents (Anti-cancer), Monoclonal Antibodies
	Reference to Finished product specifications	In house
	Proposed Pack size	Pack Size: 1’s
	Proposed unit price	Retail price As per SRO
	Shelf Life	24 months
	Storage Conditions	2^0C -8^0C
	The status in reference regulatory authorities	OPDIVO (NIVOLUMAB 100mg single dose vial) | BLA #125554 | BRISTOL MYERS SQUIBB in USFDA
	For generic drugs (me-too status)	Not available in Pakistan

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, Characterization (Elucidation of Structure and Other Characteristics), impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Geneway Bio-Technology co., Ltd Address: No. 6 Anmin Road, Huangdai Town, Xiangcheng, Suzhou, Jiangsu China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at 25±2 °C for 10 days, at 5 ±3 °C for 6months & ≤-30 °C for 12 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted specification & in-house analytical method along with Analytical method validation studies for the applied product.
	Container closure system of the drug product	Nivolunix 40mg injection is provided in 5mL clear glass vial (USP type-I glass) 20 mm rubber stopper, type -1 and 20 mm Flip off seal with red color top.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 commercial batches. The accelerated stability study data is conducted at 40° C ± 2° C & 75% ± 5% RH for 6 months. The real time stability study data is conducted at 2 OC - 8OC for 24 months.

	Module-IV	Pharmacology studies: The binding of product to human CD279 (programmed cell death 1, PD-1): • Effects on interaction between PD-1 and PD-1 ligands using the PD-1/CHO cell line and biotin-labeled recombinant human PD-L1- Fc and PD-L2-Fc fusion proteins. • Effect on immunoreactivity (on alloantigen-induced T-cell activation, antigen-specific T cell reactivity using Cynomolgus monkeys) • Activity against malignant tumors in mice with malignant melanoma B16F10 cells. • Secondary pharmacodynamics (antibody-dependent cell-mediated cytotoxicity) • Safety pharmacology (Effects on the central nervous system, Effects on the cardiovascular system, Effects on the respiratory system) Pharmacokinetic studies: (Analytical procedures-assay, antibody assay, Single-dose administration, Repeated-dose administration) Toxicology studies: Single-dose toxicity using cynomolgus monkeys, Repeated-dose toxicity in cynomolgus monkeys, Extended study of pre- and postnatal development in cynomolgus monkeys, Cross-reactivity studies, Four-week repeated intravenous dose toxicity study with ipilimumab coadministration in cynomolgus monkeys) Note: The submitted clinical trial data is from bulk manufacture not from the finish product manufacter.
	Module-V	Phase I study: • An open-label study to investigate the pharmacokinetics (PK) in 17 patients with advanced solid tumors resistant to conventional therapies. Phase II study: An open-label study to investigate the PK and other endpoints in 35 patients. Phase III study: A Phase III trial to compare the efficacy & safety of FX02 and Opidivo (Nivolumab) injection in patients with advance NSCLC who had received prior platinum-based chemotherapy. Note: **The submitted clinical trial data is from bulk manufacture not from the finish product manufacturer.**

Bio-similarity studies:	
WHO Bio-similarity guidelines	**Data submitted by the firm**
Quality Comparison Physicochemical characterization	**a) Primary Structure:** i. Amino acid sequence by LC-MS & MS/MS ii. N-terminal sequence by LC-MS. iii. C-terminal lysine by LC-MS. iv. N-glycosylation site by Liquid Chromatography with tandem mass spectrometry (LC-MS-MS) **b) Secondary Structure & high order Structure**

	i. Intact mass by LC-MS ii. Disulfide bond by LC-MS iii. Free thiol (Ellman's) iv. Circular Dichroism (Secondary Structure) by Far spectrogram. v. Thermostability by differential fluorimetry (DSF) **c) Heterogenicity** i. Glycan by LC-MS ii. Heterogenicity of glycosylation by FLD-HPLC iii. Isoelectric point by CIEF iv. Charge variant (CEX-HPLC
Biological Activity	Biological activity by: • PD-I binding activity by ELISA
Impurities	• Purity by SEC-HPLC • Purity by CE-SDS • Protein A by ELISA • DNA residual by qPCR • Host cell protein by ELISA
Stability Studies	Stability studies are provided.
Non-clinical Studies	Primary pharmacodynamics by: • Binding to PD-I • Inhibitory effect against binding of PD-I to PD-L1 or PD-L2 • One month repeated doses toxicity study in monkeys • Six months repeated doses toxicity study in monkeys
Clinical Studies	Comparative clinical study has not been submitted.
Remarks of Evaluator: i. **T**he firm has not submitted non-clinical & clinical study data from its finish product manufacturer (Exporter M/s Beacon Pharmaceuticals Limited Bangladesh) instead all non-clinical & clinical study conducted by the bulk manufacturer (Geneway Bio-Technology co., Ltd China) have been submitted. **ii.** Comparative clinical trial data has not been submitted.	

Decision: Registration Board deferred the case for submission of following by the firm:

i. Clarification of label claim (composition).

ii. Comparative clinical trial data with innovator drug.

iii. Regulatory Guidelines of country of origin (Bangladesh) indicating that the registration of above products was granted in exporting country on the basis of non-clinical & clinical trial data of bulk manufacturer of China.

B: Imported Veterinary Biologicals from Reference Countries:

1.	**Name of Importer**	**M/s Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 43 Sector-15, Korangi, Industrial Area, Karachi.**
	DSL details	Copy of DSL

		Validity : 19-06-2024 Status: License to sell drugs as wholesale
	Name of Manufacturer	M/s ADM Protexin Limited, Lopen Head, South Petherton, TA13 5JH, United Kingdom.
	Brand Name +Dosage Form + Strength	Protexin Concentrate
	Composition	Contents per kg *Enterococcus faecium* NCIMB1 30183 PXN® 33 *Streptococcus thermophilus* NCIMB 30189 PXN® 66 *Lactobacillus rhamnosus* NCIMB 30188 PXN® 54 *Lactobacillus acidophilus* NCIMB 30184 PXN® 35 *Lactobacillus bulgaricus* NCIMB 30186 PXN® 39™ Bifidobacterium bifidum NCIMB 30179 PXN® 23™ *Lactobacillus plantarum* NCIMB 30187 PXN® 47™
	Finished product specifications	Innovator' Specifications
	Pharmacological Group	Veterinary feed additive (Probiotic)
	Shelf life	24 months (2 Co -8 Co)
	Products already registered in Pakistan	The product is already registered in 100 gm
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 21689 Dated 9th August 2021, Dy. No.10629 Dated 26th April 2022 Rs. 7500/- date 04-08-2021, Rs. 67500/- date 19-04-2022
	Demanded Price / Pack size	Decontrolled/ 1000 gm (one Kg)
	General documentation	Original Legalized Free Sale Certificate (FSC): Issued by: Rural Payments Agency UK. Issued on: 27-05-2021 Copy of GMP Certificate: • Issued by: Medicines & Health Products Regulatory Agency (MHRA), UK Online verified on 25 August 2022 vide below link https://cms.mhra.gov.uk/mhra/gmp/uk-gmp-40676-insp-gmp-406765124258-0008-v
	Remarks	In specification only viable count (potency test) has been mentioned & analytical method of this test has been submitted. In stability study only this one test i.e. viable count (potency test) has been performed & submitted. Justification submitted by the firm: Justification has been su bmitted from the manufacturer that product is animal feed additive & regulated in country of origin (UK) with different regulation with respect to other pharmaceutical/Biological Drugs. And the said test has been performed as per ISO standard.
Decision: Registration Board deliberated that the instant molecule is a veterinary probiotics which come under the purview of Health &OTC division hence the Board referred the case to Committee on Placement of Therapeutic goods falling in Grey area for their recommendation.		

C: Imported Veterinary Biologicals from Non-Reference Countries:

1.	**Name of Importer**	**M/s Huzaifa International,**

		Address: Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan
	DSL details	Copy of DSL Address:M/s Huzaifa International, Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan. Validity : 20th November-2023 Status: License to sell drugs as Distributor
	Name of Manufacturer	M/s Komipharm International Co., Ltd. Address:17, Gyeongje-Ro, Siheung-Si, Gyeonggi-Do, South Korea [Before Address System CHange: 1236-6, Chongwang-Dong, Shihung-Si, Kyonggi-Do, South Korea]
	Brand Name +Dosage Form + Strength	**Pro-Vac AB**
	Composition	Each 2ml dose contains: Anthrax (Stern Strain) spore...: ≥ 0.8 X $I0^7$ CFU Blackleg spore------ ≥ 0.8 X $I0^7$ CFU
	Finished product specifications	Ph. Eu specifications
	Pharmacological Group	Poultry Vaccine
	Shelf life	24 months (When stored at 2-8 C^o at the Dark place)
	Products already registered in Pakistan	Not been found in record of this division
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No.32626 Dated 8-12-2020, Dy No. dated 21-06-2022 Rs. 100,000/- dated 08-12-2020
	Packsize:	Decontrolled/ 10 doses (20ml)
	General documentation	***Original Legalized Free Sale Certificate (FSC)*** No. M2011076**:** **Issued by:** Animal and Plant Quarantine Agency of the Ministry for Agriculture Food and Rural Affairs of the Republic of Korea • **Issued on:** 28-11-2018 ***Original Legalized GMP Certificate:*** • **Issued by:** As mentioned above **Issued on:**19-06-2018.
Decision: Registration Board deferred the case for evidence of availability of vaccine (formulation) in RRAs and for the comments of Expert Working Group on Veterinary Drugs regarding immunological relevance and need of applied strains in Pakistan. Registration Board further advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board.		

2.	Name of Importer	**M/s Hivet Animal Health Business, Lahore 1 st Floor,667-P.M.A, Johar Town, Lahore, Pakistan**
	DSL details	License to sell drug as distributor No. 05-352-0066-040985D valid till 23-Feb-2023
	Manufacturer Name	M/s Beijing Sinder-Vet Technology Co., Ltd. Address: Beijing Tianzhu Airport Economic Development Zone, Shunyi District, Shunyu Road No.118, Shunyi District, Beijing, China.
	Brand Name + Dosage Form + Strength	**Sinvac IBD**

	Composition	Each dose contains: Infectious Bursal Disease Antigen (B87 strain)…..≥10(3.0)ELD50/dose before freeze drying (0.0012ml/dose)
	Finished product specifications	Ph. Eu specifications Myvac IBD V877 (Al-Asar Enterprise)
	Pharmacological Group	Live Virus Veterinary Vaccine
	Shelf Life	18 months (2 0C -8 0C)
	Products already registered in Pakistan	Myvac IBD V877 (Al-Asar Enterprise)
	Type of Form Dy No & Date: Fee submitted	Form-5A Dy. No.18491 Dated 01-07-2021, Dy No. 9412 dated 13-04-2022 Rs. 150,000/- dated 08-12-2021
	Demanded Price / Pack size	Decontrolled ,1000dose/vial
	General documentation	***Original Legalized Free Sale Certificate (FSC):*** **Issued by:** Animal Husbandry and Veterinary Bureau of Zhucheng city. • **Issued on:** 12-01-2022 ***Legalized copy of GMP Certificate:*** • **Issued by:** **Issued on:** 29-11-2021.
	Remarks of Evaluator	
Decision: Registration Board referred the case to Expert Working Group on Veterinary Drugs for their comments regarding immunological relevance and need of applied strain in Pakistan. Registration Board further advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board.		
3.	Name of Importer	**M/s Hivet Animal Health Business, Lahore 1st Floor,667-P.M.A, Johar Town, Lahore, Pakistan**
	DSL details	License to sell drug as distributor No. 05-352-0066-040985D valid till 23-Feb-2023
	Manufacturer Name	M/s Beijing Sinder-Vet Technology Co., Ltd. Address: No.118, Shunyu Road, Beijing Tianzhu Airport Economic Development Zone, Shunyi District, Beijing, China.
	Brand Name + Dosage Form + Strength	**SINVAC ND+IB+H9**
	Composition	Each dose of 0.5ml contains: Newcastle Disease antigen (LA SOTA strain) ≥ $10^{8.5}$ EID_{50} Infectious Bronchitis Virus M41 Strain ≥ $10^{6.5}$ EID_{50} Avian Influenza antigen inactivated (H9 Subtype WD Strain ≥ $10^{7.5}$ EID_{50}
	Finished product specifications	As per Innovator
	Pharmacological Group	Inactivated veterinary vaccine
	Shelf Life	18 months (2 0C -8 0C)
	Products already registered in Pakistan	Mevac Multi IB+H9+ND by Bromed Animal Health
	Type of Form Dy No & Date: Fee submitted	Form-5A Dy. No.11187 Dated 12-04-2021, Dy No. 9412 dated 13-04-2022

		Rs. 150,000/- dated 08-12-2021
	Demanded Price / Pack size	Decontrolled ,500 doses/bottle
	General documentation	***Original Legalized Free Sale Certificate (FSC):*** **Issued by:** Animal Husbandry and Veterinary Bureau of Zhucheng city. • **Issued on:** 12-01-2022 ***Legalized copy of GMP Certificate:*** • **Issued by:** **Issued on:** 29-11-2021.
	Remarks of Evaluator	
Decision: Keeping in view legalized GMP and Free Sale Certificate indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs.		
4.	Name of Importer	**M/s Hilton Pharma (Pvt.) Ltd. Plot No. 13-14, Sector-15, Korangi, Industrial Area, Karachi**
	DSL details	License to sell drug as distributor No. 05-352-0066-040985D valid till 23-Feb-2023
	Manufacturer Name	M/s PT MEDION FARMA JAYA, JI Babakan Ciparay No 282, Babakan Ciparay, Bandung-Indonesia Plant: JI. Raya Batujajar No 29, Cimareme, Ngamprah, Bandung Barat-Indonesia.
	Brand Name + Dosage Form + Strength	**Medivac IB Variant Vaccine**
	Composition	Each dose of dose contains: Infectious Bronchitis Virus M02 Strain $\geq 10^{3.5}$ EID_{50}
	Finished product specifications	Ph. Eu specifications
	Pharmacological Group	Inactivated veterinary vaccine
	Shelf Life	18 months (2 0C -8 0C)
	Products already registered in Pakistan	Myvac IBD V877 (Al-Asar Enterprise) M02 strain not found
	Type of Form Dy No & Date: Fee submitted	Form-5A Dy. No.15310 Dated 02-06-2021, Dy. No.22447 Dated 05-08-2022 Rs. 75,000/- dated 26-05-2021, Rs. 75,000/- dated 03-08-2022
	Demanded Price / Pack size	Decontrolled ,1000 doses/bottle
	General documentation	***Original Legalized CoPP:*** **Issued by:** Mo Agriculture Directorate General of Livestock and Animal Health services Indonesia. • **Issued on:** 30-12-2020
	Remarks of Evaluator	
Decision: Registration Board referred the case to Expert Working Group on Veterinary Drugs for their comments regarding immunological relevance and need of applied strain in Pakistan. Registration Board further advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board.		

D: Miscellaneous/ Deferred Cases

1. Local human Biological applied for registration by M/s Hilton Pharma Karachi.

The following product for the local manufacturing biological drug was considered in 262nd Meeting of Registration Board held on 20-21stOctober, 2016 and the Board decided as under;

Central Licensing Board has approved the manufacturing facility for rDNA products, As product is also of rDNA origin, which is evident from the provided certificate of analysis and other documents, thus Registration Bard approved Gluwell- Base 3ml Cartridge (Insulin Glargine 100IU). Insulin glargine will be imported in crystalline form from M/s Biocon India and will be formulated locally at M/s Hilton Pharma Karachi.

But later on the Registration Board in its 270th meeting advise the division of Biological drugs to come up with working paper in the next meeting. The final guidelines regulatory requirements of Biological drugs using rDNA technology was approved in 278th meeting of Registration Board and it was mentioned in the Guidelines that "***For the already registered drugs for local manufacturing the current guidelines shall apply".***

And the firm was advised to submit Biosmilarity data in light of decision of 278th meeting of Registration Board. The data submitted by the firm was taken up in 296th meeting of Registration board wherein the Board deferred by deciding as under;

Registration Board referred the case to Committee on Biological Drugs constituted in 273rd
meeting of Registration Board for its recommendations on the requirements of toxicity studies and abnormal toxicity studies. Moreover, Registration Board nominated Lt. Gen. (R) Prof. Dr. Karamat Ahmed Karamat (HI-M, SI-M) as Chairman of said committee. However, following documents need to be submitted by the firm:

i. Legalized GMP certificate of drug substance manufacturer abroad.
ii. Legalized free sale certificate/CoPP either from country of origin or by any reference regulatory authority as evidence that the final product has been manufactured by same concentrate/ready to fill bulk.
iii. Data of sterility test performed locally on finished drug.
iv. An agreement with the source (of bulk concentrate/ready to fill) that if there shall be any critical change in manufacturing process, biological systems used to manufacture, etc. the firm shall inform DRAP immediately along with relevant documents.

The detail of the product as under;

Name of Manufacturer	M/s Hilton Pharma (Pvt.) Ltd. 13, sector 15, Korangi Industrial Area, Karachi.
Manufacturing site of Bulk.	M/s Biocon Biologics Limited, Block No. M1, M2 and M6, Q1 (QC3 and QC10) & W3, 20th km Hosur Road, Electronics City, Bengaluru, 560100, India
Brand Name +Dosage Form + Strength	Gluwell-Base 3ml Cartridge Insulin glargine (100IU/ml)
Composition	Each ml cartridge contains: Insulin glargine ……100IU
Finished product specifications	USP Specification
Pharmacological Group	Therapeutic Protein
Shelf life	2 years when stored at 2-8 ^{O}C
Products already registered in Pakistan	Lantus by Sanofi

Type of Form Dy No & Date of application, Fee submitted	Form-5, Dy No & Date of initial Application. Dy No.2924/2016(R&I) dated 27-06-2016, Dy No.4814(R&I) dated 21-02-2022, Dy No.5672(R&I) dated 01-03-2022, Dy No.19367(R&I) dated 01-07-2022, Dy No.22963(R&I) dated 15-08-2022 Rs. 20,000 dated 27-06-2016
Demanded Price / Pack size	Price: As per DPC 3ml Cartridge Pack of 1's ,3's & 5's

The *Committee on Biological Drugs* revised the Biosmilarity guidelines which was approved in 297th meeting of Registration board. And the firm submitted data as per above mentioned decision of the Board which was evaluated tabulated below;

Documents required as per 278th RB decision for Biological Drugs (Concentrated Form/Ready to fill Form)	**Documents submitted by firm**
The firms shall provide legalized GMP certificate (issued by relevant regulatory authority) of biological drug substance manufacturer abroad (who will provide concentrate / ready to fill bulk of biological drug to Pakistani manufacturers for further processing) as an evidence that the manufacturer is an authorized manufacturer of biological drug in the country of origin. Submission of valid GMP is exempted, if valid GMP status is evident from official website of regulatory authority of country of origin.	The firm has submitted legalized copy of GMP issued by Drug Control Department, Govt of Karnataka. The same site also indicated on Eudra GMP for Active Substance (Drug substance) of INSULIN GLARGINE along with others APIs.
The firms shall provide legalized free sale certificate/CoPP either from country of origin or by any reference regulatory authority (or its website) as adopted by Registration Board of finished product as evidence that the final product has been manufactured by same concentrate/ready to fill bulk.	The firm has submitted that the bulk manufacturing site of the firm is "*Block No. M1, M2 and M6, Q1 (QC3 and QC10) & W3, 20th km Hosur Road, Electronics City, Bengaluru*" while finished products are manufactured from the same bulk on other site of the company i.e. "*M/s Biocon Biologics Limited, Block B1,B2,B3,B4 Q13 of Q1 And W20, & Unit S18, 1st Floor, Block B4, Special Economic Zone, Plot No 2,3,4 And 5 Phase IV Bommasandra Jigani Link Road, Bengaluru, 560099, India*." Instead of Free Sale Certificate of finish product manufactured from the same bulk the firm has submitted DML. The firm has submitted legalized copy of Drug Manufacturing License (DML) of the M/s Biocon Biologics Limited India with list of products attached wherein Insulin Glargine 3ml,5ml,10ml vials, 3ml Cartridge & 3ml Prefilled Pen are mentioned in permitted to manufacture for domestic purpose & in the same list the export purpose only list is separately mentioned.
The firm shall provide the complete Bio-similarity studies of the finished product of same source (bulk	Provided & Evaluated below

concentrate or ready to fill) manufactured either from country of origin or by any reference regulatory authority as adopted by Registration Board to demonstrate the biosimilarity. However, it will not be required if the finished drug product was approved before implementation of biosimilarity in the said country and finished drug product is still freely available and the firm shall provide the safety, efficacy data of finished drug product as per applicable regulatory requirements at that time.	
The firm shall provide the lot release certificate of the finished product manufactured by same bulk concentrate/ ready to fill from country of export (If applicable).	The firm informed that no Lot release certificate is required for such types of product in India. (The letter is from the importer side)
The firm shall provide the 6 months accelerated and real time stability studies for drug substance & drug product manufactured locally.	Provided
The local manufacturer shall manufacture three trial batches (quantity sufficient to meet the complete testing up to the assigned shelf life both for real time and accelerated stability studies) of the finished biological product to finalize the formulation and then perform tests as per following order: i. Latest Pharmacopoeia ii. Innovator Product iii. Reference Biotherapeutic Product iv. In case aforementioned tests are not available then tests as adopted by drug substance manufacturer shall be followed.	Provided results for the following tests: Appearance, Identification, PH, Product related substances and impurities, Limit of High Molecular weight proteins, m-cresol Content, Assay (Insulin Glargin), Zinc determination, Bacterial Endotoxin test & sterility test. Test result of Abnormal toxicity study conducted from HEJ Research institute is also submitted.
The manufacturer shall perform all tests locally as mentioned on Certificate of analysis of finished product of drug substance supplier in case of non-pharmacopoeial product.	Submitted as mentioned above
The firm shall also provide the list of finished products being manufactured from same bulk concentrate or ready to fill form in any country of the world (if available).	Provided
The firm shall provide the agreement with the source (of bulk concentrate/ready to fill) that if there shall be any critical change in manufacturing process, biological systems used to manufacture, etc. the firm shall inform DRAP immediately along with relevant documents.	Submitted.
Regular monitoring through pharmacovigilance reporting system shall be observed through proper pharmacovigilance cell of the manufacturer and report will be forwarded to the National Pharmacovigilance Centre, Division of Pharmacy Services and Biological Division of DRAP. In case of any severe adverse event, immediate mandatory reporting procedure shall be followed.	The firm has provided SOP for Pharmacovigilance Surveillance. The firm has also provided Commitment on its letter head mentioning the said statement.
The firm shall inform DRAP if there shall be any adverse event or ADR reporting from the country of	Commitment provided on the letter head

manufacture of concentrate/ready to fill bulk and finished product as required vide Rules 30 of Drug (LR&A) Rule.	
If any of the conditions is not fulfilled or public health risk reported at any stage, the drug registration shall stand cancelled with immediate effect.	Commitment provided on the letter head
All the provisions as contained in the Drugs Act, 1976 and rules made there under including provisions of Lot Release certification from National Control Laboratory for Biologicals shall be strictly adhered to.	Commitment provided on the letter head
For the already registered drugs for local manufacturing, the current guidelines shall apply at the time of renewal of product.	

Bio-similarity studies of the finished product of same source (bulk concentrate or ready to fill) manufactured from country of origin.	
WHO Bio-similarity guidelines	**Data submitted by the firm**
Quality Comparison Physicochemical characterization	**d)** Protein Content at UV 280 (by RP-HPLC method) **e) Primary Structure:** v. Intact Mass determination by Liquid Chromatography-mass spectrometry (LC-MS) i. Molecular Mass (Reduced mass) determination by LC-MS i. Peptide Mapping (Reduced) by LC-MS i. Peptide sequencing by Liquid Chromatography with tandem mass spectrometry (LC-MS-MS) **f) Secondary Structure & high order Structure** vi. Peptide mass fingerprinting under non –reducing conditions for confirmation of disulfide linkage by LC-MS vii. Disulfide linkage by 2D NMR viii. Secondary Structure by FT-IR spectroscopy ix. Circular Dichroism (Secondary Structure) by Far spectroscopy. x. Circular Dichroism (Tertiary Structure) by Near spectroscopy. xi. Determination of thermal stability by mean of Differential scanning calorimetry DSC xii. Determination of Isoelectric point (pI) by means of capillary isoelectric focusing (cIEF)
Biological Activity	Biological activity was carried out for insulin glargine injections by means of four different methods:. • Cell bases metabolic assay, • Cell bases proliferation assay (Mitogenic assay) • Insulin receptor binding assay • IGF-1 receptor binding assay. Additionally in vivo bioassay /Insulin assay (USP 121 & USP 111) : Rabbit blood sugar method
Impurities	Determination of product related substances (Glycosylated species precursor, Sequence species Deamidation/Acetylation by mean of RS method
Stability Studies	Stability studies are provided.

Non-clinical Studies	**Repeat dose toxicity study:** A comparative 90-day toxicity study with recombinant Insulin Glargine (Biocon Ltd) and Lantus (Aventis Pharma) in Wistar Rats by subcutaneous route (Study no. G4668)
Clinical Studies	Phase-I study: A Single dose, randomized, double-blind, 3- way crossover, euglycemic clamp study to measure relative PK & PD of Biocon's insulin glargine (vials) with Lantus-EURP (cartrdges) and Lantus-USRLD (disposable Pens). Clinical Pharmacology Study of FFP-112 in Healthy Male Adults by Glucose Clamp Procedure-Pharmacokinetic and Pharmacodynamic Analyses. (Comparative with Lantus) Open Label, Randomized, Multicentric Study to Establish Safety and Efficacy of Recombinant Insulin Glargine Manufactured by Biocon Ltd Compared to Lantus TM in Type 1 Diabetes Mellitus Patients. **(Total 226 evaluable patients)**
Remarks of Evaluator: Instead of Free Sale Certificate of finish product manufactured from the same bulk the firm has submitted legalized copy of DML. The firm has submitted legalized copy of Drug Manufacturing License (DML) of the M/s Biocon Biologics Limited India with list of products attached wherein Insulin Glargine 3ml,5ml,10ml vials, 3ml Cartridge & 3ml Prefilled Pen are mentioned in permitted to manufacture for domestic purpose & in the same list the export purpose only list is separately mentioned.	

Decision: Registration Board deferred the case for submission of following by the firm:

i. **Valid legalized free sale certificate/CoPP either from country of origin or by any reference regulatory authority (or its website) as adopted by Registration Board of finished product as evidence that the final product has been manufactured by same concentrate/ready to fill bulk.**
ii. **Justification of performing open label safety and efficacy study instead of double-blind study.**

2. Deferred case of M/s Huzaifa International, Sargodha deferred in 264th meeting of Registration Board.

The following veterinary vaccine was deferred in 264th meeting of Registration board;

Name of Importer	M/s Huzaifa International, Address: Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan
DSL details	Copy of DSL Address:M/s Huzaifa International, Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan. Validity : 20th November-2023 Status: License to sell drugs as Distributor
Name of Manufacturer	M/s Komipharm International Co., Ltd. Address:17, Gyeongje-Ro, Siheung-Si, Gyeonggi-Do, South Korea [Before Address System CHange: 1236-6, Chongwang-Dong, Shihung-Si, Kyonggi-Do, South Korea]
Brand Name +Dosage Form + Strength	**PRO-VAC^{TM} IBD Plus**
Composition	Each dose contains Infectious Bursal Disease Virus (K7 strain)……. Min. $10^{2.5}EID_{50}$
Finished product specifications	Ph. Eu specifications
Pharmacological Group	Poultry Vaccine
Shelf life	15 months (When stored at 2 C^o -8 C^o)

Products already registered in Pakistan	
Type of Form Dy No & Date of application, Fee submitted	Form 5-A DyNo.4914 date 05-08-2015 Rs.100,000 05-08-2015
Demanded Price / Pack size	Decontrolled/ 1000 doses vial
General documentation	***Original Legalized Free Sale Certificate (FSC):*** **Issued by:**Animal and Plant Quarantine Agency of the Ministry for Agriculture Food and Rural Affairs of the Republic of Korea **Issued on:** 30-09-2014 **valid upto** 30-09-2019 ***Original Legalized GMP Certificate:*** • **Issued by:** As mentioned above **Issued on:**19-06-2018.

The case was deferred in 264th meeting of Registration Board & the board decided as under;

Deferred for evaluation by Dr. Qurban Ali, Member Registration Board.

Now the expert opinion of Dr. Qurban Ali, member Registration Board has been received on **17-08-2022** to the Director Biological Drugs via email which is reproduced as under;

Infectious bursal disease (IBD), also known as Gumboro disease is a highly contagious, immunosuppressive disease of young chickens and is responsible for major economic losses in the poultry industry worldwide. IBD virus (IBDV) is a double-stranded RNA virus, having two serotypes (1 and 2) with only serotype 1 causing the disease in young chickens. The virus infects the bursa of Fabricius causing immunosuppression that enhances the susceptibility of chicken to other infections and interferes with vaccination against other diseases.

The IBDV is highly resistant virus and tends to persist in the farm environment despite strict hygiene measures. Therefore immunization is considered the most important measure to control IBD; where protective immunity in birds depends on inducement of both humoral and cell-mediated immune responses; however, rampant usage of live vaccines worldwide has resulted in the evolution of new strains antigenic variants and very virulent strains (vvIBDV) resulting into significant losses and high mortality in chicken, and virus continuously evolving in the field with changes in antigenicity and virulence necessitating the development and use of newer vaccines with improved efficacy.

Most commercially available conventional live IBDV vaccines are based on classical virulent strains. Those classified as mild, intermediate and ''intermediate plus (or hot) vaccines. IBD-K7 was isolated in 2007 from Seonghwan, Chungnam, Korea, which was later fully characterized, sequenced, patented and deposited in 2013 with the accession number KCTC 12376BP to the Gene Bank of Korea Biotechnology Institute (Yeoseong-gu, Daejeon, Korea) as an international depositing institution. The virus was taken as vaccine candidate and translated into live intermediate IBD Vaccine fulfilling all requirements of production and testing. Studies found IBD K7 as a novel recombinant virus compared to existing viruses with some of the virogenic viral antigen properties, besides showing better immunogenicity than the mid-dose vaccine D-78 and no significant difference from the mid-dose plus vaccine of Winterfield strain. The product is lyophilized, dispensed with adjuvant, stabilizers, preservatives and diluent for use. The product can be administered as injection (i/m or s/c) or use in drinking water/ spray vaccination from at day one; where virus strain used has low virulence and higher immunogenicity than intermediate IBD vaccines.

*From afore going, vaccine **from IBD K7 strain is recommended for registration** to enhance repertoire of veterinarians for control of a difficult disease of IBD.*

Remarks of Evaluator: Free Sale certificate is expired on 30-09-2019 which was valid at the time of submission.

Decision: Registration Board referred the case to Animal Husbandry Commissioner for comments regarding immunological relevance and need of applied strain in Pakistan.

3. Deferred case of M/s Huzaifa International, Sargodha deferred in 316th meeting of Registration Board.

The following veterinary vaccine was deferred in 316th meeting of Registration board;

Name of Importer	M/s Huzaifa International, Address: Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan
DSL details	Copy of DSL Address:M/s Huzaifa International, Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan. Validity : 20th November-2019 Status: License to sell drugs as Distributor
Name of Manufacturer	M/s Komipharm International Co., Ltd. Address:17, Gyeongje-Ro, Siheung-Si, Gyeonggi-Do, South Korea [Before Address System Change: 1236-6, Chongwang-Dong, Shihung-Si, Kyonggi-Do, South Korea]
Brand Name +Dosage Form + Strength	**Pro-VacChek ND** (Lyophilized Newcastle Disease Virus Live Vaccine)
Composition	Active Ingredient (s) and Amount (s) per unit dose: Newcastle Disease Virus (Ulster 2C strain) $\geq 10^{5.0} EID_{50}$ **Excipient:** LPGG ……40% **Composition of LPGG:** Lactose……74.62g Monopotasium phosphate ……..0.53g Dipotasium phosphate……1.25g Monopotasium L-glutamate……0.83g Gelatin…….10g Distilled water……..1000mL
Finished product specifications	Ph. Eu specifications
Pharmacological Group	Poultry Vaccine
Shelf life	24 months (When stored at 2-8 C° at the Dark place)
International availability	Not Provided.
Products already registered in Pakistan	The strain Ulster 2C is available by Lachman which is inactivated virus vaccine as per our record while applied vaccine is Live virus vaccine.
Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 27460(R&I) Dated 9th August 2018 Rs. 100,000/- 2nd August, 2018
Demanded Price / Pack size	Decontrolled/ 1000 doses
General documentation	***Original Legalized Free Sale Certificate (FSC):*** **Issued by:**Animal and Plant Quarantine Agency of the Ministry for Agriculture Food and Rural Affairs of the Republic of Korea

	• **Issued on:** 12-01-2018 ***Original Legalized GMP Certificate:*** • **Issued by:** As mentioned above **Issued on:**19-06-2018.

The case was deferred in 316th meeting of Registration Board & the board decided as under;

Registration Board deferred the case for expert opinion of Dr. Qurban Ali, member Registration Board regarding the need of product (Live Newcastle Disease vaccine) and for submission of evidence of availability of formulation in RRAs by the firm.

Now the expert opinion of Dr. Qurban Ali, member Registration Board has been received on **17-08-2022** to the Director Biological Drugs via email which is reproduced as under:

Newcastle Disease (ND) is an important disease of poultry causing devastating losses with disease control presenting significant challenge to poultry industry worldwide. One of the hallmarks for ND-prevention was the discovery of lentogenic NDV viruses in America. The subsequent development of the vaccine-strains namely La Sota and B1 with derivatives like e.g. clone30 thereafter became the basis for the majority of ND vaccines. Efforts for ND prophylaxis should normally therefore aim at active immunization using combinations of live and killed lentogenic virus based vaccines. The virus strains most commonly used in vaccines are La Sota, and B1 strains as well as viruses from the asymptomatic enteric patho-types which are usually based on the V4, VG-GA or Ulster 2C viruses. These viruses are selected by manufacturers in order to improve vaccine immunogenicity while reducing the vaccine reactions. Ulster 2C strain is known to stimulate immunity in the intestinal loop rather than in the respiratory tract and does not give abnormal side effects to the vaccinated chicks. ***The product based on Ulster 2C strain is therefore recommended for registration to enable users for availability of variety of safer vaccines for their ND control plan****; which otherwise remain a national challenge for food security in the country.*

The firm also submitted evidence of ***availability of formulation in RRAs*** is product Poulvac NDW (Live Newcastle Disease Virus, strain Ulster 2C) by Zoetis UK Limited approved in Veterinary Medicines Directorate UK and same was confirmed from below mentioned link.

Veterinary Medicines Directorate

Decision: Keeping in view the legalized GMP, legalized FSC indicating product availability in country of origin, recommendation of veterinary expert and availability of formulation in UK; Registration Board approved the product subject to compliance of current Import Policy for finished drugs.

4. Request of M/s ICI Pakistan Limited, Karachi for issuing Registration letter with innovator's Specification for the below mentioned Pharmacopeial product.

The following veterinary product of M/s ICI Pakistan Limited, Karachi was approved in 282nd meeting of Registration Board as per following detail.;

Name of Manufacturer	**Brand Name & Composition**	**Documents details**	**Decision of 282nd Meeting of RB**
M/s Intervet Inc. 411 West Delaware Avenue Millsboro, Delaware 19966 USA.	**Fortegra Vaccine** (Coccidiosis Vaccine Live Oocysts) The amount of antigenic material per dose in the final	Certificate of License and Inspection; Certificate no. 1800442	Keeping in view latest valid legalized CoPP and approval of USFDA (Reference Regulatory

	container:- Minimum of sporulatedoocysts throughout dating: *Eimeriaacervulina*……..600 *Eimeria maxima*……. 200 *Eimeria maxima* MFP… 100 *Eimeriamivati*…….. 400 *Eimeriatenella*…… 200	(P. 227-229/Corr.) **Shelf life** 12 Months (2-7^{0}C) **Pack size** 10x1,000Vial	Authority); Registration Board approved the product as per current Import Policy for Finished Drugs.

It is submitted that M/s ICI Limited submitted a letter in which they informed that the product Fortegra is a live vaccine against coccidiosis in chickens for which a Ph. Eur. monograph exist and because this product was developed in US and not sold in EU it is not developed/tested according to this European monograph stated from principal. As the product is not included in respective country's Pharmacopoeia therefore, we request the issuance of registration letter by mentioning "innovator specification"

As per above decisions of the Board that innovator specification can only be given if the product is not included in any of the official Pharmacopoeia. Therefore, the request of the firm for issuance of registration letter by mentioning "innovator specification" was not entertained and same was communicated to the firm.

In response the firm has submitted clarification letter wherein the firm narrated that they are providing clarification letter provided by the manufacturer wherein the manufacturer has informed that Coccidiosis live vaccine is described in the European Pharmacopoeia (monograph 2326). However Fortegra (Coccidiosis vaccine) is developed in US and according to US guidelines. The product is not registered in Europe and therefore won't comply in all aspect with the Ph. Eur. monograph. The firm has submitted the following documents.

- Statement from Manufacturer
- Specification comparison of manufacturer's specs with Ph. Eur. monograph

The comparison is reproduced as under.

Final Product Control Tests according to Coccidiosis Monograph 2326	**Requirement according to Coccidiosis monograph 2326**	**Fortegra as approved by the USDA**	**Remarks**
Identification (confirmation of Eimeria species)	Microscope/ potency test	See Part II.D.2 code 112	For Fortegra the identity is performed on each antigen batch and during lesion scoring in the potency test identification of the species is also confirmed
Sterility test/campylobacter	Ph. Eur. 0062/2.6.1 including campylobacter selective medium	9CFR 113.27[1](e)	In addition, each antigen is treated with beta-propiolactone
Mycoplasma test	Ph. Eur. 2.6.7	Not tested	Antigens treated with beta-propiolactone

Extraneous agents testing	Ph. Eur. 2.6.25 (section 1 to 6)	Method as described in part 2.E.1 of the dossier. Salmonella 9CFR 113.30, see part II.D.2 code 108	Antigens treated with beta-propiolactone
Sporulatedoccysts count (to ensure correct formulation)	Not less than minimum on the label and not more than maximum on the label	See Part II.D. code 109	For Fortegra the number of occysts is determined on each antigen batch to formulate the vaccine correctly. The potency test ensures that the final vaccine is correctly formulated.
Potency test	Immunogenicity test described in 2326 (including Johnson and Reid Lesions scoring)	Method as described in part 2.E.1 code 208 of the dossier (Johnson and Reid Lesions scoring)	Lesion scoring system on a scale of 0-4 from Johnson and Reid is used to justify the lesion score claim in the SPC.*
		Safety test described in part 2.E.1 code 207 of the dossier	Safety test is not required according to Ph. Eur.

The case was deferred in 393rd meeting of Registration Board & the Board decided as under;

Registration Board deferred the case for further clarification by the firm as the European Pharmacopoeia specifications are stricter than that of manufacturer's specifications.

Now the firm has submitted veterinary Drugs is a separate class under the Drugs (Specifications) Rules,1978. The firm requested to issue registration letter of Fortegra Coccivac-D2 with innovator's specifications may be issued as a similar case of ICI's product Coccivac D2 was discussed and approved in 316th meeting of the Registration Board.

Decision: Registration Board deliberated that the product is manufactured in USA and is not exported to Europe, hence, manufacturer is not following Ph. Eur. Specifications. Registration Board approved the above "Innovator Specifications" for the product.

5. Locally Manufactured Veterinary Vaccines applied by M/s Grand Pharma Pvt Ltd, Lahore and deferred in 316th meeting of Reg. Board.

Following products of M/s Grand Pharma Pvt Ltd, Lahore was deferred in 316th meeting of RB as per following details;

1.	**Name and address of product manufacturer (Applicant)**	**M/s Grand Pharma Pvt Ltd** Plot # 5-A, Street No.N-5, RCCI Estate, Rawat, Islamabad
	Brand Name +Dosage Form + Strength	Vaxi-drop 1000ml
	Type of Form, Diary No. Date of R& I & fee	Form-5 Dy. No.20999 Date:21-8-2020 Rs. 20,000/- Date: 19-8-2020
	Composition	Each ml contains: Monobasic Potassium Phosphate : 0.37 mg Disodium Phosphate Dihydrate : 0.72 mg

		Sodium Chloride : 7.65mg
	Pharmacological Group	Diluent for live avian vaccines
	Finished Product Specification	Manufacturer' Spec
	Shelf Life	2 Years (15^0C -25^0C)
	Document Details	All the undertaking has been submitted by the firm. Copy of DML Copy of inspection report for GMP for viral vaccines section (killed) & Bacterial killed vaccine section.
	Pack size & Demanded Price	0.30ml per bird **Decontrolled**
	Products already registered in Pakistan	*MS Bac* (M/s Hi-Tech Pharma, Lahore.0
	Remarks of Evaluator	

Reg. Board in its 313th meeting decided as under;
"Registration Board deferred the product for submission/ confirmation of following:
i. Method of administration of vaccine
ii. Container Closure System of diluent."

It is submitted that the firm has submitted in their reply that diluent under consideration an additional packaging (in 1000 ml) of their already registered product (diluent in 36 ml packing) vide Registration # 087070 dated 28-05-2018. And the VAXI-DROP is used to dilute live avian vaccines through spray or Eye drop. *Container Closure System of diluent* is "Autoclavable plastic bottles having rubber caps with aluminum seals"

The case was taken up in 316th meeting of Registration Board & the Board deicded as under:

*Registration Board deferred for confirmation of manufacturing facility for the above diluent (pharmaceutical**)***

The firm has submitted reply that the product Vaxidrop has already been registered vide Reg No. 078070 in 36ml packing with DRAP which has been manufactured in killed Bacterial vaccine section & in the instant case 1000ml packing has been applied for registration which will also be manufactured in the same section where a filling line bottles already exist.
The firm has submitted copy of Renewal of DML issued on 29-09-2021 wherein following sections are mentioned.
1.Oral Liquid section (Vet) 2. Viral vaccine Section (Live) 3. Viral Vaccine Section (Killed) 4. **Bacterial killed vaccine section** 5. Bolus Section (General) (Veterinary) 6. Oral Powder Section (General) (Veterinary) 7. Oral Liquid Section (General)(Veterinary) 8. Oral Powder Section (Penicillin)(Veterinary) 9. Dry Powder Injection Section vials (Penicillin)(Veterinary) 10. Liquid Injection Section vials (Penicillin)(Veterinary)
Decision: Registration Board deferred the case for confirmation of International practices regarding the manufacturing section requirement for manufacturing of vaccine diluent.

6. Imported Veterinary Biological deferred in 312th meeting of RB applied by M/s Hipra Pakistan (Private) Limited, Karachi.

Name of Importer & Address	**M/s Hipra Pakistan (Private) Limited,** 3rd floor, plot no 8, block CCA, Phase 6-C, DHA, Lahore **Go down** 2nd Warehouse on Left side, Street no 5, Gajjumata Nadir Chowk, Hazara Chowk, Industrial Area Ferozpur Road, Distt Lahore
DSL Details	License to sell drug as distributor No. 0011000 0004579 valid till

	19-Feb-2022
Name of Manufacturer & Address	Laboratorios HIPRA, S.A, Avda. La Selva, 13517170 Amer (Girona) Spain
Brand Name/Dosage Form	**Avian Solvent** 1000 ml dose
Composition	Each 0.03ml dose contains: Disodium phosphate dodecahydrate.....0.087mg Potassium dihydrogen phosphate.....00006mg Sodium chloride.....0.24mg Potassium chloride.....0.006mg Patent blue (E-131).....0.003mg Water for injection.....0.03ml q.s.ad.
Finished Product Specifications	Innovator's Specifications
Pharmacological Group	Solvent for avian vaccines (to be use: Ocular-nasal,oral or spray)
Shelf Life & Storage	60 Months (Below 25^{o} C)
International Availability	Spain
Products already Registered in Pakistan	
Type of Form, Dy. No & Date of Application Fee Submitted	Form – 5A Dy. No 7602 Dated 23-03-2021 Rs. 100,000.00 dated 23-03-2021
Demanded Price&Pack Size	Decontrolled 1000 dose (30ml) Vial
General Documentation	No Separate Free Sale Certificate has been provided rather the firm has provided certificates of five different live viral vaccines (Freely authorized to sale in country of origin) wherein the diluent has been mentioned & Freely available in the
Remarks:	The firm has not submitted separate CoPP or FSC for diluent and applied for separate registration.

The firm din't submit separate CoPP or FSC for diluent and applied for separate registration & board in 312th meeting deferred the case for submission of valid legalized CoPP. The decision is reproduced as under:

> ***Registration Board deferred the product for submission of valid legalized CoPP of the product.***

In response the firm has submitted that "The CoPP clearly explains that the product is registered with the vaccine as **there is no such procedure to register solvent separately in the country of origin** and its solvent is a registered product." The firm also submitted that there is demand of the solvent here in Pakistan the complete statement of the firm is reproduced as under;

"AVIAN SOLVENT is used with live vaccines. The administration routes of live vaccines are Spray, Eye drop, mouth drop, and drinking water. The solvent is required for Eye dropping and mouth drop routes. Many breeder and layer farmers use the Eye drop or Mouth drop route to administer live vaccines, for which a solvent is required in which the vaccine is mixed and then administered to the birds, as the vaccine is in the freeze-dried tablet form. Almost 100 % of the breeder and layer farmers need solvents for the administration of some live vaccines and some broiler farmers prefer to use the eye drop method.

As the demand for the solvent is higher in the market and we cannot import a larger amount of solvent which affects our business."

Decision: Keeping in view the non-availability of diluent as separate product in country of origin; Registration Board did not accede to the request of the firm.

Cases of AD-III (Haleema Shareef)

A: Imported Veterinary Biologicals from Reference Countries.

1.	**Name and address of Importer**	**M/s Saadat International, 117 Habitat Flat Shadman II, Jail Road, Lahore.**
	Detail of DSL	**M/s Saadat International** Address: 117 Habitat Flat Shadman II, Jail Road, District Lahore Valid till: 12-Jun-2022
	Name and address of Manufacturer	**Marketing Authorization Holder:** M/s Boehringer Ingelheim Vetmedica GmbH Binger Strabe 173, 55216 Ingelheim am Rhein, Germany. **Manufacturer of Drug:** M/s Boehringer Ingelheim Animal Health USA Inc. 2621 North Belt hwy, Saint Joseph, MO 64506- USA.
	Name of exporting country	United States of America
	Brand Name +Dosage Form + Strength	**BOVELA**
	Diary No. Date of R& I & fee	Dy. No. 1315 R&I Dated 14-01-2022 Rs. 150,000/- (Slip No. 14457036611)
	Composition	**Lyophilizate for suspension for chicken** Each dose (2ml) of lyophilizate vaccine contains: Modified live BVDV*-1 non cytopathic parent strain KE-9….≥ $10^{4.0}$ $TCID_{50}$ ** Modified live BVDV*-2 non cytopathic parent strain NY-93….≥ $10^{4.0}$ $TCID_{50}$ ** *Bovine viral diarrhea virus **Tissue culture infective dose 50% **Diluent part:** Each one dose of 2ml contains: Sodium chloride …16mg Potassium Chloride…0.4mg Potassium dihydrogen phosphate…2.3mg Disodium hydrogen phosphate… 2.3mg Water for Injection q.s. … 2ml
	Pharmacological Group	Immunological
	Type of Form	Form-5A
	Finished Product Specification	Manufacturer's Specifications
	Shelf Life	24months----(2-8^{o}C)
	Document Details	Original Legalized Certificate of Pharmaceutical product (No. 06/21/16177) is submitted by the firm. Original Legalized letter of authorization is submitted by the firm.
	Pack size & Price	2000doses: Decontrolled
	Reference Regulatory Authority Availability	N/A

	Products already registered in Pakistan	Could not be confirmed
	Remarks of Evaluator	For valid copy of DSL firm has submitted application for renewal of DSL. Evidence of already registered product in Pakistan with these strains is required.
Decision: Registration Board referred the case to Expert Working Group on Veterinary Drugs for their comments regarding immunological relevance and need of applied strain in Pakistan. Registration Board advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board and for the current cases the Board advised to forward such cases to Expert Working Group on Veterinary Drugs without waiting for registration board meeting minutes.		
2.	**Name and address of Importer**	**M/s Saadat International, 117 Habitat Flat Shadman II, Jail Road, Lahore.**
	Detail of DSL	**M/s Saadat International** Address: 117 Habitat Flat Shadman II, Jail Road, District Lahore Valid till: 12-Jun-2022
	Name and address of Manufacturer	**Marketing Authorization Holder:** M/s Boehringer Ingelheim Vetmedica GmbH Binger Strabe 173, 55216 Ingelheim am Rhein, Germany. **Manufacturer of Drug:** M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France
	Name of exporting country	France
	Brand Name +Dosage Form + Strength	**Gallivac IBD S706 NEO**
	Diary No. Date of R& I & fee	Dy. No. 20796 R&I Dated 30-07-2021 Rs. 75000/- (Slip No. 0430941720)
	Composition	Each dose of vaccine contains: Live attenuated avian infectious bursal disease virus, strain S706≥ $4\log_{10}$ $CCID_{50}$ -5.3log10 $CCID_{50.}$ Dosage Form: Effervescent tablet
	Pharmacological Group	Immunological
	Type of Form	Form-5A
	Finished Product Specification	In- house
	Shelf Life	24months----(2-8^{o}C)
	Document Details	**<u>Free Sale Certificate (Original Legalized):</u>** Confirms that said product is on free sale in country of origin i.e. France. **Manufacturer:** M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France. **Issued by:** Agence nationale du medicament veterinaire (anses) France. **Dated:**03-06-2020 **<u>GMP Certificate (Original Legalized):</u>** **Issued to:** M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France **Issued by:** (anses)ANMV France

		Validity: 3years from the date of inspection i.e. conducted on 17-02-2020, 20-02-2020. **<u>Sole Agency Agreement:</u>** Original sole agency agreement is submitted by the firm.
	Pack size & Price	2000doses: Decontrolled
	Reference Regulatory Authority Availability	Product is on free sale in country of origin i.e. France
	Products already registered in Pakistan	N/A (New formulation)
	Remarks of Evaluator	**a. Firm has Submitted field efficacy studies for BUR 706 but not of Gallivac IBD S706 NEO with following justification:** *<u>Efficacy of Gallivac IBD S706 NEO can be established based on data from field efficacy studies performed with 706 vaccine as the only difference between the composition of two vaccines is the addition of a colorant and tableting excipients for the effervescent tablet.</u>* b. For valid copy of DSL firm has submitted application for renewal of DSL.
Decision: Registration Board referred the case to Expert Working Group on Veterinary Drugs for their comments regarding immunological relevance and need of applied strain in Pakistan. Registration Board further advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board.		
3.	**Name and address of Importer**	**M/s Saadat International** 117 Habitat Flat Shadman II, Jail Road, Lahore
	Detail of DSL	**M/s Saadat International** Address: 117 Habitat Flat Shadman II, Jail Road, District Lahore Valid till: 12-Jun-2022
	Name and address of Manufacturer	**Marketing Authorization Holder:** M/s Boehringer Ingelheim Vetmedica GmbH Binger Strabe 173, 55216 Ingelheim am Rhein, Germany. **Manufacturer of Drug:** M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France
	Name of exporting country	France
	Brand Name +Dosage Form + Strength	**Gallivac IBD S706 NEO**
	Diary No. Date of R& I & fee	Dy. No. 31673R&I Dated 17-11-2021 Rs. 75,000/- (Slip No. 2322179827)
	Composition	Each dose contains: Live attenuated infectious bursal disease virus, S706 strain … 4log10-5.3log10 $CCID_{50.}$ * Cell Culture Infectious Dose 50% Dosage Form: Effervescent tablet
	Pharmacological Group	Immunological, Q101AD09
	Type of Form	Form-5A
	Finished Product Specification	Manufacturer's specifications
	Shelf Life	24months (2-8^{o}C)
	Document Details	**Original legalized FSC** is submitted by the firm.

		Original Legalized Sole Agency Agreement is submitted by the firm. **GMP Certificate (Original Legalized)** attached with 2000 doses application**:** **Issued to:** M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France **Issued by:** (anses)ANMV France **Validity:** 3years from the date of inspection i.e. conducted on 17-02-2020, 20-02-2020.
	Pack size	5000 doses.
	Reference Regulatory Authority Availability	Product is on free sale in country of origin i.e. France
	Products already registered in Pakistan	N/A (New formulation)
	Remarks of Evaluator	**a. Firm has Submitted field efficacy studies for BUR 706 but not of Gallivac IBD S706 NEO with following justification:** *Efficacy of Gallivac IBD S706 NEO can be established based on data from field efficacy studies performed with 706 vaccine as the only difference between the composition of two vaccines is the addition of a colorant and tableting excipients for the effervescent tablet.* b. For valid copy of DSL firm has submitted application for renewal of DSL.
Decision: Registration Board referred the case to Expert Working Group on Veterinary Drugs for their comments regarding immunological relevance and need of applied strain in Pakistan. Registration Board further advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board.		

B; Imported Veterinary Biologicals from Non-Reference Countries:

1.	**Name and address of Importer**	**M/s. QAS International, GT Road, Gujranwala**
	Detail of DSL	M/s.QAS International, Address: Opposite Marian Hotel Near Grace Marque Subhan Ceramics Main GT Road, Gujranwala Valid till: 24-Nov-2022.
	Name and address of Manufacturer	**Manufacturer:** M/s. Veterinarski zavod SUBOTICA doo Adress: Beogradski put 123, 24000 Subotica, Serbia
	Name of exporting country	Republic of Serbia
	Brand Name +Dosage Form + Strength	Poliovin
	Diary No. Date of R& I & fee	Dy. No.29406 R&I Dated 28-10-2021 Rs. 150,000/- (Slip No 964611009823)
	Composition	Each dose contains: *Cl perfringens* type A and alpha toxoid….. anti-alpha 2.5 IU *Cl perfringens* type C and beta toxoid….. anti-beta 2.5 IU *Cl perfringens* type D and beta toxoid….. anti-epsilon 5 IU *Cl novyi* type B, …. Anti-novyi 3.5IU *Clostridium Septicum* and toxoid….. anti-septicum2.5 IU.

		Fusobacterium necrophorus… 40AU *Staphylococcus aureus* … 0.5AHU *Arcanobacterium pyogenes*… 80AU
	Pharmacological Group	Immunological products
	Type of Form	Form-5A
	Finished Product Specification	In house
	Shelf Life	24months----(2-8^{o}C)
	Document Details	**COPP (Original Legalized):** It confirms the free sale of product in exporting country and also GMP status of product manufacturer. **Sole Agency Agreement:** Original sole agency agreement is submitted by the firm.
	Pack size & Price	doses per Vial: Decontrolled
	Reference Regulatory Authority Availability	N/A
	Products already registered in Pakistan	Could not be confirmed with this combination

Remarks of Evaluator: product already registered in Pakistan could not be confirmed with this combination

Query	Response
Clarification regarding difference in address of manufacturer on CoPP (Veterinarski Zavod Subotica d.o.o Beogradski put 123, 24106 Subotica, Srbija) and on distribution agreement and form 5A (Beogradski put 123, 24000 Subotica, Srbija) is required.	Firm has submitted that "24106 is a special postal code of the part of town of Subotica where Veterinarski Zavod Subotica is located, while 2400 is the overall postal code of the entire town of Subotica. Using one or another is exactly the same. The important part of the address is the name of street, Beogradski put 123.
Clarification regarding difference in name of manufacturer on COPP (Veterinarski Zavod Subotica d.o.o) and on Letter of marketing authorization in country of origin (Veterinary institute Subotica JSC) is required.	Firm has submitted that Veterinary Institute Subotica is the English translation of the name of the company in Serbian language Veterinarski Zavod Subotica. The difference in suffix of the name d.o.o and JSC is due to the fact that the company changed its legal form in December 2020 from JSC-Joint stock company (in Serbian language AD) to limited, in Serbian language d.o.o. Letter of Decision change JSC (AD) to d.o.o is submitted.

Decision: Registration Board referred the case to Expert Working Group on Veterinary Drugs for their comments regarding immunological relevance and need of applied strain in Pakistan. Registration Board further advised DBE&R to take the comments of Expert Working Group on Veterinary Drugs for all the veterinary vaccines having new strains, before placing the case in Registration Board.

2.	**Name and address of Importer**	**M/s Orient traders international,** CM-10, Block A, Kazimabad, Model Colony, Karachi.
	Detail of DSL	**M/s Orient traders international** Address: CM-10 Block -A, Kazimabad, Model Colony, Karachi. Valid till: 25-07-2022
	Name and address of Manufacturer	**Manufacturer of Drug:** **/Marketing Authorization Holder:**

		Pharmagal-Bio, spol. s.r.o. Murgasova 5, 949 Nitra Slovak Republic.
	Name of exporting country	EU-Slovak Republic
	Brand Name +Dosage Form + Strength	Bronchipharm
	Diary No. Date of R& I & fee	Dy. No. 22597 R&I Dated 17-08-2021 Rs. 150,000/- (Slip No. 666902646)
	Composition	**Lyophilizate for suspension for chicken** Each dose(0.1ml) contains: Avian infectious Bronchitis Virus, Live, strain H120 10^3EID$_{50}$ - $10^{4.5}$ EID$_{50}$ *50% Embryo Infective dose
	Pharmacological Group	Veterinary Vaccine
	Type of Form	Form-5A
	Finished Product Specification	Ph. Eur Specifications
	Shelf Life	18months----(2-8^{o}C)
	Document Details	i. Original legalized CoPP (No. 3058/2021/I) confirming GMP and free sale status of product in country of origin is submitted by the firm. **ii.** Original legalized Product specific Sole Agency Agreement made on March 01, 2022 is submitted by the firm.
	Pack size & Price	2000doses per vial: Decontrolled
	Reference Regulatory Authority Availability	N/A
	Products already registered in Pakistan	Bronchipharm 1000 doses is already registered Product. Reg No. (107933)
	Remarks of Evaluator	
Decision: Keeping in view legalized CoPP indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs.		
3.	**Name and address of Importer**	**M/s. Brand Station, 89 A2, Wapda Town Extension, Lahore, Pakistan**
	Detail of DSL	Address: M/s. Brand Station 69 Wocland villas Lahore, near aiwind road, Lahore. Valid till: 10-08-2027
	Name and address of Manufacturer	**Manufacturer:** M/s. Yebio Bioengineering Co., Ltd Adress: No.260 Heyun Road Hongdao, Qingdao, China
	Name of exporting country	China
	Brand Name +Dosage Form + Strength	Yevac ND+IB Vaccine
	Diary No. Date of R& I & fee	Dy. No.30663 R&I Dated 09-11-2021 Rs. 150,000/- (Slip No 1748159755)
	Composition	Each dose contains: Newcastle disease virus strain LaSota $\geq 10^8$ EID$_{50}$ before inactivation. Infectious Bronchitis virus strain M41$\geq 10^6$EID$_{50}$ before inactivation.

	Pharmacological Group	Vaccine
	Type of Form	Form-5A
	Finished Product Specification	Manufacturer's specifications
	Shelf Life	24months----(2-8^{o}C)
	Document Details	Original legalized CoPP is submitted by the firm.
	Pack size & Price	500ml doses per Vial: Decontrolled
	Reference Regulatory Authority Availability	N/A
	Products already registered in Pakistan	Reg No. 090160 OLVAC A+B (Emulsion for Injection) Each 0.5ml dose contains: Inactivated Newcastle Disease virus ……$10^{8.5}$ EID50 Inactivated adenovirus of egg drop syndrome (EDS) (127 strain)……$10.^{7.5}$ EID_{50} Inactivated virus of infectious bronchitis (strain M41, NEV 14, NEV 24).....$3x10^{7.5}$ EID_{50}
	Remarks of Evaluator	i. Composition and virus strain is not mentioned on FSC.
Decision: **Keeping in view legalized legalized CoPP indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs and submission of valid legalized FSC indicating composition of product by the firm. The firm shall apply for change in address of importer as per new submitted DSL before issuance of registration letter.**		
4.	**Name and address of Importer**	**M/s Pharmakon International Enterprises,** Office No. 26, 2nd Floor, Aries Plaza, Murree Road, Shamsabad.
	Detail of DSL	**M/s Pharmakon International Enterprises,** Address: Valid till:
	Name and address of Manufacturer	**Manufacturer of Drug:** M/s JinyuBaoling Bio-Pharmaceutical Co., Ltd. No. 1 Jinyu street, Shaerqin Industrial park, Economic and tecnological Development zone, Hohhot, inner Mongolia, China.
	Name of exporting country	Peoples Republic of China.
	Brand Name +Dosage Form + Strength	Goat Pox Vaccine, Live
	Diary No. Date of R& I & fee	Dy. No. 25395 R&I Dated 13-09-2021 Rs. 150,000/- (Slip No. 33810920261)
	Composition	Each inoculation dose of vaccine contains: Attenuated Goat Pox Virus (Strain CVCC AV41) … $10^{3.5}$ $TCID_{50}$
	Pharmacological Group	Biological
	Type of Form	Form-5A
	Finished Product Specification	Manufacturer's Specifications
	Shelf Life	24months----(-15^{o}C)
	Document Details	**<u>Free Sale Certificate (Original Legalized):</u>** Manufacturer: M/s Jinyu Baoling Bio-Pharmaceutical Co., Ltd Issued by: Department Of Agriculture and Animal Husbandry Of Inner Mongolia Autonomous Region, P.R.China Issue date: 09/03/2020 **<u>GMP Certificate (Original Legalized):</u>** Issued to: M/s JinyuBaoling Bio-Pharmaceutical Co., Ltd.

		Issued by: Administrative unit: Department Of Agriculture And Animal Husbandry Of Inner Mongolia Autonomous Region, P.R.China Validity: 05-03-2021-04-03-2026 **Sole Agency Agreement:** Product specific Sole agency agreement dated 15th June, 2021 is submitted by the firm
	Pack size & Price	25doses per Vial: Decontrolled
	Reference Regulatory Authority Availability	N/A
	Products already registered in Pakistan	Could not be confirmed (no any registered product)
	Remarks of Evaluator	Currently there is no any registered Goat pox vaccine. Firm has submitted application for renewal of DSL.
Decision: Registration Board referred the case to Animal Husbandry Commissioner for comments regarding immunological relevance and need of applied strain in Pakistan.		

C: Miscellaneous/ Deferred Cases

1. Imported Veterinary Biological applied by M/s Forward Solution deferred in 316th meeting of Registration Board.

Name and address of Importer	**M/s. Forward Solutions, Plot No.19-B, Abdul Sattar Edhi Road, Near Qazalbash Chowk, Lahore.**
Detail of DSL	M/s. Forward Solutions Address: Plot No.19-B, Abdul Sattar Edhi Road, Near Qazalbash Chowk, Lahore. Copy of DSL No. 05-352-0066-028137D Valid till 10-Feb-2022
Name and address of Manufacturer	M/s FARTO S.P.A Italy Address: Via Emilia, 285-40064 Ozzano Emilia Bologna Italy. Email: fatro@fatro.it
Name of exporting country	Italy
Brand Name +Dosage Form + Strength	Olvac A+B (emulsion for injection)
Diary No. Date of R& I & fee	Dy. No. 29616 (R&I) Dated 07-01-2020, Rs. 100,000/- Dated 07-01-2020
Composition	Each dose of 0.5ml contains: Inactivated Newcastle Disease Virus…. $10^{8.5}EID_{50}$ Inactivated adenovirus Egg Drop Syndrome (127 strains) …$10^{7.5}EID_{50}$ Inactivated virus of infectious bronchitis (strains M14, NEV14, NEV 24)…. $3\times10^{7.5}EID_{50}$
Pharmacological Group	Biologicals
Type of Form	Form-5A
Finished Product Specification	In-House
Shelf Life	Stability studies of three batches at (2^0C-8^0C) for 24months is submitted by the firm. 24 months (2^0C-8^0C)
Document Details	**Original Legalized COPP:** Firm has submitted Certificate of Pharmaceutical Product confirming that product is in the markets of exporting country and

	plant and facilities conform to the Good manufacturing practices in force within the European community. **Composition of product from COPP:** Inactivated Newcastle Disease Virus…. $10^{8.5}EID_{50}$ Inactivated adenovirus Egg Drop Syndrome (127 strains) …$10^{7.5}EID_{50}$ Inactivated virus of infectious bronchitis (strains M14, NEV 14, NEV 24) …. $3\times10^{7.5}EID_{50}$ **Sole Agency Agreement:** Scanned copy of Sole Agency Agreement between M/s FARTO Italy and M/s. Forward Solutions.
Pack size	1000 dose Vial (500mL)
Reference Regulatory Authority Availability	N/A
Products already registered in Pakistan	Could not be confirmed with these strains
Remarks of Evaluator	i. Original or notarized sole agency agreement is required as scanned copy is submitted. ii. Composition of Inactivated infectious bronchitis virus is different on Form 5A and COPP.
Previous Decision (M-316)	Registration Board deferred the product for submission of following by the firm: i. Original or notarized sole agency agreement. ii. Clarification regarding difference of composition of Inactivated infectious bronchitis virus on Form 5A and COPP.
Evaluation by BE&R	Now the firm has submitted revised Form 5A with composition similar to that of COPP and original sole agency agreement. *Subject product is additional pack of following already registered product. OLVAC A+B(500 doses) (Emulsion for Injection) Each 0.5ml dose contains: Inactivated Newcastle Disease virus ……$10^{8.5}$ EID50 Inactivated adenovirus of egg drop syndrome (EDS) (127 strain)……$10^{7.5}$ EID50 Inactivated virus of infectious bronchitis (strain M41, NEV 14, NEV 24).....$3x10^{7.5}$ EID50
Decision: **Keeping in view legalized CoPP indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs.**	

2. Imported Veterinary Biological applied by M/s Saadat International, Lahore deferred in 316th meeting of Registration Board.

Name and address of Importer	**M/s Saadat International, 117 Habitat Flat Shadman II, Jail Road, Lahore.**
Detail of DSL	**M/s Saadat International:** Address: 117 Habitat Flat Shadman II, Jail Road, District Lahore Valid till: 12-Jun-2022
Name and address of Manufacturer	**Marketing Authorization Holder:** M/s Boehringer Ingelheim Vetmedica GmbH Binger Strabe 173, 55216 Ingelheim am Rhein, Germany.

	Manufacturer of Drug: M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France
Name of exporting country	France
Brand Name +Dosage Form + Strength	**Gallimune H9+ND**
Diary No. Date of R& I & fee	Dy. No. 19297 R&I Dated 09-07-2021 Rs. 150,000/- (Slip No. 07658493298)
Composition	Each 0.3 ml dose contains: Inactivated Avian Influenza Virus, H9N2 (iraq)strain at least7log2HI.U. Inactivated Newcastle Disease Virus, Ulster 2C strain at least 16HI.Ufr
Pharmacological Group	Vaccine
Type of Form	Form-5A
Finished Product Specification	Manufacturer's Specifications
Shelf Life	24months----(2-8^{o}C) Stability studies for 27 months at 2-8 ^{o}C
Document Details	**GMP certificate (Original Legalized):** Certificate No. 20/265668 Issued to: M/s Boehringer Ingelheim Animal Health Rue De L aviation, 69800 ST PRIEST-France (Manufacturer) Issued by: French agency for veterinary medicinal products. Validity: Three years from the date of inspection (conducted on February 17th 2020 to February 20th 2020). **Sole Agency Agreement:** **Boehringer Ingelheim Vetmedica GmbH** (the marketing authorization holder of the product), a company incorporated under the laws of Germany, with its principal office at Binger Strabe 173, 55216 Ingelheim am Rhein, Germany (BIV GmbH) herewith appoints; Saadat International 117 Habitat Flat Shadman II Jail Road Lahore our sole agent in Pakistan for Gallimune H9+ ND, the product is manufactured and supplied to Saadat International by BIV GmbH affiliated company: Boehringer Ingelheim Animal Health France. **COPP (Original Legalized):** Certificate No. 20-268470
Pack size	300ml bottle
Reference Regulatory Authority Availability	N/A
Products already registered in Pakistan	Gallimune 208 ND+Flu H9 M.E. Emelsion For Injection. [Each Dose Of Vaccine Contains: - Inactivated Avian Influenza Virus H9N2 Strain Minimum Titer Before Inactivation...108 EID50. Inactivated Newcastle Disease Virus, Ulster 2c Strain Minimum Titer Before Inactivation 1068 EID50].
Remarks of Evaluator	In response to this division's letter dated 12th January 2022 applicant has submitted following documents: Field trial data. Finished Product Specifications: Manufacturer. Following justification regarding this statement on the COPP that product is not licensed to be placed in the market of country of origin is required. "Gallimune H9+ND is not licensed to be placed in the France market because avian influenza caused by H9N2 subtype is not present in poultry farms of this country. Therefore:

	No Free certificate could be obtained for any H9 vaccine. All the H9 vaccines manufactured in France are for exportation purpose only for the countries that have the H9 as endemic disease, so the authority can only provide certificate of origin and/or Certificate of Pharmaceutical product". Following documents are still required: Finished product specifications in light of 267th RB meeting.
Previous Decision (M-316)	Registration Board deferred the product for submission of evidence of availability of formulation in reference regulatory authorities.
Evaluation by BE&R Division	*The firm has submitted that Gallimune H9+ND is not registered in reference regulatory authorities (same as all the vaccines contain H9N2 formulations) because avian influenza caused by the H9N2 subtype is not present in poultry farms of these countries.*
Decision: Registration Board deferred the product for submission of evidence of availability of formulation in country of origin or in any other reference regulatory authorities.	

3. Request for Withdrawal of diluent by M/s Better Traders International, 24-Z, Saifullah Shaheed Road, Madina Town, Faisalabad.

Following six products of M/s. Better Traders International are approved as combo pack with diluent subject to the conditions that firm shall submit valid legalized FSC indicating diluent in combo pack before issuance of registration letter.
Now the firm vide their letter dated 10-05-2022 requested for withdrawal of the diluent and issuance of registration letters without diluent for the following products approved by Board in its 313th and 316th Registration Board meeting as per following details:

Sr. No.	Name of Importer and Manufacturer	Brand name and Composition	Decision
1.	**Importer:** M/s Better Traders International, 24-Z/E, Saifullah Shaheed Road, Madina Town, Faisalabad. **Manufacturer:** M/s AVAC Vietnam Co., Ltd. Address: Highway A, Ngoc Lick, Trung Tac Province, Hung Yen City Veitnam	**AVAC IB- H120** Infectious Bronchitis Vaccine, Live Each dose contains: - Attenuated IB Virus strain H120 and stabilizers …. Not less than 10^2 EID_{50}	**Decision M-313** Keeping in view legalized GMP and FSC indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs. The firm shall submit valid legalized FSC indicating diluent in combo pack before issuance of registration letter. Chairman Registration Board is authorized for issuance of letter.
2.		**AVAC ND- Lasota** Live vaccine Each dose contains: - Newcastle Virus strain Lasota…. Not less than 10^6 EID_{50}	
3.		**AVAC GUMBORO PLUS** Newcastle Disease Vaccine. Each dose contains not less than 10^2 EID_{50} attenuated infectious Bursal Disease(IBD)Virus strain intermediate Plus and Stabilizers	
4.		**Avac ND -IB Live**	**Decision M-316**

		Live Each dose contains not less than 10^6 EID_{50} Hitchner B1 of Newcastle Disease Virus and 10^2 EID_{50} H120 strain of infectious Bronchitis Virus.	Keeping in view legalized GMP and FSC indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs. The firm shall submit valid legalized Free Sale Certificate indicating diluent in combo pack before issuance of registration letter. Chairman Registration Board is authorized for issuance of letter after submission of said FSC.
5.		**Avac ND -IB K** Inactivated. Each dose contains not less than 10^6 EID_{50} Lasota of Newcastle Disease Virus and 10^2 EID_{50} H120 strain of infectious Bronchitis Virus and oily emulsion adjuvant.	
6.		**Avac Gumboro INT** Live vaccine Each dose contains not less than 10^3 $TCID_{50}$ attenuated Infectious Bursal (IBD) Disease Virus strain W2512.	

Decision: Registration Board acceded to the request of the firm for registration of products without diluent.

4. Request for change in address of manufacturer for Product Inactivated FM D virus antigen of strains of one or more types A, O, Asia- 1 approved in 288th meeting by M/s. Orion Group, Faisalabad.

Following product of M/s. Orion Group, Faisalabad is approved in 288th Registration Board meeting as per following details:

Sr. No.	Name of Manufacturer	Brand Name & Composition	Packing, Demanded Price, Shelf Life & Specifications	Decision (M-288th):
1.	M/s Federal State Enterprise "Shchelkovo biokombinant", Biokombinant Township, Shelkovskii district, Moscow region, 141142, Russian Federation.	Each 2ml of vaccine contains: Inactivated FM D virus antigen of strains of one or more types A, O, Asia-1…….1ml Adjuvant Montanide ISA 206……..1ml	50ml (25 doses) Bottle Decontrolled 18 months (2°C – 8°C) Ph. Eur. Specs.	Keeping in view the valid legalized GMP certificate and valid legalized FSC indicating product availability in country of origin; Registration Board approved the above product subject to compliance of current Import policy for finished drugs. Registration Board advised DBER to send an email to Federal Service for Veterinary and Phytosanitary Surveillance, Russia regarding verification of authorization of All-Russian Scientific and Research Institute for Certification (JSC"VNIIS") for issuance of GMP certificate. The firm will submit

				revised valid legalized FSC with correct brand name and composition before issuance of registration letter. The same will also be verified during inspection of manufacturer abroad. Registration Board has authorized its Chairman for issuance of registration letter after said verification.

For composition The Board decided that ***the firm will submit revised valid legalized FSC with correct brand name and composition before issuance of registration letter*** and now the firm has submitted new FSC in line with decision of Board with following name and composition*:*

Composition discussed in Board	**Composition on newly submitted FSC**
The cultural monovalent and polyvalent emulsified inactivated vaccine against foot-and-mouth disease Each 2ml of vaccine contains: Inactivated FM D virus antigen of strains of one or more types A, O, Asia-1…….1ml Adjuvant Montanide ISA 206……..1ml	**Emulsified Inactivated Vaccine against Foot-and-Mouth Disease containing serotypes A, O, Asia-l** Each 2 ml of the vaccine contains: Inactivated FMD virus antigen (not less than 6PD50 for each serotype A, O, ASIA-I)…. 1 ml. adjuvant Montanide ISA 206….. 1 ml.

Now firm M/s. Orion Group, Faisalabad, has applied for exemption from inspection of manufacturer abroad (Russia) for product approved in 288th RB meeting as the manufacturer "M/s. Federal State Enterprise "Shchelkovo biokombinant, Biokombinant Township, Shelkovskii district, Moscow region, 141142, Russian Federation" is issued with Eudra GMP.
For above manufacturer when the EUDRA-GMDP website is checked for confirmation, a difference in the name and address of manufacturer abroad is observed between what is approved in 288th meeting minutes and what is present on EUDRA-GMPD website which is recorded in the table below:

In 288th meeting minutes	**In Eudra GMDP**
M/s Federal State Enterprise "Shchelkovo **biokombinant**", **Biokombinant Township, Shelkovskii district, Moscow region, 141142, Russian Federation.**	M/s. Federal State Enterprise Shchelkovo **Biocombinat** **Biocombinat, Losino-Petrovsky, 141142, Russian Federation**

For a difference in spellings of name of manufacturer firm has informed that this might happen because of translation from Russian to English language.

It is further submitted that address of manufacturer is checked from website of manufacturer and it is observed that address of the manufacturer is same to that present on EUDRA-GMDP certificate which could be perused on following web link (https://biocombinat.ru/en/contacts/).

Now the firm has applied for change in address of manufacturer and submitted following:

i. A Fee challan of Rupee 7500/- (Slip No. 4209186338).
ii. A copy of letter from manufacturer stating that M/s. Federal State Enterprise Schelkovo Biocombinat is working under the same name and in the same manufacturing facility since the year 1924. The observed difference in the address previously as BIOCOMBINAT TOWNSHIP, SHELKOVSKII DISTRICT, MOSCOW REGION 141142 and currently as BIOCOMBINAT LOSINO-PETROVSKY, 14112, RUSSIAN FEDERATION, is only as the address details has been renamed recently.

Decision:

Keeping in view GMP certificate available on official website of EUDRA; Registration Board approved the change in address of manufacturer from M/s Federal State Enterprise "Shchelkovo biokombinant", Biokombinant Township, Shelkovskii district, Moscow region, 141142, Russian Federation to M/s. Federal State Enterprise Shchelkovo Biocombinat, Biocombinat, Losino-Petrovsky, 141142, Russian Federation subject to compliance of current Import Policy for finished drugs and submission of either of following by the firm:

i. Valid legalized GMP certificate from country of origin indicating new address of manufacturer abroad.
ii. Approval of new address issued by municipal authority of country of origin indicating that only address is changed while site remains the same.

5. Imported Veterinary Biologicals applied by M/s Bromed Animal Health, Lahore deferred in 313th meeting of Registration Board.

Following products of M/s Bromed Animal Health, Lahore were deferred in 296th meeting of Registration Board as per following details:

i.	**Name of Importer**	**M/s. Bromed Animal Health 246-A, West Wood Colony, Lahore.**
	DSL details	M/s. Bromed Animal Health Address: 246-A, West Wood Colony, Lahore Valid till: 18 Oct 2022
	Name of Manufacturer	**Product License Holder:** Middle East For Veterinary Vaccine. Second Industrial Zone -Extention Part No. 21,22,24,25 El Salhya El Gdeda Elsharkya Governate, Egypt.
	Brand Name +Dosage Form + Strength	ME VAC Eli Var2
	Composition	(Live Vaccine) Each dose contains: Live attenuated Avian Infectious Bronchitis Variant 2 Virus (EG/IBV 12) $\geq 10^3$ EID_{50} Live attenuated New Castle Disease Virus (NDV2)$\geq 10^6$ EID_{50}.
	Finished product specifications	Manufacturer's Specification
	Pharmacological Group	Biologicals
	Shelf life	24 months (2^0C-8^0C)
	International availability	Egypt
	Products already registered in Pakistan	Not found in combination with applied strain
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 31086 R&I Dated 23-11-2020 Rs. 100,000/- Dated 23-11-2020

	Demanded Price / Pack size	1000 doses
	General documentation	Valid Legalized GMP Certificate dated 18-03-2019 valid till 17-03-2022. Legalized FSC issued on 26-07-2020 issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt confirms that product is on free sale in the market of Egypt. Copy of Product specific Sole agency agreement. Copy of registration license of above product for export issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt indicating demanded pack size.
	Remarks of Evaluator	
	Decision: *Registration Board deferred the product for submission of following:* *i. Source of strains used in product.* ii. *Scientific literature confirming similarity & Immunological relevance of applied strains with circulating strains of Pakistan.*	
ii.	**Name of Importer**	**M/s. Bromed Animal Health 246-A, West Wood Colony, Lahore.**
	DSL details	M/s. Bromed Animal Health Address: 246-A, West Wood Colony, Lahore Valid till: 18 Oct 2022
	Name of Manufacturer	**Product License Holder:** Middle East For Veterinary Vaccine. Second Industrial Zone -Extention Part No. 21,22,24,25 El Salhya El Gdeda Elsharkya Governate, Egypt.
	Brand Name +Dosage Form + Strength	ME VAC Eli Var2
	Composition	(Live Vaccine) Each dose contains: Live attenuated Avian Infectious Bronchitis Variant 2 Virus (EG/IBV 12) $\geq 10^3$ EID_{50} Live attenuated New Castle Disease Virus (NDV2)$\geq 10^6$ EID_{50}.
	Finished product specifications	Manufacturer's Specification
	Pharmacological Group	Biologicals
	Shelf life	24 months (2^0C-8^0C)
	International availability	Egypt
	Products already registered in Pakistan	Not found in combination with applied strain
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 31085 R&I Dated 23-11-2020 Rs. 100,000/- Dated 23-11-2020
	Demanded Price / Pack size	5000 doses
	General documentation	Valid Legalized GMP Certificate dated 18-03-2019 valid till 17-03-2022. Legalized FSC issued on 26-07-2020 issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt confirms that product is on free sale in the market of Egypt.

		Copy of Product specific Sole agency agreement. Copy of registration license of above product for export issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt indicating demanded pack size.
	Remarks of Evaluator	
	Decision: *Registration Board deferred the product for submission of following:* *i. Source of strains used in product.* ii. *Scientific literature confirming similarity & Immunological relevance of applied strains with circulating strains of Pakistan.*	
iii.	**Name of Importer**	**M/s. Bromed Animal Health 246-A, West Wood Colony, Lahore.**
	DSL details	M/s. Bromed Animal Health Address: 246-A, West Wood Colony, Lahore Valid till: 18 Oct 2022
	Name of Manufacturer	**Product License Holder:** Middle East For Veterinary Vaccine. Second Industrial Zone -Extention Part No. 21,22,24,25 El Salhya El Gdeda Elsharkya Governate, Egypt.
	Brand Name +Dosage Form + Strength	ME VAC ND 7 Plus
	Composition	(Inactivated Vaccine) Each dose contains: Inactivated vNDV Genotype VII "rgNDV1/ME-G7/2017" $\geq 10^{8.5}$ EID_{50}/dose before inactivation. Inactivated NDV LaSota strain, "NDV/chicken/Egypt/11478/11" $\geq 10^{8.5}$ EID_{50}/dose before inactivation
	Finished product specifications	Manufacturer's Specification
	Pharmacological Group	Biologicals
	Shelf life	24 months (2^0C-8^0C)
	International availability	Egypt
	Products already registered in Pakistan	Reg No. 084989 Medivac ND G7B Emulsion
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 31088 R&I Dated 23-11-2020 Rs. 100,000/- Dated 23-11-2020
	Demanded Price / Pack size	1000 doses
	General documentation	Valid Legalized GMP Certificate dated 18-03-2019 valid till 17-03-2022. Legalized FSC issued on 28-06-2020 issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt confirms that product is on free sale in the market of Egypt. Copy of Product specific Sole agency agreement. Copy of registration license of above product for export issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt indicating demanded pack size.
	Remarks of Evaluator	*Composition of submitted locally registered product is different*
	Decision: *Registration Board deferred the product for submission of following:*	

	i. Source of strains used in product. ii. *Scientific literature confirming similarity & Immunological relevance of applied strains with circulating strains of Pakistan.*	
iv.	**Name of Importer**	**M/s. Bromed Animal Health 246-A, West Wood Colony, Lahore.**
	DSL details	M/s. Bromed Animal Health Address: 246-A, West Wood Colony, Lahore Valid till: 18 Oct 2022
	Name of Manufacturer	**Product License Holder:** Middle East For Veterinary Vaccine. Second Industrial Zone -Extention Part No. 21,22,24,25 El Salhya El Gdeda Elsharkya Governate, Egypt.
	Brand Name +Dosage Form + Strength	**Mefluvac H9+ND7 0.3**
	Composition	Inactivated Bivalent Virus Vaccine Against New Castle Disease Each dose contains: Low pathogenic Avian Influenza H9N2 $\geq 10^{8.5}$ EID_{50}/dose before inactivation Recombinant Newcastle Disease Virus $\geq 10^{8.5}$ EID_{50}/dose before inactivation
	Finished product specifications	Manufacturer's Specification
	Pharmacological Group	Biologicals
	Shelf life	24 months (2^0C-8^0C)
	International availability	Egypt
	Products already registered in Pakistan	Not verifiable Firm has submitted Gallimune 208 manufactured by Boehriger Ingelheim Germany and Nobilis Influenza H9N2+ND manufactured MSD Merck USA as innovator reference.
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 13954 R&I Dated 24-05-2021 Rs. 150,000/- Dated 21-05-2021
	Demanded Price / Pack size	1000 doses
	General documentation	Valid Legalized GMP Certificate dated 18-03-2019 valid till 17-03-2022. Legalized FSC issued on 26-05-2021 issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt confirms that product is on free sale in the market of Egypt. Copy of Product specific Sole agency agreement. Copy of registration license of above product for export issued by General Organization for Veterinary service, Ministry of Agriculture and Land Reclamation Egypt indicating demanded pack size.
	Remarks of Evaluator	
	Decision: *Registration Board deferred the product for submission of following:* *i. Source of strains used in product.* ii. *Scientific literature confirming similarity & Immunological relevance of applied strains with circulating strains of Pakistan.*	

Now the firm has submitted source of strain and following response/ relevancy: -

Sr.	Product Name	Virus strain as per FSC/ CoPP	Same/ circulating strain in Pakistan	Already registered products of same strain	Manufacturer/ agent name
i.	MEVAC Eli Var 2	*NDV2* EG/IBV12	VG/GA ND60 NDV2-NDV60 E/IBV12 Pak973	Avinew MEVAC ND Elite MEVAC IBVAR2 GPVAC IB Plus	Marial/ Saadat MEVAC/ Bromed MEVAC/ Bromed Grand Pharma
ii.	MEVAC Eli Var2	*NDV2* EG/IBV12	VG/GA ND60 NDV2-NDV60 EG/IBV12 Pak973	Avinew MEVAC ND Elite MEVAC IB Var2 GPVAC IB Plus	Marial/ Saadat MEVAC/ Bromed MEVAC/ Bromed Grand Pharma
NOTE: MEVAC Eli Var2 is a bivalent vaccine and it is a combination of already approved two vaccines MEVAC ND Elite & MEVAC IB Var2 in Registration Board Meeting No.312					
iii.	MEVAC ND7 Plus	vNDV Genotype vii, "rg NDV1/ME-G7/2017"} NDV/chicken/ Egypt/11478 AF/2011* *Lab number in Egypt	ND G7 Lasota	Medivac ND G7B Emulsion Reg.No.0884989 MEVAC ND Broiler	Hilton Pharma MEVAC/ Bromed
iv.	MEFLUVAC H9+ND7 0.3	H9N2 (A/chicken/ Egypt/ ME 543V/ 2016) * vNDV genotype vii, "rg NDV1/ME-G7/2017"} *Lab Number in Egypt	AI H9N2 ND G7	MEVAC Multi IB+H9+ND MEFLUVAC H9 0.3 Medivac ND G7B Emulsion Reg.No.084989	MEVAC/ Bromed MEVAC/ Bromed Hilton Pharma
Note: MEVAC ND7 strain used in MEVAC ND7 Plus and MEFLUVAC H9+ND7 has shown highest identity with Pakistani isolates reported recently.					
Evaluation by DBE&R: *For product at serial i & ii virus strain on FSC is NDV2 and the firm claimed in their letter that it is NDV2-NDV60 strain.*					

Decision;

Registration Board referred the case to Expert Working Group on Veterinary Drugs for comments regarding immunological relevance and need of applied strains in Pakistan.

6. Issuance of Registration letter to Al-Asar Enterprises with corrected composition for Product MYVAC IBD V877 (2000 doses).

Following product of M/s Al-Asar Enterprises is approved in 312th Registration Board meeting however there was typographic error in composition:

Sr. No.	Approved composition in 312th Registration Board meeting	Corrected Composition	Remarks
1.	**MYVAC IBD V877** Freeze dried live vaccine containing Infectious bursal disease V877 strain ≥ **$20^{2.5}$** EID_{50} per bird dose in 2000 dose for active immunization of Infectious Bursal Disease.	**MYVAC IBD V877** Freeze dried live vaccine containing Infectious bursal disease V877 strain ≥ **$10^{2.5}$** EID_{50} per bird dose in 2000 dose for active immunization of Infectious Bursal Disease.	Approved by the Chairman Registration Board in the light of delegation of powers in line with FSC. Accordingly Registration letter with correct composition is issued.

Decision:

Registration Board noted the above information.

7. Issuance of Corrigendum to Al-Asar Enterprises with corrected composition for Product MYVAC IBD V877 (1000 doses).

Following product of M/s Al-Asar Enterprises is approved in 260th Registration Board meeting however there was typographic error in composition:

Sr. No.	Approved composition in 260th Registration Board meeting	Corrected Composition	Remarks
1.	**MYVAC IBD V877** (Infectious Bursal Disease V877 vaccine) Each dose contains: Infectious **bronchitis** virus strain V877 ……..$10^{2.5}EID_{50}$	**MYVAC IBD V877** (Infectious Bursal Disease V877 vaccine) Each dose contains: Infectious **bursal** virus strain V877 ……..$10^{2.5}EID_{50}$	Approved by the Chairman Registration Board in the light of delegation of powers in line with FSC. Accordingly, corrigendum with correct composition has been issued to the firm.

Decision:

Registration Board noted the above information.

Cases of AD-IV (Kashif Mehsud)

A: Miscellaneous/ Deferred Cases

1. Extension in labeling exemption for Vaxigrip Tetra (Reg. No. 105066)

M/s Sanofi Aventis Pakistan Limited, Karachi submitted that Annual Influenza vaccination is considered to date as the most effective method for preventing seasonal flu and its complications. The firm further submitted that vaccines by Sanofi Pasteur are manufactured globally at a single source to fulfill the requirement of the whole world. Therefore, it is not possible for manufacturer to follow the packaging and labeling rules of every country at the time of export

plus production, packaging, quality controls of these sterile and temperature sensitive products require specialized methods and techniques of handling under highly controlled environment. The firm requested to extend the exemption of Urdu Text, Registration number and MRP on packs of Vaxigrip Tetra. The firm has submitted the following documents:

i. Fee Challan of Rs. 7500
ii. Copy of SOPs for control of local repacking operations.
iii. An undertaking that to print the Registration Number and Maximum Retail Price (MRP) on each pack of above product at their Karachi site bearing DML No. 000007, before releasing the goods into the market.
iv. Copy of registration letter dated 07-10-2020.
v. Copy of permission of Extension in labeling exemption for Vaxigrip Tetra (Reg. No. 105066) vide letter No. F.3-5/2014-DDC(BD)(Vol-VII) (M-316) dated 02-06-2022.

In this context, it is submitted that the initial request of the firm for exemption of labeling text for Vaxigrip Tetra (Reg. No. 105066) was approved by Registration Board in its 295th meeting for one year from the date of issuance of registration letter. The registration letter was issued on 07-10-2020, hence, the permission was valid till 07-10-2021 and again exemption of labeling text for Vaxigrip Tetra (Reg. No. 105066) was approved by Registration Board in its 316th meeting for one year from the expiry of the permission i.e 7-10-2021 which is valid till 06-10-2022.
It is suggested to grant two to three years permission if agreed to avoid unnecessary workload.

Decision:

Registration Board acceded to the request of the firm and extended the permission, for one year from the date of expiry of previous permission i.e. 06-10-2022, to import Vaxigrip Tetra (Reg. No. 105066) in Standard Export Packs and to locally print MRP and Registration Number along with Urdu Text and other parameters as per Drugs (Labelling & Packing) Rules, 1978 before sale of drug at M/s Sanofi Aventis, Plot 23, sector 22, Korangi Industrial area, Karachi to comply the requirement as per Drugs (Labelling & Packing) Rules, 1986. This permission shall be valid for one (01) year only after issuance of registration letter.

Registration Board further advised DBE&R to prepare agenda for next meeting regarding time span for such permissions.

2. M/s Saadat International, Lahore has applied for change of name of manufacturer (Site remains the same) of their already registered biological product Aftovaxpur (Reg. No. 018499).

M/s Saadat International, Lahore has applied for change in name of manufacturer (Site remains the same) of their already registered biological product as per following details:

Sr. No.	Reg. No.	Brand Name	Existing Name of Manufacturer	Demanded Name of Manufacturer
1.	018499	Aftovaxpur (Foot & Mouth Disease inactivated Vaccine)	M/s Merial Animal Health Ltd. United Kingdom	M/s Boehringer Ingelheim Animal Health Ltd. Ash Road, Pirbright Surrey GU24 ONQ, United Kingdom.

Decision of 316th R.B Meeting:

"Registration Board deferred the case for verification of approval status of product in reference regulatory authorities."

The firm has submitted legalized copy of registration letter of the stated product in Germany and legalized copy of renewal of Registration letter of the stated product in France.

Decision:

Registration Board approved the change of name of manufacturer from M/s Merial Animal Health Ltd. United Kingdom to M/s Boehringer Ingelheim Animal Health Ltd. Ash Road, Pirbright Surrey GU24 ONQ, United Kingdom for the above mentioned product subject to submission of valid legalized Free Sale Certificate from any of reference regulatory authority and the Chairman Registration board is authorized to issue PRV letter.

3. Extension in shelf life of Emergency Use Authorized product Convidecia Vaccine in Vial applied by Mis AJM Pharma deferred in 317th meeting.

M/s AJM Pharma has applied for extension in shelf life of their already Emergency Use Authorized product Convidecia Vaccine in Vial as per following details:

Reg. No.	Brand Name	Existing shelf life	Demanded shelf life
107886	Convidecia Vaccine in vial	6 months (2°C to 8°C)	12months (2°C to 8°C)

Decision of 317th R.B Meeting:

"Registration Board deferred the case and advised the firm to submit the import data of the product since its Emergency Use Authorization."

The Firm has submitted invoices endorsed by DRAP (I & E) Karachi and WHO approval for the above stated product with 12 months of shelf life which has been verified online.

Decision;

Keeping in view the approval of WHO; Registration Board approved the extension in shelf life of Convidecia Vaccine in vial (Reg. No. 107886) from 6 months to 12 months.

4. Delegation of Functions:

Registration Board, in its various meetings (262,276,277,284,288,290,292,295,296,297,307 and 316) has authorized its Chairman for certain functions, under Rule 24(10) of Drugs (Licensing, Registering & Advertising) Rules, 1976, in order to facilitate timely disposal of various cases / post-registration variation cases/ contravention of various provisions of the Drugs Act, 1976.

Following functions are hereby reframed and compiled as follows:

Sr. No.	Functions
1.	Relaxation / exemption in urdu version only for drugs imported for critical ailments like AIDS, cancer, vaccines, sera etc subject to the condition that same shall be printed at any licensed premises prior to marketing.
2.	Export Registration of finished drugs for following categories except Narcotic, Psychotropic drugs and precursor chemicals. • Generic version / me too drugs of already registered formulations. • Formulations which have already been registered for export purposes. • Formulations which are approved by reference regulatory authorities (as approved by Registration Board) and yet not registered for local sale.
3.	Change of name of the manufacturer of imported drug(s).
4.	Increase/ decrease in shelf life of registered drug.
5.	Grant of additional packing of already registered same drugs/medicines except injectables. (For Veterinary Drugs only)
6.	Action initiated on safety of drugs.
7.	Change of packing from: • PVC to Alu-Alu and vice-versa • strip to blister and vice-versa • strip/blister to bottle and vice-versa • glass bottle to PET/HDPE bottle and vice-versa

	• PET bottle to HDPE bottle and vice-versa • Vial to ampoule and vice-versa • Glass vial/ampoule to plastic ampoule and vice-versa • Glass vial/ampoule to pre-filled syringe and vice-versa
8.	Change in labeled storage conditions of imported product
9.	Change of source/grant of additional source of half-finished products like pellets, bulk liquid and granules etc. of registered drugs.
10.	Constitution of panel of inspector for product specific inspection, verification of stability data, GMP inspection and dosage form specific inspection of manufacturer abroad etc.
11.	Correction of typographic errors in recording minutes and registration letters like composition, brand names, demanded price, pack size, address (as per DML/DSL) etc or other typing mistakes.
12.	Change in the packing design/packaging components/ change in label, carton/change in shape, colour of Capsule, Tablets and shape of blister/ aluminum foil.
13.	Change of brand names of registered drug(s).
14.	To grant approval of exemption from inspection of manufacturer abroad as per Import Policy for inspection of finished drugs.
15.	To grant approval for issuance of registration letter(s) on recommendation of inspection panel nominated for inspection of manufacturer abroad.
16.	Correction in formulation in accordance with standard formulations approved by reference regulatory authorities i.e. change from uncoated to film/ sugar/enteric coated tablet or vice versa and correction in base / salt / ester / form of API.
17.	Grant of registration of diluents as combo packs for already registered/approved drugs provided that such diluents shall be provided free of cost.
18.	Issuance of registration letters in approved cases of ciprofloxacin granules for oral suspension containing ciprofloxacin base where revision / correction of salt form and granules of the formulation is required after submission of requisite fee. All registration holders of ciprofloxacin granules for oral suspension shall ensure the supply of ciprofloxacin granules along with the solvent / diluent having following composition as per the innovator product. • Soya lecithin • Medium chain triglycerides • Flavor • Sucrose • Purified water.
19.	Approval of change of registration status from old title/name of the firm to the new title/name of the firm (If site remains the same)
20.	Approval of change/correction of finished product specifications in different scenarios mentioned as under: i. Products registered with manufacturer specifications but formulation exist in official monograph (as decided by Registration Board in 267th meeting) ii. Products registered with any pharmacopoeial specification (e.g. USP) but formulation do not exist in that particular pharmacopeia but another pharmacopeia (e.g. BP). iii. Correction in specification while issuance of registration letters in accordance with decisions taken in 264th, 266th & 267th meetings of Registration Board. iv. Product approved/registered with any pharmacopoeial specification but formulation do not exist in any official monograph. v. Change of specifications from one official pharmacopeia to another official pharmacopeia.

	vi. Manufacturer/innovator specifications for a product are more stringent than official pharmacopoeial specifications.
21.	Grant of renewal of registration (locally Manufactured) which have been received within time as required under Rule 27 of Drug (LR&A) Rules 1976.
22.	Grant of extension in cases of contract manufacturing of already registered products if these are on same terms and conditions.
23.	Change of contract manufacturer/ manufacturing site of already registered products.
24.	Issuance of show cause notice for cancellation of registration after termination of agency authorization by Manufacturer / Product License Holder.
25.	Issuance of show cause notice for cancellation of registration after cancellation of DML
26.	Approval of product license holder/Market Authorization Holder including incorporation of exporter (if required) by the firm.

The above-mentioned functions of post registration variations and pre-registration variations may be delegated to the Director Biological Drugs to avoid un-necessary delays and for timely disposal of the cases if agreed please.

Decision:

Registration Board constituted the following Committee to formulate recommendations on functions of Registration Board to be delegated to Director Biological Drugs.

1. **The Director Biological Drugs.**
2. **The Secretary Registration Board**
3. **Mr. Manzoor Ali Bozdar Additional Director PE&R**

AGENDA ITEM NO.I: PERSONAL HEARING CASES

CASE No. 01: MANUFACTURE & SALE OF MISBRANDED DEX-NEO CREAM REG. NO. 067664, BATCH NO. 299 MANUFACTURED BY M/S. ZANCTOK PHARMACEUTICAL LABS, HYDERABAD.

The Federal Inspector of Drugs-IV, DRAP inspected the premises of M/s. Zanctok Pharmaceuticals Karachi dated 18-11-2021 and following sample of drug taken on Form-3 for the purpose of test/analysis. Details are:

S. No.	Product Name	Manufactured by	Reg. no.	Batch no.	Mfg. Date	Exp. Date	Remarks of CDL
01	Dex-Neo cream	M/s. Zanctok Pharmaceutical Labs, Hyderabad	067664	299	11-2021	10-2023	The inner most label (tube) does not contain date of expiry as required under rule 3 of the Drugs (labelling & Packing) Rules 1986. Hence, sample is declared **"Misbranded"** under the Drug Act, 1976.

The sealed sample of above drugs was sent by FID to Federal Government Analyst, Central Drugs Laboratory, Karachi for the test/analysis vide this office memorandum No. SHM-NTF-64-66/2021-FID(K)-IV dated 19-11-2021.

The sealed portion of sample was also sent by FID to Chairman, Drug Registration Board, DRAP, Islamabad vide office letter of even number dated 19-11-2021.

The Federal Government Analyst, Central Drugs Laboratory, Karachi declared the sample as Misbranded under the Drugs Act, 1976, vide test report No.KQ.348/2021 dated 25-01-2022.

In the light of above test report of Federal Government Analyst, Central Drugs Laboratory, Karachi, FID issued an explanation letter of even number dated 31-01-2022 to M/s. Zanctok Pharmaceuticals Hyderabad to explain their position in the matter for manufacturing/selling of above-mentioned Misbranded drug.

M/s. Zanctok Pharmaceuticals Hyderabad explained their position vide letter dated 07-02-2022. The firm's stance was reproduced as:

> "Keeping in view all the above-mentioned facts, it is stated that we owe to rectify the improper labeling (i.e no expiry date mentioned on primary packaging which was missed during engraving labeling on tubes due to machine problem) of our product Dex-Neo cream from the very next following batch with immediate effect."

In light of FGA report, M/s Zanctok Pharmaceuticals Hyderabad involved in manufacturing and selling of Misbranded drug Dex Neo cream Batch no. 299 and violated section 23(1)(a)(iii) of the Drugs Act 1976 and rules framed under.

Further, FID recommended that action under section 42 of the Drugs Act, 1976.

Section 42 of the Drugs Act 1976 reproduced as:

> "Where any person has been found to have contravened any of the provisions of this Act or the rules in respect of any registered drug, the Registration Board may, after giving such person an opportunity of being heard, cancel the registration of such drug or suspend such registration for a specified period."

Decision of 316th Meeting of Registration Board.

> "The Board after thorough deliberations, considering the facts of the case, decided to issue show cause notice for suspension/cancellation/ prosecution in Drug Court of the subject cited drug to M/s. Zanctok Pharmaceuticals Hyderabad and called them for personal hearing before Registration Board."

Decision of 316th meeting of Registration Board has been communicated vide letter No. F.03-11/2022-QC (316-RB) dated 27-05-2022.

Firm has replied vide Ref No. ZPL/046/2022 dated 30-05-2022 where in firm agreed for personal hearing.

Firm has been called for Personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

M/s Zanctok Pharmaceutical Laboratories submitted vide Ref No. ZPL/117/2022 dated 30-08-2022 that:

> "[…] Unfortunately, we have received the above subject letter on 30-08-2022 in afternoon through Whats App. We still have not received the letter through Pakistan post/courier. We believe due to heavy rain and flood in Hyderabad, no post was received to the factory. Due to receiving of the letter in late hours (Last Day), we are not getting flight for tomorrow to Islamabad. Therefore, we request you to move the hearing date to next month […]"

Decision: **Registration Board after considering the facts of the case and request of the firm to grant another opportunity of personal hearing and acceded to the request and provide them another opportunity of personal hearing.**

CASE NO. 02: MANUFACTURE & SALE OF ADULTERATED & SUB-STANDARD STERILE WATER FOR INJECTION REG. NO. 000040, BATCH NO. 799 MANUFACTURED BY M/S. ZAFA PHARMACEUTICAL LABORATORIES (PVT.) LTD., KARACHI.

The Federal Inspector of Drug-III / Assistant Director-XII, DRAP, Karachi inspected the premises of M/s. National Institute of Child Health (NICH) Rafeeqi Shaheed Road Karachi. on

28-05-2021 wherein the sample of drug along with other drugs were taken for the purpose of test/analysis on prescribed Form-3.

The Federal Government Analyst, Central Drugs Laboratory, Karachi declared the above said sample as "Adulterated and Sub-Standard" quality vide their test report No.KQ.134/2021 (Initial) dated 11th June 2021 and test report No. KQ.134/2021 (Final) dated 30th, July 2021.

S. No.	Name of Drug	Reg; No	Batch No.	Mfg. Date	Exp. Date	Mfg.by	Result of CDL	Basis of Result
01	Zafixime 500mg Injection	027228	440	01-2021	01-2023	M/s. Zafa Pharmaceutical Laboratories (Pvt) Limited, Karachi.	Standard	-
-	Strile Water for Injection 5ml Ampoule	030217	799	12-2020	12-2025	---do---	Adulterated & Substandard	**Containing white fibers visible to the naked eye.**

In the light of above test reports of Federal Government Analyst, Central Drug Laboratory, Karachi an explanation letter of even number dated 11th June 2021 and 02nd, August 2021 issued by FID to M/s. Zafa Pharmaceutical Laboratories (Pvt) Limited, Plot No. B-10, Block-B, S.I.T.E. North Karachi, for explaining their position in the matter of manufacturing/selling of above mentioned Adulterated and Sub-Standard drug.

M/s. Zafa Pharmaceutical Laboratories (Pvt) Limited, Plot No. L-1/B, block 22, Federal "B", Area Karachi, 75950 vide their letter No. Nil dated 23th August,2021 requesting for retesting of Drug Zafixime 500mg Injection Batch No. 440, from NIH Islamabad. under section 22(5) of the drug Act 1976 for testing.

FID submitted the request of firm for retesting dated 25-08-2021.

M/s. Zafa Pharmaceutical Laboratories (Pvt) Limited, again requested for Appellate testing dated 07-10-2021.

Proceedings and Decision of 313th Meeting of Registration Board.

The Board after thorough deliberations and considering the facts of the case decided to ask/request Federal Government Analyst, Karachi to provide OOS investigation and complete testing record on which the product is declared as of Adulterated and Substandard quality.

The decision of Board has been communicated dated 16-12-2022 after approval of minutes.

M/s. Zafa Laboratories replied dated 11-01-2022, the conclusion of firm is reproduced as:

"In light of above investigation, product Water for Injection 5ml, Batch no. 799 was found as per specification. Therefore, OOS is not required against complaint."

Response received from Central Drugs Laboratory, Karachi received through WhatsApp dated 14-03-2022 wherein the remarks of OOS Investigation Form are reproduced as:

"Containing white fibers (WFI) visible to the naked eyes. The sample is of adulterated and substandard quality.

Technical Evaluation of the case:

- Water for injection was declared adulterated and substandard, containing white fibers visible to the naked eyes.
- Defects may not be equally distributed over the batch that's why it is not necessary for a Board or retention portion to be defective. Allowing retesting may result in false negative results and pose the risk to patient which can be avoided otherwise.
- Moreover, the remarks of CDL may be considered for further investigation of quality defect considering the statistical validity of sample size.

Proceedings and Decision of 316th Meeting of Registration Board.

The Board after thorough deliberations and considering the facts of the case decided:

i. To issue show cause notice for suspension/cancellation/ prosecution in Drug Court of the subject cited drug to M/s. Zafa Pharmaceutical Laboratories (Pvt.) Ltd., Karachi and called them for personal hearing before Registration Board.

Mr. Adnan Rizvi, Member of Board has recorded his note of dissent i.e. the sample should be sent to NIH for appellate testing.

Decision of 316th meeting of Registration Board has been communicated vide letter No. F.03-11/2022-QC (316-RB) dated 27-05-2022.

Firm has replied vide letter Nil dated 02-06-2022 wherein they again requested to send sample for appellate testing to NIH for physical testing.

Firm has been called for personal hearing.

Proceedings and Decision of 320th Meeting of Registration Board.

M/s. Zafa Pharmaceutical Laboratories (Pvt) Limited, Karachi submitted vide Ref No. Nil dated 29-08-2022 that the concerned technical person was not available to attend the hearing due to unavoidable circumstances (rain and flood). They further requested for personal hearing in next meeting.

Decision: **Registration Board after considering the facts of the case and request of the firm to grant another opportunity of personal hearing and acceded to the request and provide them another opportunity of personal hearing.**

CASE NO. 03: MANUFACTURE & SALE OF ADULTERATED & SUBSTANDARD ABEX INJECTION, REG. NO. 086072, BATCH NO. 21AL2, MFG. DATE 02-21, EXP. DATE 02-23, MANUFACTURED BY M/S. SEMOS PHARMACEUTICALS (PVT.) LTD., KARACHI.

FID, DRAP, Karachi inspected the premises of M/s. JPMC, (Central Pharmacy) Rafeeqi Shaheed Road Karachi. on 23-04-2021, wherein following sample of drug along with other drugs were taken for the purpose of test/analysis on prescribed Form-3.

The Federal Government Analyst, Central Drugs Laboratory, Karachi declared the above said sample as "Adulterated and Sub-Standard" quality vide their test report No.KQ.100/2021 (Initial) and (Final) dated 26th May 2021 and 15th June 2021**.**

S. No.	Name of Drug	Reg. No	Batch No.	Mfg. Date	Exp. Date	Mfg. By	Result of CDL	Basis of Result
01	Injection Abex	086072	21AL2	02/2021	02/2023	M/s. Semos Pharmaceuticals (Pvt) Ltd. Plot #11, Sector 121-A, North Karachi. Industrial Area, Karachi.	Adulterated & Sub-standard	**After reconstitution, containing black particles visible to naked eye.**
02	Ampoule of Water for Injection	026762	WF2-243C	JAN-2021	JAN-2026	M/s. Surge Labortories (Pvt) Ltd. 10th Km, Faisalabad Road, Bikhi, District Sheikhupura	Standard	-

In the light of above test report KQ.100/2021 (Initial) dated 26th May 2021 of Federal Government Analyst, Central Drug Laboratory, Karachi an explanation letter of even number dated 27th May 2021 and 17th June 2021 were accordingly issued to M/s. Semos Pharmaceuticals (Pvt) Ltd. Plot #11, Sector 121-A, North Karachi. Industrial Area, Karachi. for explaining their position in the matter of manufacturing/selling of above mentioned Adulterated and Sub-Standard drug

M/s. Semos Pharmaceuticals (Pvt) Ltd. Plot #11, Sector 121-A, North Karachi. Industrial Area, Karachi vide their letter No. SP/L TR047 dated 28th June 2021 requesting for retesting of Drug Abex Injection Batch No. 21AL2 from NIH Islamabad.

FID stated that in the light of above, portion of sample lying with the Board may be got retested from Appellate Laboratory National Institute of Health (N.I.H) Islamabad.

Proceedings and Decision of 313th Meeting of Registration Board.

The Board after thorough deliberations and considering the facts of the case decided to ask/request Federal Government Analyst, Karachi to provide OOS investigation and complete testing record on which the product is declared as of Adulterated and Substandard quality.
The decision of Board has been communicated dated 16-12-2022 after approval of minutes.

M/s. Semos Pharmaceuticals, Pvt Ltd., Karachi dated 27-12-2021, the firm mentioned that they have checked retention samples and recall samples as described process but didn't see any particles after reconstitution.

Firm also highlighted the remarks of CDL report reproduced as:

- As per requirements of USP general chapter <790> additional units may be inspected (As per ANSI/ASQ Z 1.4 or ISO 2859-1 standard for sampling) to gain further information on the risk of particulates in the batch.
- It is also mentioned in USP <790> that because of complaint and regulatory concern inspect 20 units, but they have received 10 units only. That's why they have requested to inspect more samples as per CDL remarks.

For the greater public interest and precautionary measures, they revalidated the Cephalosporin sterile area after replacing the filters where necessary i.e. HEPA filters for tunnel sterilization etc and other HEPA filters were also re-validated where necessary. They conducted DOP test on the filters. They further requested for appellate testing under section 22(4) of the Drugs Act 1976.

Response received from Central Drugs Laboratory, Karachi dated 14-03-2022 wherein wherein the remarks of OOS Investigation Form are reproduced as : "Adulterated and Substandard".

Technical Evaluation of the case:

- Product is declared as adulterated and substandard after reconstitution, containing black particles visible to naked eyes.
- Firm has conducted risk assessment however the risks are defined by firm in low to moderate range. DOP test was also conducted but no remarks was mentioned in the report.
- Defects may not be equally distributed over the batch that's why it's not necessary for a Board portion or retention portion to be defective. Allowing retesting may result in false negative results and pose the risk to patient which can be avoided otherwise.
- Moreover, the remarks of CDL may be considered for further investigation of quality defect.

Decision of 316th Meeting of Registration Board.
The Board after thorough deliberations and considering the facts of the case decided:

i. To issue show cause notice for suspension/cancellation/ prosecution in Drug Court of the subject cited drug to M/s. Semos Pharmaceuticals (Pvt.) Ltd., Karachi and called them for personal hearing before Registration Board

Mr. Adnan Rizvi, Member of Board has recorded his note of dissent i.e. the sample should be sent to NIH for appellate testing.

Decision of 316th meeting of Registration Board has been communicated vide letter No. F.03-11/2022-QC (316-RB) dated 27-05-2022.

Firm has replied vide Ref. No. SP/LTR/062 dated 01-06-2022 wherein they again requested to send sample for appellate testing to NIH for physical testing and ready to appear before the Board.

Firm has been called for personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

M/s. Semos Pharmaceuticals, Pvt Ltd., Karachi submitted vide Ref No. SP-LTR/065 dated 31-08-2022 that their flight had been delayed at the last moment and no other flight was available in short span of time. They further requested for another date for personal hearing.

Registration Board after considering the facts of the case and request of the firm to grant another opportunity of personal hearing and acceded to the request and provide them another opportunity of personal hearing.

Case No. 04: MANUFACTURE & SALE OF SUB-STANDARD INDOBID CAPSULE, REG. NO. 007106, BATCH NO. 386, MANUFACTURED BY M/S ADAMJEE PHARMACEUTICALS (PVT) LTD., KARACHI.

FID Karachi vide letter No. F.ARS-107-109/2021-FID-II (K) dated 02nd August 2021 wherein the FID Karachi has informed that the sample was received in CDL, Karachi wherein, the Federal Government Analyst has declared following samples of Indobid Capsule as of **"Substandard quality"**.

Name of Product	Manufactured by	Reg. no.	Batch no.	Mfg. Date	Exp. Date	CDL Remarks
Indobid Capsule	M/s Adamjee Pharmaceuticals (Pvt) Ltd., Karachi	007106	386	01-2021	01-2025	Substadard on basis of Dissolution.

Results of CDL on the basis of which sample under reference has been declared as Sub-Standard quality are reproduced as under:-

S.No.	Test	Specification	Result	Reference
1	Description	Hard gelatin capsules consist of white body and blue coloured cap, containing off white powder.	Complies	Mfg. Specs.
2	Identification	The identification test must identify Indomethacin.	Complies	BP 2020
3	Dissolution	Each unit is not less than 70%	**Does not Comply.**	BP 2020
4	Assay Indomethacin (Lebel claim 25mg/ capsule)	90.0% to 110.0%	103.2%-Complies	BP 2020

Remarks: The sample is "Sub-Standard" quality under the Drugs Act, 1976.

The FID Karachi has further informed that the firm has sent the explanation letter to explain their position dated 13th July 2021 regarding the violation of Drug Act 1976 and DRAP Act 2012.
The firm has submitted their reply dated 30th July 2021, wherein they requesting for retesting of Drug Indobid Capsules B.No.386 from NIH Islamabad.
In light of Supreme Court judgement of "C.P.1692-L/2020, C.P.1792-L/2020 and C.P.5-L/2021" and firm's request for appellate testing, the case is submitted for consideration of Board.
Proceedings and Decision of 312th Meeting of Registration Board.

The case has been deferred till the finalization of Appellate Testing Guidance Document/Protocol.

The agenda of "Handling requests of Appellate Testing- Guidance document for registration Board" was discussed in 313th meeting of Registration Board. The Board after thorough deliberations and considering the facts of the case decided as:

i. The firm will provide OOS investigation and complete testing record of the concerned batch along with scientific justifications/grounds with the request of Appellate testing under section 22(4) of the Drugs Act 1976.
ii. Federal Government Analyst, Karachi will provide OOS investigation and complete testing record of such reports.
iii. Registration Board advised QA&LT Division to present all cases of Appellate Testing with these both set of documents along with technical report of the case.

OOS investigation was asked by firm and CDL vide office letter dated 23-12-2021.

The firm submitted the response dated 16-02-2022. They provided the results of initial test, Keeping sample and warrantor portion and request for appellate testing. However, OOS investigation was not provided.

CDL submitted the response dated 15-03-2021 wherein they mentioned: OOS is validated.

Technical Evaluation of the case:

i. The product was declared substandard on dissolution.
ii. CDL performed the test as per BP 2020 while firm performed on manufacturer specs.
iii. Audit trail was not provided by firm.
iv. Data is not time stamped hence data integrity cannot be verified.

Proceedings and Decision of 317th Meeting of Registration Board:

Out of Specification (OOS) investigations and testing records submitted by M/s. Adamjee Pharmaceuticals (Pvt) Ltd., Karachi and CDL, DRAP Karachi was presented before Registration Board. The Board deliberated the case in detail as follows:

i. M/s. Adamjee Pharmaceuticals (Pvt) Ltd., Karachi requested for Appellate testing. In compliance to the decision of 313th meeting of Registration Board firm and CDL were asked to submit Out of specification (OOS) investigation vide office letter dated 23-12-2021. The firm submitted the response dated 16-02-2022. They provided the results of initial test, Keeping sample and warrantor portion and request for appellate testing. However, OOS investigation was not provided. While CDL submitted the response dated 15-03-2022 wherein they mentioned that OOS is validated.
ii. Review of documents revealed that the product "Indobid Capsule" (Reg# 007106) was registered vide letter No.F.3-4/83-Reg(M-51) dated 16-01-1984 and no specification was mentioned in registration letter. Later on the subject product was included in BP specifications Minutes of 317th meeting of Registration Board (16-17 May, 2022) | 877 while the firm is still manufacturing and testing the product per manufacturer specifications. Further in 197th meeting of Registration Board held on 3-4 th May 2006, the Board decided as:

"All the firms shall adopt the specifications mentioned in the official pharmacopoeias for all the formulation except those drugs not included in the

official pharmacopoeias. For these drugs manufacturers may adopt their own specifications till the inclusion of that formulation in the official pharmacopoeias. after this decision firms will not be allowed to adopt their own specifications for the drugs, which are included in any of the official pharmacopoeias, listed in the Section 3 of Drugs Act, 1976."

Decision: Keeping in view position narrated above, the Board concluded that the firm is still manufacturing/testing the said product as per manufacturer specifications despite of the fact that it is included in the official pharmacopoeia (BP). Therefore, Board did not accede the firm's request of appellate testing. Thus, the Board decided to issue show cause notice for suspension/cancellation/ prosecution in Drug Court of the subject cited drug to M/s. Adamjee Pharmaceuticals (Pvt) Ltd., Karachi and called them for personal hearing before Registration Board.

Decision of 317th meeting of Registration Board has been communicated vide letter No. F.03-30/2022-QC (317-RB) dated 21-06-2022.

Firm has replied vide Ref. No. Nil dated 28-06-2022 wherein they mentioned that they are the only company in Pakistan manufacturing Indomethacin capsule. They further said that they already imported a huge quantity of the said product foil, therefore they will change it to official pharmacopeia after consumption of the present foil.

Firm has been called for personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

M/s. Adamjee Pharmaceuticals, Pvt Ltd., Karachi submitted vide Ref No. Nil dated 31-08-2022 that their flight had been delayed. They further requested for personal hearing in next meeting.

Decision: Registration Board after considering the facts of the case and request of the firm to grant another opportunity of personal hearing and acceded to the request and provide them another opportunity of personal hearing.

Case No. 05: MANUFACTURE & SALE OF SUB-STANDARD LEFIN PEDIATRIC SUSPENSION, REG. NO. 000404, BATCH NO. 332V, MANUFACTURED BY M/S. LEAMA CHEMI PHARMA (PVT) LTD. PESHAWAR.

The Federal Inspector of Drug Peshawar inspected the premises of M/s. Leama Chemi Pharma (Pvt) Ltd. Peshawar on 12-08-2021 wherein the sample of drug along with other drugs were taken for the purpose of test/analysis on prescribed Form-3.

Name of Product	Manufactured by	Reg. no.	Batch no.	Mfg. Date	Exp. Date	CDL Results
Lefin Pediatric Suspension	M/s. Leama Chemi Pharma (Pvt) Ltd. Peshawar.	000404	332V	06/21	05/23	Sub-Standard on the basis of Assay.

02. Results of CDL on the basis of which samples under reference has been declared as Substandard quality are reproduced as under:-

S.No.	Test	Acceptance Criteria	Result	Reference
1.	Description	Pink coloured suspension in ambered glass bottles.	Complies.	Mfg. Specs.
2.	Identification	The identification test must identify Paracetamol.	Complies.	BP 2020
4.	**Assay** Paracetamol. (Label Claim 120mg/5ml)	95.0% to 105.0%	**70.45%-** **Does not comply.**	BP 2020

Remarks: *The sample is of "Sub-Standard" quality under the Drugs Act, 1976.*

FID has sent the explanation letter to explain their position dated 26-10-2021 regarding the violation of Drug Act 1976 and DRAP Act 2012.

The firm has submitted their reply dated 29-11-2021, wherein they requesting for retesting of product Lefin Pediatric Suspension Batch no. 332V.

The agenda of "Handling requests of Appellate Testing- Guidance document for registration Board" was discussed in 313th meeting of Registration Board. The Board after thorough deliberations and considering the facts of the case decided as:

i. The firm will provide OOS investigation and complete testing record of the concerned batch along with scientific justifications/grounds with the request of Appellate testing under section 22(4) of the Drugs Act 1976.
ii. Federal Government Analyst, Karachi will provide OOS investigation and complete testing record of such reports.
iii. Registration Board advised QA&LT Division to present all cases of Appellate Testing with these both set of documents along with technical report of the case.

The firm's response received dated 14-02-2022. Firm has submitted testing method on UV and it seems that assay method on HPLC was added afterwards as document show doesnot show serial No. on HPLC method.

CDL submitted the response dated 15-03-2021 wherein they mentioned: OOS is validated.

Technical Evaluation of the case:

i. The product was declared substandard by CDL on the basis of assay.
ii. CDL performed the test as per BP 2020.
iii. Testing method of firm was not a control document.
iv. HPLC was not standard method, they mentioned UV for assay in testing method.
v. Firm performed assay on HPLC dated 10-12-2021 while the parameters i.e mobile phase, standard preparation, sample preparation, wavelength, flow rate were not as per BP 2020.

Parameters	BP Parameters	CDL parameters	Firm's Parameters
Flow rate	1.5ml/min	1.5ml/min	1ml/min
Column temperature	35	35	-

Detection wavelength	245nm	245nm	256nm
Inject volume	50ul	50ul	10ul

vi. Audit trail was not provided by firm.
vii. Data is not time stamped hence data integrity cannot be verified.

Proceedings of 317th Meeting of Registration Board.

Out of Specification (OOS) investigations and testing records submitted by M/s. Leama Chemi Pharma (Pvt) Ltd. Peshawar and CDL, DRAP Karachi was presented before Registration Board. The Board deliberated the case in detail as follows:

i. Registration Board considered the case of M/s. Leama Chemi Pharma (Pvt) Ltd. Peshawar requested for Appellate testing. In compliance to the decision of 313th meeting of Registration Board, the firm and CDL were asked to submit Out of specification (OOS) investigation vide office letter dated 23-12-2021. The firm submitted the response dated 14-02-2022. Firm has submitted testing method on UV and it seems that assay method on HPLC was added afterwards as document does not show serial No. on HPLC method. While CDL submitted the response dated 15-03-2022 wherein they mentioned: OOS is validated.
ii. Review of documents revealed that the product "Lefin Pedriatic Suspension" (Reg# 015203) was registered vide letter No.F.3-3/97-Reg.II(M-125) dated27th June 1997 and no specification was mentioned in registration letter. Later on the subject product was included in BP specifications while the firm is still manufacturing and testing the product per manufacturer specifications. Further in 197th meeting of Registration Board held on 3-4th May 2006, the Board decided as:

> "All the firms shall adopt the specifications mentioned in the official pharmacopoeias for all the formulation except those drugs not included in the official pharmacopoeias. For these drugs manufacturers may adopt their own specifications till the inclusion of that formulation in the official pharmacopoeias. after this decision firms will not be allowed to adopt their own specifications for the drugs, which are included in any of the official pharmacopoeias, listed in the Section 3 of Drugs Act, 1976."

Decision: Keeping in view position narrated above the Board concluded that the firm is still manufacturing/testing the said product as per manufacturer specifications despite of the fact that it is included in the official pharmacopoeia (BP). Therefore, Board did not accede the firm's request of appellate testing. Thus, the Board decided to issue show cause notice for

suspension/cancellation/ prosecution in Drug Court of the subject cited drug to M/s. Leama Chemi Pharma (Pvt) Ltd. Peshawar.and called them for personal hearing before Registration Board.

Decision of 317th meeting of Registration Board has been communicated vide letter No. F.03-30/2022-QC (317-RB) dated 21-06-2022.

Firm has replied vide Ref. No. Nil dated 30-06-2022 wherein they provided HPLC analysis and requested to accept the same.

Firm has been called for personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

Mr. Irfan Wahid, QCM (CNIC# 17301-1469985-7) and M. Ibrar Khalid, Production Incharge (CNIC# 17301-1666657-5) appeared before the Board. They said that they performed the assay by UV spectroscopy and after the substandard report received they performed the assay by HPLC method.

Decision: **Registration Board after considering the facts of the case and thorough deliberations decided to suspend the registration of the said product for six (06) months or till the verification of root cause analysis, Corrective and preventive action (CAPA) by the firm and verification of aforementioned points and Product Specific Inspection by following panel whichever is later.**

- **Director DTL Peshawar.**
- **Additional Director, DRAP, Peshawar**

Case No. 06: MANUFACTURE & SALE OF SUBSTANDARD CIPRACEPT 250MG TABLET, REG. NO. 096357, BATCH NO. TCA-103, MFG. DATE 01-2021, EXP. DATE 01-2023, MANUFACTURED BY M/S. MISSION PHARMACEUTICALS, KARACHI.

FID, DRAP, Karachi inspected M/s. Mission Pharmaceuticals (Pvt.) Ltd., A-94, SITE Super Highway, Karachi on 25-02-2021 to check the GMP compliance level of the firm, wherein following sample of drugs along with other drugs were taken for the purpose of test/analysis on prescribed Form-3:

Name of Drug	Reg; No	Batch No.	Mfg. Date	Exp. Date	Mfg. By	Result of CDL
Cipracept 250mg Tablet (R. No. 096357)	TCA-103	TCA-103	01-2021	01-2023	M/s. Mission Pharmaceuticals (Pvt.) Ltd., Karachi.	Sub-Standard on the basis of Dissolution

FID sent sealed samples of above drug was sent to Federal Government Analyst, Central Drugs Laboratory, Karachi for the test/analysis vide this office memorandum No. ARS-69-70/2021-FID-II (K) dated 26-02-2021

The Government Analyst, Central Drugs Laboratory, Karachi vide test report No.KQ.51/2021 dated 23rd April, 2021 declared the sample of the above-named drug as **"Sub-Standard"** quality under the Drugs Act, 1976, which is violation of Section 23(1) (a) (v) of Drugs Act, 1976 and rules framed there under.

FID issued an explanation letter of even numbers dated 28th April, 2021 and 24th May, 2021 to M/s. Mission Pharmaceuticals (Pvt.) Ltd., A-94, SITE Super Highway, Karachi for explaining their position in the matter for manufacturing, selling & distributing of above-mentioned substandard drug with the directions to recall the above batch from the market.

FID submitted that M/s. Mission Pharmaceuticals (Pvt.) Ltd., Karachi did not challenge the test report of CDL, Karachi. Firm mentioned that they checked dissolution test and found it well in limits as specified by USP.

FID submitted that M/s. Mission Pharmaceuticals (Pvt.) Ltd., Karachi has violated the Section 23(1) (a) (v) of Drugs Act, 1976, and recommended that:

i. Registration of their under-reference product may kindly be suspended/cancelled for a certain period.
ii. PSI may be carried out by panel of inspectors.
iii. Recalled stock should be destroyed as per SOP.

FID further submitted the name of MD and technical persons as provided by the firm:

i. Muhammad Aleem Mirza, Managing Director (CNIC No. 42201-7437635-3)
ii. Pahlwan Tanwari, Production Incharge (CNIC No. 42201-1989136-9)
iii. Jubair Ali Watio, Manager Quality Control (CNIC No. 45208-8699076-5)

The names provided by firm have been verified by Licensing Division. A show cause has been issued to following dated 07-01-2022.

M/s Mission Pharmaceuticals, S.I.T.E Super Highway, Karachi.	Mr. Muhammad Aleem Mirza, Managing Director M/s Mission Pharmaceuticals, Karachi.
Pahlwan Tanwari, Production Incharge, M/s Mission Pharmaceuticals, Karachi	Jubair Ali Watio, Manager Quality Control, M/s Mission Pharmaceuticals, Karachi.

M/s. Mission Pharmaceuticals, Karachi replied vide letter: MP/C-005/22 dated 03-03-2022. They mentioned that

> *"[…] they found that this batch was over wet mixing due to this reason although tablet passes in disintegrator test but in dissolution test is not released in given time period. Normal wet mixing time is 10-15 minutes but by operator mistake has run the mixer for 35 minutes. Granules become dense and after finding the blend all in process test hadness, disintegration test and friability was found in limit […]."*

Firm further requested to be heard in person to share investigation and CAPA.

Firm has been called for personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

M/s. Mission Pharmaceuticals, Karachi submitted vide Ref No. MP/08/026/22 dated 29-08-2022 that they requested to extend the date as they received letter dated 29-08-2022, unable to reach on time due to flood in Sindh.

Decision: **Registration Board after considering the facts of the case and request of the firm to grant another opportunity of personal hearing and acceded to the request and provide them another opportunity of personal hearing.**

CASE NO. 07: MANUFACTURE & SALE OF SUB-STANDARD DIAGYL SUSPENSION, BATCH NO. 162 BY M/S SWISS PHARMACEUTICALS (PVT) LTD, KARACHI.

FID-VI, Karachi visited the premises of premises of M/s Swiss Pharmaceuticals (Pvt) Ltd., A/159 SITE, Super Highway, Karachi on 12-06-2018 and taken the following sample U/S 18(1) (c) of the Drugs Act, 1976 for the purpose of test/analysis on prescribed Form-3:

Name:	Diagyl Suspension 60ml
composition	Each 5ml contain 200mg Metronidazole
Registration No:	020229
Batch No:	162
Manufacturing Date:	06-2018
Expiry Date:	06-2021
Manufactured By:	M/s Swiss Pharmaceuticals (Pvt) Ltd., A/159 SITE, Karachi

02. The FID-VI, Karachi has forwarded one sealed portion of sample to Central Drugs Laboratory, Karachi vide memorandum No.ARS-57-59/2018-FID-VI (K) dated 12-06-2018 as required under Section 19(3)(i) of the Drugs Act, 1976.

03. The Federal Government Analyst, CDL, Karachi declared the sample as of Sub-standard quality on the basis of Assay content (Percentage determined: 208.2%, Limit: 95.0%- 105.0%) vide test/analysis report No.R.KQ. 468/2018 dated 20th July, 2018.

04. In light of the above said test report; the FID served an explanation letter vide reference No. ARS-57-59/2018-FID-VI (K) dated 26-07-2018 to M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Super Highway, Karachi for explaining their position in the matter of manufacturing, selling and distributing of above mentioned substandard drug with direction to recall the above said batch from the market. The FID-VI inspected the premises as the results were very alarming and could be lethal if the drug under reference was distributed to masses. The stock were fresh and present at their nation wise distributor so the firm quarantined it till further investigation.

05. In response M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Super Highway, Karachi submitted their reply vide reference No. Nil dated 08-08-2018 wherein they submitted that the same out of specification assay results were due to **Mixing Error.** They also submitted that the whole batch quantity is lying under their quarantine and they want to destroy it under the supervision of FID. However they didn't apply for retesting from Appellate laboratory, NIH, Islamabad.

06. The FID-VI, Karachi provided the names of responsible persons which are as under:

S.No.	Name	Designation	CNIC
1	Muhammad Umair Feroz	Director	42000-0375898-3
2	Zahid Hussain Khan	Quality Control Incharge	42401-7324156-3
3	Munawar Sultana	Production Incharge	42101-2796675-4

07. The Division of Drug Licensing, DRAP Islamabad was requested to verify the names provided by the FID-VI, Karachi and provided the following names being responsible persons and technical persons.

M/s Swiss Pharmaceuticals (Pvt) Ltd., A/159 SITE, Karachi.	Hafiz_Ferozuddin (Director/Chief Executive) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi.
Hafiz Muhammad Umair, (Director) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi.	Hafiz Muhammad Aamir, (Director) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi.
Hafiz Muhammad Saad, (Director) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi.	Ms. Munawar Sultana (Production Incharge) (42101-2796675-4) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi
Zahid Hussain (Quality Control Incharge) (42401-7324156-3) M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi	

08. The FID has provided that M/s Swiss Pharmaceuticals (Pvt) Ltd, Karachi has violated the section 23(1) (a) (v) of the Drugs Act, 1976 and rules framed there under and recommended to the Board that the recalled stocks is ordered to be incinerated and firm may be issued warning to uplift the GMP standards so that such failures may satisfactory be mitigated/addressed in future.

09. Show cause notice has been issued to the technical staff/management of the firm – responsible persons U/S 7(11) of the Drugs Act, 1976 vide letter no. 3-59/2018-(QC) dated 19-11-2018 that why the following action(s) should not be initiated against you:

i. Prosecution in the Drug Court.
ii. Cancellation/Suspension of Drug Registration.
iii. Any other action the Board may deem fit.

10. The show cause notice was served to the firm and accused persons but the firm did not submit their reply in response to show cause notice.

Proceeding and Decision of the 287th Meeting of Registration Board.

Mr. Hafiz Muhammad Umair (Director) and Mr. Zahid Hussain (Quality Control Incharge) of M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi appeared on behalf of M/s Swiss Pharmaceuticals (Pvt.) Ltd., A/159 SITE, Karachi to plead instant case of Substandard drug Sub-Standard Diagyl Suspension, Batch No. 162 before the Board in its 287th meeting on 04th January, 2019. Representatives of firm informed that problem occurred due to improper mixing during manufacturing operation. The Board after hearing the accused deliberated the matter in depth in the light of available record/ investigation report of FID decided as under:

I. Submission of product development data by the firm.

II. Product Specific Inspection including verification of product development data by the following panel:

- Director, Drug Testing Laboratory, Karachi.

- Area Federal Inspector of Drugs.

III. Suspension of the Registration of the said product for six (06) months or till the verification of product development data and satisfactory report by the panel whichever is later.

The decision of Registration Board had been communicated vide letter No. 03-92/2018-QC (287-RB) dated 28-02-2019.

FID-VI, DRAP, Karachi vide reference No.F.07-10/2020-FID-VI (K) dated 24th February, 2020 addressed to the Director QA&LT, DRAP, Islamabad regarding the subject of *"INSPECTION OF M/S HANDS PAKISTAN PLOT NO. 158, GADAP ROAD, MALIR KARACHI- STOCK ORDERED NOT OT DISPOSE OF ON FORM-1"* wherein ha has submitted that during the inspection of M/S Hands Pakistan Plot No. 158, Gadap Road, Malir Karachi on 24-02-2020 he recovered the stocks of Suspension Diagyl (R. No. 020229) for which the registration Board in its 287th meeting had suspended the registration of the said product for six months or till the verification of product development data and satisfactory report by the panel whichever is earlier. The available stocks of the suspended drug product were ordered "Not to dispose of on Form-1" under Section 18(1) of the Drugs Act, 1976 and violations of Board's decision.

S. No.	Name of Drug	Batch No.	Quantity	Mfg. Date	Exp. Date	Mfg. by
01	Susp. Diagyl 60ml	166 to 181	1 x 60ml x 134 x 100	10-2019	10-2022	M/s Swiss Pharmaceuticals (Pvt.) Ltd., Karachi.

Furthermore, samples of the said product along with other drugs were also drawn for test/analysis purpose on prescribed Form-3 and sent to the Federal Government Analyst, CDL, Karachi.

FID, DRAP, Karachi requested the permission for extension in the period of order made "Not to dispose of" on form-1 under the Drugs Act, 1976/DRAP Act, 2012. The permission was granted by Chairman, Registration Board and communicated to FID vide office letter F.No.3-59/2018-(QC) dated 08-05-2020 with directions to submit the complete case.

FID-VI, DRAP, Karachi vide reference No.F.07-10/2020-FID-VI (K) dated 04th March, 2020 addressed to the Director QA&LT, DRAP, Islamabad regarding the subject of "SURPRISED "INSPECTION OF M/S SWISS PHARMACEUTICALS PVT LTD, A -159,SITE SUPER HIGHWAY KARACHI STOCK ORDER NOT TO DISPOSE OF ON FORM I" wherein he has submitted that he was directed to inspect an unauthorized premises alleged to store expired drugs/ medicines and selling those after re labeling. Accordingly the undersigned along with Dr. Waqar Ahmed Assistant Director DRAP Karachi proceeded for visit and reached at Plot No. C-36 SITE-II Super Highway Karachi. The alleged Plot was found owned by M/s Swiss Pharmaceutical (Pvt.) Ltd., and was very adjacent to their registered plot No. A/159 SITE Super Highway Karachi. The said plot is declared as their ware house on Drug Sale license and used for storage of expired goods and same was seen stored there. This plot is connected to their main plot No. A/159 through ill defined stores where firm had stored some chemicals, packing materials and finished goods. Among the finished good panel found fresh stock of syrup Diagyl, B.No.170 and 171, the registration of which was suspended by the Board for six months are till the verification of product development data by the nominated panel vide DRAP Islamabad letter No.F.03-92/2018-QC (287-RB) dated 28th February 2019. But instead of complying the decision of the board concerned, the firm resumed the manufacturing of suspended drug. The suspected stocks were ordered not to dispose of initially for 28 days under section 18(1) of the Drug Act 1976.

S. No.	Name of Drug	Batch No.	Quantity	Mfg. Date	Exp. Date	Mfg. by

01	Susp. Diagyl 60ml	170	1 x 60ml x 100 x 110	12-2019	12-2022	M/s Swiss Pharmaceuticals (Pvt.) Ltd., Karachi.
02	Susp. Diagyl 60ml	171	1 x 60ml x 100 x 174	01-2020	01-2023	-do-

M/s Swiss Pharmaceuticals (Pvt.) Ltd., A-159 SITE Super Highway Karachi was directed to explain their position for manufacturing and selling of above suspended product vide this office letter of even number dated 24th February 2020. M/s Swiss Pharmaceutical (Pvt.) Ltd A-159 SITE Super Highway Karachi submitted their reply vide letter dated 03-03-2020 admitting their mistake and seeking further instruction

FID, DRAP, Karachi recommended that the registration of the alleged product may be cancelled after necessary legal procedure in this connection. The complete case is forwarded to your good office for further necessary action/instruction into the matter, please.

The permission was granted by Chairman, Registration Board and communicated to FID vide office letter F.No.3-59/2018-(QC) dated 08-05-2020 with directions to submit the complete case. Reminder-I issued dated 15-06-2020.

FID-VI, DRAP, Karachi vide reference No.F.ARS-07-10/2020-FID-VI (K) dated 25-06-2020 regarding the subject of "Manufacture and sale of substandard drugs by M/s Swiss Pharmaceuticals (Pvt.) Ltd. Karachi" Wherein he has stated that he inspected M/s. Swiss Pharmaceutical (Pvt.) Ltd., A-159, SITE Super Highway, Karachi on 17-02-2020 and on 24-02-2020 FID, DRAP, Karachi inspected M/s. HANDS Pakistan, Plot No. 15, Gadap Road, Malir, Karachi.

During the inspections of both premises, following suspected samples were drawn along with other samples on prescribed Form-3 for test/analysis purpose:

S. No.	Name of Drug	Batch No.	Mfg Date	Exp. Date	Mfg by	Taken From	Result of CDL
01.	Susp. Diagyl 60ml	170	12-2019	12-2022	M/s. Swiss Pharmaceuticals	M/s. Swiss Pharmaceuticals	Substandard
02.	-do-	171	01-2020	01-2023	-do-	-do-	
03.	-do-	167	10-2019	10-2022	-do-	M/s. HANDS Pakistan, Malir, Karachi	

In the light of above test report of Government Analyst, Central Drugs Laboratory, Karachi an explanation letters of even numbers dated 09th March 2020 and 06th April 2020 were accordingly issued to M/s. Swiss Pharmaceuticals (Pvt.) Ltd., A-159 SITE Super Highway, Karachi

M/s. Swiss Pharmaceuticals (Pvt.) Ltd., A-159 SITE Super Highway, Karachi has submitted unsatisfactory reply and did not challenge the reports vide their letter dated 01th April 2020.

FID recommended that the firm has violated Section 23(1) (a) (v) and 23(l)(a)(x) of Drugs Act, 1976 for manufacturing and selling of Substandard and Suspended drug, which is punishable under Section 27 of Drug Act, 1976 and rules framed there under therefore, it is recommended that:-

1. The Drug Manufacturing License No. 000438 of M/s. Swiss Pharmaceuticals (Pvt.) Ltd., Karachi may be suspended/cancelled for certain period after due deliberation of Registration Board/Licensing Board.
2. The registration of the alleged product **(Suspension Diagyl)** may be cancelled for violation

of decision of Registration Board
3. Through panel GMP inspection may be conducted.

Names of Responsible persons along with copies of CNICs as provided by the firm;

i. M/s. Swiss Pharmaceuticals (Pvt.) Ltd., A-159 SITE Super Highway, Karachi
ii. Muhammad Umair Feroze, Director (42000-0375898-3)
iii. Munnawar Sultana, Production Incharge (42101 -2796675-4)
iv. Safdar Khan Kayani, QC Incharge (42401-1779995-5)

M/s Swiss Pharmaceuticals (Pvt.) Ltd., vide reference No. nil dated 22-07-2020 received on 10-08-2020 addressed to the Chairman, Registration Board wherein M/s Swiss Pharmaceuticals has submitted that due to pandemic of COVID-19 and lockdown situation in Karachi, their staff were not able to attend office and due to this, they were inept to join office to respond your letters. Now we therefore, confirm through this letter to challenge the testing report of Central Drug testing Laboratory, Karachi in Appellate laboratory. Their request for retesting of the said product, which is not within the prescribed period under the law so their request was not acceded.

PSI report in compliance to 287th meeting:

FID inspected M/s. Swiss Pharma dated 01-02-2021 w.r.t. decision of 287th meeting of Registration Board communicated vide letter No. 03-92/2018-QC (287-RB) dated 28-02-2019. The observation, findings and conclusion of report submitted by FID reproduced as:

"OBSERVATIONS OF CURRENT INSPECTION:
During the current inspection the panel inspected in details the respective production areas and QC Lab. The panel also reviewed in details the following documents.
1. The root cause analysis (RCA) carried out by the firm after failure of the product.
2. The Corrective and preventive action (CAPA) taken to avoid the occurrence and recurrence of such failures in future.
3. Respective utility which might be the possible source of failure.
4. SOP relating to QA and QC system and quality manual were also checked in detail.
FINDING OF THE PANEL:
After thorough inspection, people meet, documents reviewed the panel observed as follows:
1. In compliance to the directions contained in afore-mentioned DRAP Islamabad letter the firm started to investigate the root-cause of the failure against their approved SOP.
2. The firm had found during the detailed RCA that it was propeller/stirrer that was stopped in holding vessel during the filling operation that actually affected in the variation of in potency of the Diagyl Suspension 200mg/5mL, Batch Number 162.
3. After assessing the RCA of the failure the firm had taken CAPA for better product and process performance in the light of their approved SOP for Change Control Management. At present physical indicator with the tank is installed i.e. light system indication with the holding vessel propeller /mixer that indicates any type of malfunctioning propeller/mixer either mechanical or electrical failure during operation. (RCA attached
4. The firm also revised their Sampling procedure c f QA that will indicate any process failure during operation and incorporated in sampling SOP (SOP attached)

5. Re-trained their staff/operator (Training record checked and found satisfactory).
6. During suspension period three trial batches were also manufactured with revised formulation to further assess the product stability during its shelf-life. The respective data was reviewed in detail and found satisfactory results. (Copy annexed)
7. Overall the panel found that necessary RCA has been carried out by the firm and appropriate CAPA have been taken to avoid such failures again. Moreover stability trend of said product also found satisfactory during inspection. The Panel also found GMP conditions appropriate during the inspection.
8. The panel has checked the physical stock of Diagyl Suspension Batch No. 162 and found with the Firm, also the firm is agreed to incinerate the whole batch in the presence of DRAP Representative by third party and will submit the certificate of incineration to the DRAP Office.
Conclusion: Based on the above stated facts the panel concluded that the failure in assay was because of the utility failure and found other documents satisfactory, also firm did not utilize the stock of Diagyl Suspension B# 162 and is agreed to incinerate in the presence of DRAP representative, thus recommends the resumption of production of Diagyl Suspension."

The names provided by FID have been sent to the Division of Drugs Licensing to verify/provide the names for the period of October, 2019 for further processing of the case vide letter F.No.3-59/2018-QC dated 24-07-2020 with subsequent reminders dated 18-08-2020, 21-09-2020, 09-02-2021 and 06-12-2021. After verification of names from Licensing Division, a Show cause has been issued to firm dated 12-04-2022.

M/s. Swiss Pharmaceuticals (Pvt.) Ltd., Karachi replied vide ref no. nil dated 27-04-2022 wherein they requested to include their case in upcoming DRB meeting with PSI report for removal of suspension and approval to resume production as per the Drugs Act, 1976.

Evaluation of case:
Initially one sample was declared as Substandard which was discussed in 287th meeting of Registration Board held on 04-01-2019 where Board decided as under:

I. Submission of product development data by the firm.
II. Product Specific Inspection including verification of product development data by the following panel:
- Director, Drug Testing Laboratory, Karachi.
- Area Federal Inspector of Drugs.

III. Suspension of the Registration of the said product for six (06) months or till the verification of product development data and satisfactory report by the panel whichever is later.

Meanwhile, FID further submitted that he inspected:

1. M/S HANDS PAKISTAN PLOT NO. 158, GADAP ROAD, MALIR KARACHI dated 24-02-2020 and recovered the stocks of Suspension Diagyl (R. No. 020229) for which the registration Board in its 287th meeting had suspended the registration of the said product for six months or till the verification of product development data and satisfactory report by the panel whichever is earlier.
2. Plot No. C-36 SITE-II Super Highway Karachi. The alleged Plot was found owned by M/s Swiss Pharmaceutical (Pvt.) Ltd., and was very adjacent to their registered plot

No. A/159 SITE Super Highway Karachi. The said plot is declared as their ware house on Drug Sale license and used for storage of expired goods and same was seen stored there. This plot is connected to their main plot No. A/159 through ill-defined stores where firm had stored some chemicals, packing materials and finished goods. Among the finished good panel found fresh stock of syrup Diagyl, B.No.170 and 171, the registration of which was suspended by the Board.

FID also sampled 03 Batches (167, 170, 171) of Diagyl suspension for test/analysis from above mentioned premises which were also declared Substandard by CDL, Karachi.

The PSI was conducted after 2 years of the decision of Board only for Batch no 162 and panel recommended for resumption despite of that firm has not comply with the decision of Board and manufactured multiple batches of the product after suspension. Further, 03 more batches have been declared Substandard on assay.

The firm representatives have been called for personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

No person appeared before the Board on behalf of M/s. Swiss Pharmaceutical (Pvt.) Ltd., Karachi. Therefore, to meet the ends of justice, the Board decided to give one final opportunity of personal hearing to management of M/s. Swiss Pharmaceutical (Pvt.) Ltd., Karachi in its forthcoming meeting.

Case No. 08: NON-SUBMISSION OF METHOD OF TESTING OF SASTALKA LIQUID BY M/S. SWAT PHARMACEUTICALS, SAIDU SHARIF SWAT

FID I Peshawar has submitted a letter vide No. F. 3-20/2021-DRAP-4842 dated 16-12-2022 wherein he said that he received test report (Form-6) from the Federal Government Analyst, Central Drugs Laboratory with the following remarks;

- Sample could not be tested due to non-receipt of method of testing.

Details are:

Name of Product	Reg No.	Batch No.	Mfg. Date	Exp. Date	Claimed to be manufactured by	Report No. and Date	Remarks of CDL
Sastalka Liquid	003048	L017	06-21	06-23	M/s. Swat Pharmaceuticals, Saidu Sharif Swat.	IP.59/2021 dated 27-08-2021	Sample could not be tested due to non-receipt of method of testing.

FID also seek further course of action in such matters to finalize the case.

The case has been reviewed and a show cause has been issued to M/s. Swat Pharmaceuticals, Saidu Sharif Swat after approval from Chairman, Registration Board to explain the position vide F.No.13-27/2022-QC dated 14-03-2022. No reply received.

Firm has been called for personal hearing.

Procedings and Decision of 320th Meeting of Registration Board.

No person appeared before the Board on behalf of M/s. Swat Pharmaceuticals, Swat. Therefore, to meet the ends of justice, the Board decided to give one final opportunity of personal hearing to management of M/s. Swat Pharmaceuticals, Swat in its forthcoming meeting.

Case No. 09: CASE REFERED BY PQCB, PUNJAB REGARDING SUBMISSION OF FAULTY METHOD OF ANALYSIS OF PRODUCT CIFEROL TABLET SUBMITTED BY M/S MEDISAVE PHARMACEUTICALS, LAHORE.

Assistant Director (Lic), vide letter No. F. 1-88/2005-Lic (Vol-I) dated 10-08-2021 forwarded the subject mentioned case to the division of QA&LT DRAP, Islamabad.

In the subject mentioned case, Secretary, PQCB, Punjab vide letter No. PQCB/F-DRAP/229/21 dated 15-03-2021 has submitted as under:

"Provincial Inspector of Drugs, Kot Khawaja Saeed Teaching Hospital Lahore vide letter no. 662 DI/MMS dated 20-1-2021 requested guidance regarding test/analysis of below mentioned drug, for which case was filed by DTL Lahore vide letter no.01-143004811/11919/DTL dated 13-08-2020.

Sr no	*DI Area*	*DTL Letter No. and Date*	*Manufacturer*	*Product Name & Batch No.*	*Mfg & Expiry Date*	*Reason*
1.	*Kot Khwaja Saeed Teaching Hospital, Lahore*	*01 14300481 1/11919/ DTL dated 1308-2020*	*Medisave Pharmaceuticals*	*Ciferol Tablet (70mg + 70mcg) (Alendronate Sodium & Cholecalciferol) Batch no. 20E158*	*05-20 & 05-22*	*Method of analysis Alendronate Sodium and Cholecalciferol is not aavailable in any compendia and Product specification mentioned on label is MS. But manufacturer method of assay is not working properly.*

2. As method Is not specific and does not give reproduceable results therefore, the case is being file / disposed of.

PROCEEDINGS & DECISION BY THE BOARD;

Subject issue was considered by the Provincial Quality Control Board, under section 11 of the Drugs Act 1976 in its 220 meeting held on 02-02-2021.

Secretary PQCB apprised the Board about background of the subject matter which was discussed at length. The Board observed that all the manufacturers/ drug registration certificate holders are legally bound to provide product specification and method of analysis to the Government analyst/Drug Testing Laboratories, as when required. Decided by Registration Board In its 290 Meeting held on 3 and 4 July 2019, disseminated vide letter No. F. No 3- 37/2019-QC (290RB) dated 26th September, 2019. The need for product specifications /method of analysis become more critical when the drug is not available in official pharmacopoeias and/or the manufacturer has its own customized specifications/method for analysis.

In continuation of the above firm provides the in-house method of subject drug. However. Government Analyst of DTL-Lahore found that the given method of firm is not workable (faulty) and under such circumstances It is not possible to analyse the sample and therefore the case is filed.

The Board expressed its serious concerns over casual behavior on the part of the firms in this regard. Furthermore, the Board decided to recommended the Drug Regulatory Authority of Pakistan (DRAP) Islamabda for cancellation of registration of the above-mentioend drug, in the best public interest."

Proceedings and Decision of 312th meeting:

The Board after thorough deliberations and considering the recommendations of Secretary, PQCB, Punjab decided as under:

i. Issue Show cause notice firm for cancellation /suspension of their registered product.

In compliance to the decision of 312th meeting of the Registration Board, the firm was issued show cause notice vide F.No.03-33/2021-QC (312-RB) dated 28-10-2021. Till date no reply has been received from the firm.

The representatives of the firm are called before the Board for personal hearing.

Proceedings and Decision of 313th meeting:

The firm was called for personal hearing but no one appeared before the Board. The Board decided to grant M/s. Medisave Pharmaceuticals Lahore one final opportunity of personal hearing before the Board in its forthcoming meeting.

The representatives of firm are called before the Board for personal hearing.

Proceedings and Decision of 320th meeting:

Mr. Tariq Mahmood (Plant Manager) appeared on behalf of M/s. Medisave Pharmaceuticals, Lahore and submitted that M/s. Medisave Pharmaceuticals Lahore has provided correct testing method to DTL Lahore and the same has already been communicated to PQCB Lahore also. The Board keeping in view the details of case as provided by Secretary PQCB Lahore and reply of the firm decided as under:

i. **Area FID Lahore to conduct sampling of product Ciferol Tablet 70mg + 70mcg (Alendronate Sodium & Cholecalciferol) for the purpose of test/analysis by CDL Karachi.**

ii. **The firm will provide method of testing along with reference standard to CDL Karachi for testing of said product.**

Case will be placed before Registration Board after receiving above report from CDL Karachi

Case No. 10: **STOCKS OF DRUGS SEIZED UNDER SECTION 18 (1) OF THE DRUGS ACT, 1976 - M/S, PAK RISEN PHARMACEUTICALS, HATTAR.**

FID-I Peshawar vide letter No. F. 3-20/2021-PakRisen-DRAP-3242 dated 12-08-2021 informed regarding the inspection of the firm M/s. Pak Risen Pharmaceuticals, Plot No. 3, Phase-I-II, Industrial Estate, Hattar on 06-08-2021 and has requested for the permission to continue the safe custody of seized stocks till the decision of case.

02. Details of stocks are given as under:

s. No.	Name of item	Reg. No.	B. No.	Mfg. date	Exp. date	Mfg. by	Qty.
1	Pakcezone 250mg inj	040388	DV-2I08	06/21	05/23	M/s Pak Risen Pharmaceuticals, Plot No. 3, Phase I II, Industrial Estate, Hattar.	1 Pack
2	Metrozine 100ml infusion alongwith Original Batch manufacturing record (36 pages)	040412	LV-2125	06/21	05/23	-do-	1 Pack
3	Metrozine 100ml Infusion alongwith Original Batch manufacturing record (36 pages)	040412	LV-21I0	03/21	02/23	-do-	1 Pack

02. The same was granted to FID-I Peshawar vide letter F. No. 13-43/2021-QC dated 21-10-2021. Furthermore, FID I Peshawar was instructed to provide complete investigation of case for further processing of the matter.

03. FID I Peshawar has submitted following reason to declare the sample of product Pakcezone 250 inj and Metrozine 100ml Infusion as misbranded product:

S. No.	Product name	Mfg date	Exp date	Mfg by	Reason to declare subject sample as Misbranded
1	Pakcezone 250mj Injection B. No. DV-2I08	06/21	05/23	M/s Pak Risen Pharmaceuticals, Plot No. 3, Phase I II, Industrial Estate, Hattar.	The product Pakcezone (Reg. No. 040388) is Ceftriaxone 250mg Injection while one side of packing (where MRP & Mfg. License No. is printed) bears Pakcezone Injection as 500mg.
2	Metrorize 100ml Infusion B. No. LV-2125	06/21	05/23	-do-	The batch record and all the documents indicate that product is manufactured in the month of July 2021 as mfg. date. However label bears manufacturing date as 06/2021. The record reveals that preprinted labels with old mfg. date i.e., 06/2021 were used and besides misbranded, its

					deliberate manipulation of documents and data integrity is deliberately breached.
3	Metrorize 100ml Infusion B. No. LV-2110	03/21	02/23	-do-	The batch record and all the documents indicate that product is manufactured in the month of April 2021 as mfg. date. However, label bears manufacturing date as 03/2021. The record reveals that preprinted labels with old mfg. date i.e., 03/2021 were used and besides misbranded, its deliberate manipulation of documents and data integrity is deliberately breached

03. FID I Peshawar vide letter No. 11-53/2005-PakRisen-DRAP 4690 dated 06-12-2021 submitted the complete case and recommended as under:

"Recommendations

Based on conclusion of the cases vide column 10 above, there is sufficient evidence to believe that the drug product namely;

1. *Packzone 250mg Injection (040388), Batch No. DV-2108 Mfg. date 06/21 and expiry date 05/23*
2. *Metrorize 100ml Infusion (040412), Batch No. LV-2125, Mfg. date 06/21 and expiry date 05/23 &*
3. *Metrorize 100ml Infusion (040412), Batch No. LV-2110, Mfg. date 03/21 and expiry date 02/23*

are misbranded under Section 3 (s)(iv) of the Drugs Act, 1976, prohibited under section 23(a)(iii) and is punishable under section 27(2)(b) of the Drugs Act, 1976 of the DRAP Act, 2012. The case of the firm regarding GMP noncompliance was discussed in 283rd meeting of Central Licensing Board (CLB). The board suspended the production of the firm and constituted three member's panel for the inspection of the firm for rectifications of reported GMP noncompliance (Annex-V). It is proposed that the direction may be issued to the firm for avoiding above referred violations and to submit CAPA in this regard, to be verified by already constituted panel by the CLB n its 283rd Meeting. In case, firm fails to comply and reported by the panel, matter may be treated under the above referred provisions of the Drugs Act, 1976/ DRAP Act, 2012."

04. in the light of investigations of the FID-I Peshawar, show-cause notice was issued accordingly to following:

i) M/s. Pak risen Pharmaceuticals, Plot No. 3, Block B, Phase I-II, Industrial Estate, Hattar through its Proprietor

ii) Sabir Khan S/o Nannay Khan (Proprietor), M/s. Pak risen Pharmaceuticals, Plot No. 3, Block B, Phase I-II, Industrial Estate, Hattar.

05. In response to the show cause notice issued to the management of firm, reply received is given as under:

> *"It is stated with great concern that we have received Show cause NoticefF.No.13-43/2021- QC) on dated 8th Feb 2022 regarding sales of Misbranded Drugs.*
>
> *Dear Sir, we have gone through this case (sample seized by the Honorable FID) in detail and conducted a proper and deep investigation and we found a conclusion that at the time of Honorable FID Sir's inspection the collection of seized sample were done by our store attendant (non technical) as responsible technical persons were accompanying the honorable FID in inspection at that situation of stampede as finished goods store & other storage places & areas were empty (as wittiness by the FID) those samples were collected from controlled shelf of Q.C retain sample room where we use to keep misprinted and faulty/rejected stuff (one sample each) just to study and training of our Q.A/Q.C Staff & Those samples were not to be meant for market dispatch/ For sale by any means at all.*
>
> *The actual position is that the Batch of Pakcezone 250mg Batch # DV-2108 sent to market for sale was truly proof readed and checked and then released. The false/misprinted was caught at the spot and was discrded in the presence of QC staff. The production department was intimated on time.*
>
> *In addition to that in Ser.No.2 & Ser.No.3 Metrorise Case (Batch # LV-2125, LV-2110) we have not increased rather decreased their expiry by one month because of the shortage of labels and extreme demand in market, in effort not to effect market demand (human health) and customer's need for their patients we did So, but honorable FID has recognized us that it's too against the law so, we assure you/him that we will not repeat this practice in future again.*
>
> *Moreover we have written about all the in-questioned (Claimed Misbranded) Products to our sole distributor Lyall Pur Pharma (Detail Enclosed) just on FID's Direction and advice for their recall But we are informed that they have zero stock of these Products.*
>
> *Still we apologizes you for this staff negligence work. We expect and request you for not being harsh and show a kind response please."*

06. The accused are called before the Board for personal hearing.

Proceedings and Decision of 320th meeting:

No person appeared before the Board on behalf of M/s. Pak Risen Pharmaceuticals, Hattar. Therefore, to meet the ends of justice, the Board decided to give one final opportunity of personal hearing to management of M/s. Pak Risen Pharmaceuticals Hattar in its forthcoming meeting.

AGENDA ITEM NO. II: APPELLATE TESTING CASES

Case No. 11: **SUBSTANDARD MECONOR INJECTION MANUFACTURED BY M/S. NORTECH PHARMACEUTICALS (PVT.) LTD., ISLAMABAD.**

Federal Government Analyst CDL Karachi vide test report No. F. 5-3(I)/2021-CDL/S-803 dated 02-07-2021 it was informed that the sample of product "MecoNor Injection" Batch No. A-003 (Mfg. date 11-2020, Exp date 10-2022) sent to CDL Karachi by FID-I Islamabad has been declared as of substandard quality. Details of the test report are given as under:

S. No.	Test	Acceptance Criteria	Result	Reference
1.	Description	Reddish pink coloured solution in amber glass ampoule.	Complies	Mfg. Specs.
2.	Identification	The identification test must identify Mecobalamin.	Complies	Mfg. Specs.
3.	pH	5.5 to 6.5	**4.98** **Does not comply**	Mfg. Specs.
4.	Bacterial Sterility	Must be sterile	Complies	BP 2020
5.	**Assay.** Mecobalamin. (Label claim 500mcg/ampoule)	92.5% to 108.5%	106.2% Complies	Mfg. Specs.

02. FID-I Islamabad vide letter No. F. 3-4/2011-FID-I dated 23-09-2021 forwarded the request of M/s. Nortech Pharmaceuticals (Pvt.) Ltd., Islamabad dated 15-09-2021 for appellate testing of their sample of product namely "MecoNor Injection" batch No. A-003 declared substandard by CDL Karachi on 02-07-2021 (Report received by firm on 07-09-2021).

03. It is submitted the Registration Board in its 313th meeting decided as under:

*"**Proceedings and Decision of 313th Meeting of Registration Board.***

The Board after thorough deliberations and considering the facts of the case decided as:

i. The firm will provide OOS investigation and complete testing record of the concerned batch along with scientific justifications/grounds with the request of Appellate testing under section 22(4) of the Drugs Act 1976.

ii. Federal Government Analyst, Karachi will provide OOS investigation and complete testing record of such reports.

iii. Registration Board advised QA&LT Division to present all cases of Appellate Testing with these both set of documents along with technical report of the case."

04. Therefore, in the light of decision of Registration Board, a letter vide No. F. 03-27/2021-QC dated 22-12-2022 was issued to M/s. NorTech Pharmaceuticals (Pvt.) Ltd., Islamabad for submission of OOS investigation and complete testing record of the concerned batch of product MecoNor Injection along with scientific justifications/grounds with the request of Appellate testing under section 22(4) of the Drugs Act 1976 and to Federal Government Analyst CDL Karachi for submission of OOS investigation and complete testing record of report vide No. F. 5-3(I)/2021-CDL-S-803 dated 02-07-2021.

Technical evaluation of OOS report by QC section:

05. M/s. NorTech Pharmaceuticals Islamabad vide letter dated 03-01-2022 provided OOS investigation wherein they submitted the following:

- Testing method for pH of injection MecoNor (Mecobalamin) is non-pharmacopeial and the same was provided to CDL Karachi 23-06-2021.
- CDL Karachi concluded the test report while referring the controlled limits 5.5-6.5 of pH instead to limits provided by the firm i.e. 5.0-7.0.

06. However, on evaluation of the OOS report provided by the firm, it was observed that in Analysis report (Finished product) dated 24-12-2020, the pH of the batch in question of product Meconor injection was found to be 6.00 whereas in Analysis report (Finished product) dated 07-09-2021, the pH was found to be 5.7.

07. It seems that product is not stable as evident from the variation of more than ±0.1 in pH values as determined by the manufacturer itself.

Proceedings and Decision of 320th meeting:

The OOS investigation submitted by the firm and CDL Karachi were placed before the Board. The Board after thorough discussion and evaluation of the provided OOS investigation reports decided to accede with the request of M/s. Nortech Pharmaceuticals Islamabad to perform appellate test/analysis of Board's portion of sample for parameters that have been reported out of specifications (i.e. pH) by CDL Karachi of their product Meconr Injection Batch No. A-003 from NIH Islamabad.

Case No. 12: **MANUFACTURE AND SALE OF SUBSTANDARD REM-D 100MG/20ML IV INFUSION MANUFACTURED BY M/S. LIVEN PHARMACEUTICALS, KASUR.**

Federal Government Analyst CDL Karachi vide test report No. F. 5-3(LHR)/2021-CDL/S-1304 dated 03-11-2021 wherein it was informed that the sample of product "REM-D Infusion (Remdesivir 100mg/20ml)" Batch No. RD109 (Mfg. date 09-2021, Exp date 09-2022) sent to CDL Karachi by FID-II Lahore has been declared as of substandard quality. Details of the test report are given as under:

S. No.	Test	Acceptance Criteria	Result	Reference
1.	Description	Clear, colorless solution in glass vial	Complies	Innovator's Specs.
2.	Identification	The identification test must identify Remdisivir	Complies	Innovator's Specs.
3.	pH	3.0 to 4.0	4.0 Complies	
4.	Bacterial Sterility	Must be sterile	**Does not comply**	Innovators Specs.
5.	Bacterial Endotoxin	Not more than 1.0 E.U per mg	Complies	USP 43
6.	**Assay** Remdesivir, (Label claim 5mg/ml)	90.0% to 110.0%	97.4% Complies	USP 43 Innovator's Specs.

02. FID-II Lahore vide letter No. 17406/2021-DRAP(L-II) dated 19-11-201 forwarded the request of M/s. Liven Pharmaceuticals Kasur dated 05-11-2021 for appellate testing of Board's portion of sample of their product namely "REM-D Infusion" batch No. RD109 declared substandard by CDL Karachi on 03-11-2021.

03. It is submitted the Registration Board in its 313th meeting decided as under:

"Proceedings and Decision of 313th Meeting of Registration Board.

The Board after thorough deliberations and considering the facts of the case decided as:

i. *The firm will provide OOS investigation and complete testing record of the concerned batch along with scientific justifications/grounds with the request of Appellate testing under section 22(4) of the Drugs Act 1976.*
ii. *Federal Government Analyst, Karachi will provide OOS investigation and complete testing record of such reports.*
iii. *Registration Board advised QA&LT Division to present all cases of Appellate Testing with these both set of documents along with technical report of the case."*

04. In the light of decision of Registration Board, a letter vide No. F. 03-42/2021-QC dated 23-12-2021 was issued to M/s. Liven Pharmaceuticals Kasur for submission of OOS investigation and complete testing record of the concerned batch of product REM-D Infusion along with scientific justifications/grounds with the request of Appellate testing under section 22(4) of the Drugs Act 1976 and to Federal Government Analyst CDL Karachi for submission of OOS

investigation and complete testing record of report vide No. F. 5-3(LHR)/2021-CDL-S-1304 dated 03-11-2021.

Technical evaluation of OOS report by QC section:

05. M/s. Liven Pharmaceuticals Kasur vide letter dated 29-12-2021 provided OOS investigation repot of their product REM-D Infusion (Batch No. RD109). On evaluation of OOS investigation provided by Firm and CDL it was observed that CDL Karachi has performed Sterility testing as per USP 43. USP 43 method advises to use 2% or 20 (Whichever is less) containers if batch size is more than 500 units. The batch size of product is question is 1000 units. However, the firm has not provided the reference of method for sterility testing and has not provided the information regarding the numbers of units used for sterility testing.

Proceedings and Decision of 320th meeting:

The OOS investigation submitted by the firm and CDL Karachi were placed before the Board. The Board after thorough discussion and evaluation of the provided OOS investigation reports concluded that the firm is conducting bacterial sterility of the products on a non-pharmacopoeial method which is not validated therefore, the Board did not acceded the firm's request of appellate testing and decided to issue show cause notice for suspension/cancellation of the product namely Rem-D 100mg/20ml infusion manufactured by M/s. Liven Pharmaceuticals Kasur and call them for personal hearing before Registration Board in its forthcoming meeting.

Additional Agenda:

A. Pharmaceutical Evaluation & Registration Division:

The Authority in its 144th, as a one time exercise, approved out of queue consideration of submitted registration applications of following drugs in order to ensure their smooth and continuous supply in the market:

i. Paracetamol (Tablets, Infusion and Syrup / Suspension)
ii. Albumin bound Paclitaxel Injection
iii. Heparin and Enoxaprin Injection

PE&R and BE&R Divisions are advised to process the cases of abovementioned drugs without waiting for formal approval of minutes.

A: Paracetamol:

Applications submitted on Form 5:

1.	Name and address of manufacturer/ Applicant	Quaper Pvt.Ltd.,26-A small Industrial Estate, Lahore road, Sargodha.
	Brand Name + Dosage Form + Strength	Q-DOL CF TABLET
	Composition	Each Tablet Contains: Paracetamol…….…….500 mg Pseudoephedrine HCl……60 mg Chlorpheniramine Maleate…….4 mg
	Diary No. Date of R & I & fee	Dy. No 11792 dated 06-03-2019; Rs.20,000/- dated 06-03-2019.
	Pharmacological Group	NSAID, Antihistamine, Decongestant
	Type of Form	Form-5
	Finished product Specification	BP
	Pack size & Demanded Price	10*10's, As per SRO
	Approval status of product in Reference Regulatory Authorities	Not Confirmed
	Me-too status	Panadol CF Tablet by GSK (Reg# 013113)
	GMP status	Firm was granted GMP certificate dated 19-06-2019 on the basis of GMP inspection conducted on 28-01-2019 for Tablet (General). Panel inspection of firm for grant of additional sections was also conducted on 16-06-2020 & 18-06-2020 and firm was recommended for grant of following additional sections as per approved layout plan: 1. Tablet (General) section 2. Capsule (general) section 3. R&D laboratory 4. Sachet (general)

	Remarks of the Evaluator	Deficiency letter was issued to the firm and asked to provide evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.	Firm has submitted reply vide dairy No 22716 dated 11-08-2022 for standardization of their formulation and submitted revised Form-5 along with master formulation and outline of manufacturing method with revised label claim as under: Each Tablet Contains: Paracetamol……500 mg (B.P Specification) Me Too: Paracetamol 500mg tablet of M/s Siza, (Reg# 008731) RRA: MHRA Approved
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee that is Rs. 30,000/- for revision of formulation as per reference product as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.		
2.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd. 43-E, Sundar Industrial Estate, Lahore	
	Brand Name +Dosage Form + Strength	Molpa 665mg Tablet	
	Diary No. Date of R& I & fee	Form-**5D** Dy.No 16118 dated 07-03-2019 Rs.50,000/- dated 07-03-2019	
	Composition	Each XR Film Coated Tablet Contains: Paracetamol…665mg	
	Pharmacological Group	Analgesics and antipyretics anilide Paracetamol (Acetaminophen) ATC code: N02B E01	
	Form	Form-5D	
	Finished product Specifications	USP	
	Pack size & Demanded Price	14, 28, 56, 98's As per SRO	
	Approval status of product in Reference Regulatory Authorities	Paracetamol 665mg MR tablet (approved by TGA of Australia)	
	Me-too status	Panadol Extend by GSK (097070)	
	GMP status	GMP certificate dated 31-07-2018 Valid till 2 years	
	Remarks of the Evaluator.	stability data is needed	
	Decision: Deferred for submission stability study data as per the guidelines provided by the Board in its 293rd meeting.		
3.	Name and address of manufacturer / Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road,Lahore	
	Brand Name +Dosage Form + Strength	Molta Injection 300mg/2ml	
	Diary No. Date of R& I & fee	Form-5 Dy.No 13992 dated 07-03-2019 Rs.20,000/- dated 07-03-2019	
	Composition	Each 2ml Contains: Paracetamol…300mg	

	Pharmacological Group	Analgesics and antipyretics anilide Paracetamol (Acetaminophen) ATC code: N02B E01
	Form	Form-5
	Finished product Specifications	Neutro Specifications
	Pack size & Demanded Price	2 ml glass ampoule 5's As SRO
	Approval status of product in Reference Regulatory Authorities	Paracare by M/S Advacare Pharma (USFDA) (Not verifiable from USFDA site)
	Me-too status	Panum injection by M/S English pharma (040140)
	GMP status	GMP certificate dated 14-04-2022 valid till 2 year
	Remarks of the Evaluator.	RRA not verified
	Decision: Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board	
4.	Name and address of manufacturer / Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road, Lahore
	Brand Name +Dosage Form + Strength	Molta Tablets 665mg
	Diary No. Date of R& I & fee	Dy.No 13997 dated 07-03-2019 Rs.50,000/- dated 07-03-2019
	Composition	Each XR Film Coated Tablet Contains: Paracetamol…665mg
	Pharmacological Group	Analgesics and antipyretics anilide Paracetamol (Acetaminophen) ATC code: N02B E01
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	14, 28, 56, 98's As per SRO
	Approval status of product in Reference Regulatory Authorities	Paracetamol 665mg MR tablet (approved by TGA of Australia)
	Me-too status	Panadol Extend by GSK (097070)
	GMP status	GMP certificate dated 14-04-2022 valid till 2 year
	Remarks of the Evaluator.	stability data is needed
	Decision: Deferred for submission stability study data as per the guidelines provided by the Board in its 293rd meeting.	
5.	Name and address of manufacturer / Applicant	M/s GT Pharma Pvt Ltd. 23km, Raiwind Road, Lahore
	Brand Name +Dosage Form + Strength	Paramol 1000mg Injection
	Diary No. Date of R& I & fee	Form-5 Dy.No 15050 dated 07-03-2019 Rs.20,000 dated 07-03-2019
	Composition	Each 100ml Vial Contains: Paracetamol … 1000mg / 100ml Vial (10mg /ml)
	Pharmacological Group	Analgesics and antipyretics anilide Paracetamol (Acetaminophen) ATC code: N02B E01
	Form	Form-5
	Finished product Specifications	GT Specifications

	Pack size & Demanded Price	1's As per SRO (Glass vial with stopper)
	Approval status of product in Reference Regulatory Authorities	Paracetamol 10mg/ml Solution for Infusion of MHRA approved
	Me-too status	Paedal Infusion of M/S Regal Pharmaceutical (082000)
	GMP status	GMP certificate dated 13-10-2021 valid till 2 years
	Remarks of the Evaluator.	Liquid injectable liquid ampoule section present
	Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of applicable fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021	
6.	Name and address of manufacturer / Applicant	M/s Amros Pharmaceuticals A-96, S.I.T.E, Super Highway, Karachi
	Brand Name +Dosage Form + Strength	Amrocetal Infusion 1000mg/100ml
	Diary No. Date of R& I & fee	Form-5 Dy.No 15369 dated 07-03-2019 Rs.20,000/- dated 07-03-2019
	Composition	Each 100ml Contains: Paracetamol…1000mg
	Pharmacological Group	Analgesics and antipyretics anilide Paracetamol (Acetaminophen) ATC code: N02B E01
	Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	3x10's As per SRO 100 ml glass vial with Bromo butyl stopper
	Approval status of product in Reference Regulatory Authorities	Paracetamol 10mg/ml Solution for Infusion of MHRA approved (100 ml glass vial with Bromo butyl stopper)
	Me-too status	Paedal Infusion of M/S Regal Pharmaceutical (082000)
	GMP status	13-10-2020 GMP certificate valid till 2 year is provided section available are • injectable section (general and cephalosporin) • injectable section (Veterinary)
	Remarks of the Evaluator.	injectable section (general and cephalosporin) present
	Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of applicable fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021	

Applications Submitted on Form 5F:

7.	Name, address of Applicant / Marketing Authorization Holder	M/s British Pharmaceuticals. 23-Km Sheikhupura Road, Lahore
	Name, address of Manufacturing site.	M/s British Pharmaceuticals. 23-Km Sheikhupura Road, Lahore

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 22083 dated 03-08-2022
	Details of fee submitted	Rs.30,000/- dated 27-07-2022
	The proposed proprietary name / brand name	**Bripara 500mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol USP…..500mg
	Pharmaceutical form of applied drug	tablet
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	BP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Paracetamol 500mg Tablets by M/s Dr. Max Pharma Netherlands.
	For generic drugs (me-too status)	Panadol 500mg Tablets Manufactured by M/s Pharmatec Pakistan (Pvt) Ltd and marketed by M/s GlaxoSmithKline Pakistan. (Reg. No.: 101138)
	GMP status of the Finished product manufacturer	Renewal of DML granted dated 12-01-2022.
	Name and address of API manufacturer.	M/s Zenith Chemical industry Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 48 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Paracetamol 500mg Tablets of M/s GlaxoSmithKline Pakistan.
	Analytical method validation/verification of product	Method validation studies have submitted including, system suitability, specificity, linearity, accuracy, precision repeatability, Intermediate precision and robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s Zenith Chemical industry Lahore.		
API Lot No.	ZPAR20-350		
Description of Pack (Container closure system)	Alu-PVC blister packed		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 12 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9 & 12 (Months)		
Batch No.	B1	B2	B3
Batch Size	5000 Tablets	5000 Tablets	5000 Tablets
Manufacturing Date	04-2021	04-2021	04-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	• --
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of certificate of Good Manufacturing Practices (GMP) issued by Hebei Food and Drug Administration. (valid till 08-07-2023).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Section #.	Deficiencies
3.2.S.4	• Drug substance analytical method verification studies shall be submitted by M/s British pharmaceuticals.
3.2.P.1	Drug product description declares it as film coated tablet whereas submitted composition is for uncoated tablet.
3.2.P.2.2.1	Clarification shall be submitted for reporting f2 factor value as 100 for CDP studies in three dissolution mediums of pH 1.2,4.5 & 6.8.
3.2.P.5.3	Performance of accuracy & precision parameter during analytical method verification studies has not been conducted as per recommendations of ICH Q2 (R1) guidelines.
3.2.P.8.3	• Document for the procurement of drug substance shall be submitted. • Complete analytical record for the performance of dissolution test during stability studies shall be submitted. • Complete raw data sheets wherein details of sample solution preparation, standard solution preparation, weight of standard & sample and calculation formula applied for the test Assay & Dissolution test shall be submitted for complete stability studies.

Decision: Deferred for;

- **Submission of drug substance analytical method verification studies by M/s British pharmaceuticals.**
- **Clarification since drug product description declares it as film coated tablet whereas submitted composition is for uncoated tablet.**
- **Clarification shall be submitted for reporting f2 factor value as 100 for CDP studies in three dissolution mediums of pH 1.2,4.5 & 6.8.**
- **Performance of accuracy & precision parameter during analytical method verification studies has not been conducted as per recommendations of ICH Q2 (R1) guidelines.**
- **Performance of accuracy & precision parameter during analytical method verification studies has not been conducted as per recommendations of ICH Q2 (R1) guidelines.**
- **Submission of document for the procurement of drug substance shall be submitted.**
- **Submission of complete analytical record for the performance of dissolution test during stability studies.**
- **Submission of complete raw data sheets wherein details of sample solution preparation, standard solution preparation, weight of standard & sample and calculation formula applied for the test Assay & Dissolution test for complete stability studies.**

8.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy.No 3185 dated 02-02-2022
	Details of fee submitted	Rs.30,000/- dated 20-12-2021
	The proposed proprietary name / brand name	**Acetaget 500mg Tablets**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol USP…..500mg
	Pharmaceutical form of applied drug	White colored, round shaped, core tablet, plain on both sides.
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	USP Specs.
	Proposed Pack size	20 x 10's 50 x 10's
	Proposed unit price	Rs. 540 (20 x 10's)/-, Rs. 1350 (50 x 10's)/-
	The status in reference regulatory authorities	Paracetamol 500mg Tablets by M/s Dr. Max Pharma Netherlands.
	For generic drugs (me-too status)	Panadol 500mg Tablets Manufactured by M/s Pharmatec Pakistan (Pvt) Ltd and marketed by M/s GlaxoSmithKline Pakistan. (Reg. No.: 101138)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	**M/s HEBEI JIHENG (GROUP) PHARMACEUTICAL CO., LTD.** Southeast Xijingming Village, Donganzhuang Township, Shenzhou County, Hengshui City, Hebei Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (31512021, 31512025, 31512026)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Paracetamol 500mg Tablets by M/s Pharmatec Pakistan (Pvt) Ltd and marketed by M/s GlaxoSmithKline Pakistan, by performing quality tests (Appearance, Average weight, Disintegration time, Assay and Dissolution). CDP has been performed against the same brand that is Paracetamol 500mg Tablets by Pharmatec Pakistan (Pvt) Ltd and marketed by GlaxoSmithKline Pakistan, in Acidic media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The f2 values are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including, system suitability, specificity, linearity, accuracy, precision repeatability, Intermediate precision and robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s HEBEI JIHENG (GROUP) PHARMACEUTICAL CO., LTD. Southeast Xijingming Village, Donganzhuang Township, Shenzhou County, Hengshui City, Hebei Province, China.		
API Lot No.	0000170088		
Description of Pack (Container closure system)	Alu-PVDC blister packed in unit carton (20 x 10's),(50 x 10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 12 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9 & 12 (Months)		
Batch No.	551DS01	551DS02	551DS03
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	05-10-2020	12-10-2020	12-10-2020
Date of Initiation	12-10-2020	13-10-2020	13-10-2020
No. of Batches	03		

Administrative Portion

13.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine (Ebastine) Tablets 10mg & 20mg on 6th May, 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The

<table>
<tr><td></td><td></td><td>case was approved and the inspection report confirms following points:
The HPLC software is 21CFR Compliant as per record available with the firm.
Audit trail on the testing reports is available.
Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
Related manufacturing area, equipment, personnel and utilities are GMP compliant.</td></tr>
<tr><td>14.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Firm has submitted copy of certificate of Good Manufacturing Practices (GMP) issued by Hebei Food and Drug Administration. (valid till 08-07-2023).</td></tr>
<tr><td>15.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>31909052</td><td>1909ZP24</td><td>500kg</td><td>25-10-2019</td></tr>
</table></td></tr>
<tr><td>16.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td></tr>
<tr><td>17.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.</td></tr>
<tr><td>18.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted record of digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
<tr><td colspan="3">Remarks of Evaluator:
<table>
<tr><th>Section #.</th><th>Deficiencies</th><th>Firm’s response</th></tr>
<tr><td>3.2.S.4</td><td>Chromatographic conditions for the performance of Assay test, in the analytical procedure submitted from drug substance manufacturer, are different form that recommended by USP monograph of “Acetaminophen”.
Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for shall be submitted.</td><td>This is to bring to your kind attention that API manufacturer has made minor adjustment in the test procedure for Assay as described in USP monograph. The adjustment is made to make analytical method simpler and efficient. The analytical method is further validated that confirms that proposed method is suitable for intended use. Moreover, M/s Getz Pharma has developed test procedure for Acetaminophen in accordance with USP monograph and Analytical Method Verification studies have been performed accordingly.

Please refer to Annex 1 for Analytical Method Verification studies including specificity, linearity, repeatability and range performed by the Drug Product manufacturer.</td></tr>
</table></td></tr>
</table>

		This is to bring to your kind attention that we have used 100% API without any placebo in Analytical Method Verification Studies of Acetaminophen; therefore, requirement of accuracy is not applicable. Further, we have performed linearity to check area response of the sample as the concentration of the sample raised within working range of sample i.e., 50% - 150%.
3.2.S.5	COA of reference/working standard shall be submitted, used for the analysis of drug substance by M/s Getz pharma.	COA of reference/working standard used for the analysis of drug substance by M/s Getz Pharma has been submitted.
3.2.P.5	Submitted drug product specifications refer to USP, whereas the analytical procedure for Assay test is not as per USP monograph of "Acetaminophen tablets". Justification shall be submitted in this regard. Analytical method verification studies are not for the Assay method as recommended by USP monograph of "Acetaminophen tablets".	This is to inform you that the concentration of standard and sample solution preparation are exactly same as recommended in USP monograph of "Acetaminophen Tablets. However, we have modified chromatographic conditions for Assay method using chromatographic conditions for Related Substances since USP allows the use of alternate methods like in case of ease of testing. Therefore, we have adopted different chromatographic condition for Assay method. Further we have completely validated said Assay method and found to be accurate and precise that will produce equivalent results as USP. • In contrary to the claim of firm the alternate method adopted for Assay test is not as per method of related substances.
3.2.P.8.3	Assay test in the submitted stability studies have not been conducted as per analytical procedure recommended by "Acetaminophen tablets". Justification shall be submitted in this regard.	This is to inform you that for stability studies we have followed different Assay method from USP as discussed in point 3.2.P.5. Further, we have completely validated said Assay method and found to be accurate and precise that will produce equivalent results as USP.

Decision: The Board Deferred the case for scientific justification for performing assay testing during the stability studies using a different method than described by USP.

9.	Name, address of Applicant / Marketing Authorization Holder	M/s Variant Pharmaceuticals (pvt) ltd., Plot No. 5, M-2, Pharmazone, 26km Mian Sharaqpr road, District Sheikhupura, Pakistan.
	Name, address of Manufacturing site.	M/s Variant Pharmaceuticals (pvt) :td., Plot No. 5, M-2, Pharmazone, 26km Mian Sharaqpr road, District Sheikhupura, Pakistan.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17402 dated 14-06-2022
	Details of fee submitted	PKR 30,000/-: dated 08-06-2022
	The proposed proprietary name / brand name	Paracetamol 500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol……500mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	BP
	Proposed Pack size	10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved.
	For generic drugs (me-too status)	Panadol 500mg tablet by GSK.
	GMP status of the Finished product manufacturer	DML is issued w.e.f 13/02/2020 vide letter no. F.1-1/2016-Lic dated 24/02/2020.
	Name and address of API manufacturer.	Ms Pharmagen Limited Kot Nabi Bukshwala, 34 km Ferozpur roaD Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, impurity testing for impurity A-G, analytical procedure and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

		B: LE00510911/001/2016, LE00510911/002/2016, LE00510911/003/2016
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Comparative dissolution profile is submitted against Calpol 500mg Tablet by GSK in 0.1N HCl, Phosphate Buffer and Acetate Buffer. The values of F2 are in acceptable range (B: PK3H). Pharmaceutical equivalence is established against Edarbi 40mg tablet (B: 483803) by performing all the quality tests.
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Ms Pharmagen Limited Kot Nabi Bukshwala, 34 km Ferozpur roaD Lahore.		
API Lot No.	00510911/078/2020		
Description of Pack (Container closure system)	Alu-alu blister pack		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 tablets	2000 tab	2000 tab
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	25-10-2021	27-10-2021	29-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 06/2019-DRAP(AD/607409-5300 dated 11/01/2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The assay is performed by UV method as per BP.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Pharmaceutical equivalence and comparative dissolution profile is performed against Calpol Tablet mfg by M/s GSK.

Sr. No.	Observations	Response
1	In section 1.5.6 the specifications mentioned are USP/BP, please specify the monograph according to which the applied product is developed.	"Specifications of finished drug product is BP, in dossier, due to typographical error both specifications were mentioned but in module 2.3 and on covering letter the specifications are mentioned as BP".
2	Analytical method verification studies for drug substance performed by drug product manufacturer.	Verifications studies are submitted for drug substance performed by drug product manufacturer.
3	Invoice for procurement of API	Copy of invoice no. 322 dated 05/09/2021 is submitted.

Decision: Approved.

10.	Name, address of Applicant / Marketing Authorization Holder	M/s Fahmir Pharma Pvt Ltd. Main Mandianwala stop, 26 km, Lahore Jaranwala road, Tehsil Sharaqpur sharif, Distt. Sheikhupura"
	Name, address of Manufacturing site.	M/s Fahmir Pharma Pvt Ltd. Main Mandianwala stop, 26 km, Lahore Jaranwala road, Tehsil Sharaqpur sharif, Distt. Sheikhupura"
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22082 dated 14-06-2022
	Details of fee submitted	PKR 30,000/-: dated 08-06-2022
	The proposed proprietary name / brand name	Panamir 500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol……500mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	BP

	Proposed Pack size	1x10's , 2x10's, 3x10's, 5x10's 10x10's, 10x20's, (500's 1000's Jar Pack)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved.
	For generic drugs (me-too status)	Panadol 500mg tablet by GSK.
	GMP status of the Finished product manufacturer	Not provided
	Name and address of API manufacturer.	**Zenith chemical Industry Lahore** 16 km off Ferozpur Road, behind Wapda Grid Station 1 KM of Chandra Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, impurity testing for impurity A-G, analytical procedure and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months B: P11-001, P11-002, P11-003
	Module-III (Drug Product):	The official monograph of the applied product is present in B.P. The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Panadol 500mg tablet by GSK Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form) (B:PPXI). CDP has been performed against the same brand that is Panadol 500mg Tablet by Fahmir Pharma in 0.1N HCl, Acetate buffer (4.5pH) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range (B:PPXI).

	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Zenith chemical Industry Lahore 16 km off Ferozpur Road, behind Wapda Grid Station 1 KM of Chandra Road, Lahore		
API Lot No.	ZPAR20-350		
Description of Pack (Container closure system)	Alu-Pvc blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	Trail -1	Trail -2	Trail -3
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	08-09-2021	09-09-2021	10-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 141/2019-DRAP (AD-813875-228 issued by DRAP valid till 16-12-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Invoice No. 00011/0321 dated 05/03/2021 is submitted (Local)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The assay is performed by UV method as per BP.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Observations	Response
1	Provide 6 months stability study data (Accelerated and Real time) according to the conditions of zone IV_A since 3 months data is submitted.	

2	Analytical method verification studies for drug substance performed by drug product manufacturer.	
3	The submitted process validation documents describe the process of film coating while the applied product is uncoated, please clarify. Moreover, as per the BMR provided in the submitted dossier, the applied product is film coated while as per the manufacturing method and master formula no step of film coating is involved.	
4	Please submit compatibility of excipients with the drug substance.	
5	Provide record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	
6	GMP certificate / Last inspection report of finished product manufacturer is required.	

Decision: Deferred for;

- **Submission of 6 month stability study data (Accelerated and Real time) according to the conditions of zone IV_A since 3 months data is submitted.**
- **Submission of analytical method verification studies for drug substance performed by drug product manufacturer.**
- **Clarification since the submitted process validation documents describe the process of film coating while the applied product is uncoated, please clarify. Moreover, as per the BMR provided in the submitted dossier, the applied product is film coated while as per the manufacturing method and master formula no step of film coating is involved.**
- **Submission of compatibility of excipients with the drug substance.**
- **Submission of record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).**
- **Submission of GMP certificate / Last inspection report of finished product manufacturer is required.**

11.	Name, address of Applicant / Marketing Authorization Holder	M/s Reliance Pharma Plot # 8, Street No. S-8, RCCI, Industrial Estate, Rawat Islamabad-Pakistan
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt) Ltd Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10339 dated 22/04/2022
	Details of fee submitted	PKR 75,000/-: dated 30/03/2022
	The proposed proprietary name / brand name	Relimol Infusion

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml Contains: Paracetamol …1000mg
	Pharmaceutical form of applied drug	Clear and colorless liquid filled in clear and colorless glass vials.
	Pharmacotherapeutic Group of (API)	Analgesics and antipyretics
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	1 glassVial (100ml)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Acetaminophen 1g/100ml Infusion by Baxter Healthcare Coporation (United states), FDA Approved.
	For generic drugs (me-too status)	Provas Infusion by Sami Pharmaceuticals (Pvt) Ltd. Reg No: 053223
	GMP status of the Finished product manufacturer	GMP certificate valid till 10/02/2022 New license Applied on 22/12/2021.
	Name and address of API manufacturer.	M/s HEBEI JIHENG PHARMACEUTICAL CO., LTD. No.1 Weiwu Street Industrial Park Hengshui City, Hebei Province, 053000 China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time 60months : 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated 6 months: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (011608001, 011608002 & 011608003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (Liquid particle count) and its verification studies, batch analysis and justification of specification, reference standard,

		container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the reference product OFIRMEV Infusion by Mallinckrodt Pharmaceuticals. Batch No 1019689 by performing quality tests (Physical appearance, pH, Liquid Particle count, Percent assay). CDP is not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**M/s HEBEI JIHENG PHARMACEUTICAL CO., LTD.** No.1 Weiwu Street Industrial Park Hengshui City, Hebei Province, 053000 China.		
API Lot No.	011803173		
Description of Pack (Container closure system)	Clear glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 36 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 & 36 (Months)		
Batch No.	0718801	0718802	0718803
Batch Size	5000 Vials	5000 Vials	5000 Vials
Manufacturing Date	07-2018	07-2018	07-2018
Date of Initiation	07-08-2018	15-08-2018	13-09-2018
No. of Batches	03		

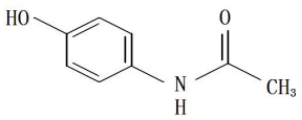
REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

19.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A

20.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of drug production license certificate No. JI20150076 issued by Hebei Drug Administration valid till 30/08/2025 has been submitted.
21.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of clearance certificate dated 31-05-2018 is submitted .
22.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
23.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted.
24.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
REMARKS OF EVALUATOR		

Sr. No.	Section	Observations/ Deficiencies	Response submitted by Firm and Evaluation
1	1.4.3	• Provide notarized copy of contract manufacturing agreement • Provide documents confirming number of approved sections of the applicant (DML holder) • Provide details of already registered drug products of contact giver on contract manufacturing,	• Notarized copy of Contact manufacturing agreement. Copy of agreement • Section approval letter of Applicant (DML holder) 4 sections • List of already registered drug products of contact giver on contract manufacturing. 6 Products
2	2.3.S.3.1	• Submit conclusion from the list of studies performed (e.g IR, UV, NMR, MS, Elemental analysis.)	• Based on the analysis of the Paracetamol samples produced in Hebei Jiheng Pharmaceutical Co. Ltd. , and with the comparison to results of the Paracetamol EP CRS (Batch No.: 4.1), we confirm that Paracetamol sample matches the chemical structure below,  which is defined as the structure of Paracetamol in EUR. Ph. 8. The crystal form of the product is identical with EP CRS Lot 4.1. the summary is provided in **ANNEXURE 2.**
3	2.3.S.4.4	• Submit discussion and justification for any incomplete	• Complete testing is performed and revised COA is attached in **ANNEXURE 3**

		analysis of the drug substance/API by drug product manufacturer. • The COA of API of DP manufacturer mentions reference of API manufacturer both USP and BP.	Evaluation The COA mentions supplier/manufacturer as M/s Global pharmaceuticals. • We use BP specification as reference for testing; USP was only referred for verification purpose.
4	2.3.P.1	• The quantity of API per unit is 1020mg per 100ml whereas the applied strength is 1000mg/100ml. clarification is required with respect to composition of FPP.	• As per Standard for fill volume we go for the upper limit therefore the fill volume of paracetamol infusion is 102ml for which we use 1020mg of paracetamol API. Evaluation Submit scientific rationale for batch formula. The BMR mentions the Quantity of API 1000mg/100ml. Potency adjustment has not been done.
5	2.3.P.2.2.1	The pharmaceutical equivalence studies of applied formulation is with Orfimex 100ml infusion whose marketing status is discontinued as per USFDA database.	As we have already approved paracetamol infusion Brand Name: ACETAMOL 100ml INFUSION- manufacturer Vision Pharmaceuticals Pvt. Ltd. We will submit pharmaceutical equivalence with Brand leader as soon as possible.
6	2.3.P.5.1	The specification of drug Product does not include the test of osmolality which has been both determined by innovator and generic product the pH of both generic and innovator product is between 5 – 7 whereas your claimed specification are pH 4 – 7.	We have now included the test for osmolality in our standard analytical procedures. The revised standard analytical procedure and COA is attached in **ANNEXURE 4**
7	2.3.P.5.6	Provide justification of specification of all the tests specified in section 2.3.P.5.1	Specification of product is as per Innovator specs.
8	3.2.S.4.2	Detailed analytical procedures for testing of drug substance shall be provided by the drug product manufacturer for API.	A detailed analytical procedure for testing of drug substance by the drug product manufacturer for API has been provided.
9	3.2.S.4.3	Analytical method verification studies including specificity, Accuracy and repeatability (method precision) performed by the drug product manufacturer shall be submitted for API.	Analytical method verification studies including specificity, Accuracy and repeatability (method precision) performed by the drug product manufacturer for API has been provided.
10.	3.2.S.4.4	A discussion and justification shall be provided for any incomplete analysis of the drug substance/ API by drug product manufacturer.	• Complete testing is performed and revised COA has been submitted. • We use BP specification as reference for testing; USP was only referred for verification purpose.
Decision: Deferred for; • **Justification for not performing pharmaceutical equivalence against the reference / innovator's product.**			

	• **Clarification regarding the specification of drug Product does not include the test of osmolality which has been both determined by innovator and generic product the pH of both generic and innovator product is between 5 – 7 whereas your claimed specification are pH 4 – 7.** • **Clarification since potency adjustment has not been made.** • **Submission scientific rationale for submitted batch formula.**	
12.	Name, address of Applicant / Marketing Authorization Holder	M/s. Saibins Pharmaceuticals, Islamabad. **Office Address:** House No.697 Street No.70 Sector I-8/3 Islamabad. **Factory Address:** Plot # No 316 Industrial Triangle Kahuta Road Islamabad.
	Name, address of Manufacturing site.	M/s Hamaz Pharmaceuticals (Pvt) Ltd. 13-KM Lutfabad, Bosan Road, Multan.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8314 dated 30/03/2022
	Details of fee submitted	PKR 75,000/-: dated 22/10/2021
	The proposed proprietary name / brand name	Saimol Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Paracetamol ….1gm
	Pharmaceutical form of applied drug	Solution for infusion
	Pharmacotherapeutic Group of (API)	other analgesics and antipyretics, ATC Code: N02BE01
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	1’s, 10’s or 20’s
	Proposed unit price	Glass vial,As per SRO
	The status in reference regulatory authorities	Paracetamol …. NASID (Acetaminophen) Reference: USFDA,Reference ID: 3839318
	For generic drugs (me-too status)	Bofalgan 1g/100ml Infusion M/s Bosch Pharmaceuticals
	GMP status of the Finished product manufacturer	Last GMP inspection conducted on 13-04-2021, and the report concludes that “All the observations pointed out during inspection were discussed with the management of the firm and they were committed to overcome before next periodic inspection. Based on the above observations and keeping in view their attitude for better compliance, their current compliance level is rated as Good.”

	Name and address of API manufacturer.	M/s. Pharmagen Limited, Kot Nabi Bukshwala, 34 KM Ferozepur Road, Lal
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity, specifications, analytical procedures and its verification, batch analysis container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:Lab.Exp.001/2016,lab.Exp.002/2016, Lab.Exp.003/2016
	Module-III (Drug Product):	The firm has submitted detail of manufacturer, description of manufacturing process and controls, specifications, analytical procedure batch analysis,container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against Bofalgan Infusion 1g by Bosch pharmaceuticals performing quality tests (pH, Assay, Uniformity of dosage form).
	Analytical method validation/verification of product	Complete validation studies have not been performed.

STABILITY STUDY DATA

Manufacturer of API	M/s. Pharmagen Limited, Kot Nabi Bukshwala, 34 KM Ferozepur Road, Lahore.
API Lot No.	5301-20-029
Description of Pack (Container closure system)	100 ml Type II colorless glass vial with bromobutyl stopper and an aluminum cap
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 36 months Accelerated: 12 months
Frequency	Real Time: 0, 3,6,9,12,18,24months (Completed) Accelerated: 0, 1,2,3,4,5,6,12 months (Completed)

Batch No.	ET901	ET902	ET903
Batch Size	2500vials	2500vials	2500vials
Manufacturing Date	07.03.2019	12.03.2019	16.03.2019
Date of Initiation	13.05.2019	13.05.2019	13.05.2019
No. of Batches	03		

Administrative Portion

25.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
26.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate No. 06/2019-DRAP (AD/607409-530) issued by DRAP.
27.	Documents for the procurement of API with approval from DRAP (in case of import).	• Local Manufacturer
28.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Analytical method is on HPLC supporting data is of UV.
29.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
30.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S. No	Sections	Observations/Deficiencies/ Short-comings
1.	1.4.3.	➢ Provide notarized copy of Contract manufacturing agreement. ➢ Provide documents confirming number of approved sections of the applicant (DML holder) and evidence of SVP section. ➢ Provide details of already registered drug products of contract giver on contract manufacturing.
	MODULE II	Correct all relevant details as mentioned in module III.
2.	3.2.S.3.2	Submit list of Drug Substance / API-related impurities and process-related impurities shall be submitted along with acceptance limits.
3.	3.2.S.4.2	Detailed analytical procedures for the testing of drug substance shall be provided by Drug product manufacture for API.
4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted for API.
5.	3.2.S.4.4	A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer. Submit reference for Specifications of API tested by FPP manufacturer.
6.	3.2.S.4.5	Submit justification of specifications.
7.	3.2.S.7 Stability	The stability testing of API does not include all the tests of BP. The test of LOD has been changed to water content in specification as mentioned in 3.2.S.7.1. Justification is required with respect to incomplete testing of API.
8.	3.2.P.1	The quantity of the ingredients used in the applied formulation vary vastly from innovator i.e. 3850 mg mannitol has been used in the innovator

		product whereas, your formulation has 76.6 mg. Justification is required with respect to quantitative composition.
9.	3.2.P.2.3	Submit discussion of the parameters relevant to the performance of the Drug Product (e.g. pH, ionic strength, dissolution, particle size distribution, polymorphism, rheological properties).
10.	3.2.P.3.2	The batch formula mentioned in section 3.2.P.3.2 is different then 3.2.P.2.2.1 and BMR submitted in section 2.3.R.1.1.
11.	3.2.P.3.3	The manufacturing process does not mention the filtration step. Clarification is required.
12.	3.2.P.3.5	Submit process validation report for commercial batches.
13.	3.2.P.5.1	The specification does not include tests for extractable volume, osmolality and dissolved oxygen as paracetamol is known to be unstable in the presence of oxygen.(Apotel 10 mg/ml PAR) Submit acceptance criteria for all the tests of specifications as you have mentioned "should meet the requirements'. The pH of FDA innovator product is approximately 5.5 and generic product is pH 4.5 – 6.0 whereas, your limit is 3-7.5 .Justification is required. The range of assay is 100%-103%. Justifications is required.
14.	3.2.P.4.3	Analytical method validation should include all the steps of validation as only accuracy,linearity and precision has been discussed.
15.	3.2.P.5.4	The copies of complete analysis of at least two batches shall be provided.
16.	3.2.P.6	COA of primary / secondary reference standard including source and lot number shall be provided.
17.	3.2.P.8.3	Submit stability data as per DRAP CTD guidance document. The testing of the drug product should be as per section 3.2.4.2 .The drug product testing is on UV as per submitted supporting documents whereas, as per method it was on HPLC.

Decision: The Board deferred the case for submission of documents and clarification of points mentioned above.

13.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.12950 dated 27/05/2022
	Details of fee submitted	PKR 30,000/-: dated 27/05/2022
	The proposed proprietary name / brand name	Acetaget Solution for IV Infusion 1g/100ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Paracetamol USP….1g
	Pharmaceutical form of applied drug	Clear colorless liquid, filled in clear glass vial.

	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	100ml x 1's
	Proposed unit price	Rs. 240/-
	The status in reference regulatory authorities	Paracetamol Accord 10mg/ml Solution for Infusion by M/s Accord Healthcare Limited, UK. MHRA Approved.
	For generic drugs (me-too status)	Bofalgan Infusion 1g/100ml manufactured by M/s Bosch Pharmaceuticals (Pvt.) Ltd., Karachi. (Reg. No.: 070607).
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Liquid Injectable (General) section approved.
	Name and address of API manufacturer.	**M/s HEBEI JIHENG (GROUP) PHARMACEUTICAL CO., LTD.,** No. 1, Weiwu Street, Hengshui Industrial Park, Hebei province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (31512021, 31512025, 31512026)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the comparator brand that is Bofalgan Infusion 1g/100ml by M/s Bosch Pharmaceuticals (Pvt.) Ltd.

		(Karachi) by performing quality tests (Appearance, Clarity of Solution, pH, Nominal Volume & Assay).		
	Analytical method validation/verification of product	Method validation studies have submitted including, system suitability, specificity, linearity, accuracy, precision repeatability, Intermediate precision, robustness, stability of solution and range.		
STABILITY STUDY DATA				
Manufacturer of API		M/s HEBEI JIHENG (GROUP) PHARMACEUTICAL CO., LTD., No. 1, Weiwu Street, Hengshui Industrial Park, Hebei province, China.		
API Lot No.		012010134		
Description of Pack (Container closure system)		Clear colorless liquid, filled in clear glass vial; further packed in secondary carton. (100ml x 1's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		570DS08	570DS09	570DS10
Batch Size		120 vials	120 vials	120 vials
Manufacturing Date		29-07-2021	29-07-2021	29-07-2021
Date of Initiation		03-09-2021	03-09-2021	03-09-2021
No. of Batches		03		
Administrative Portion				
31.	Reference of previous approval of applications with stability study data of the firm (if any)	Onsite inspection report of Getz Pharma product Emclide (Empagliflozin & Linagliptin) Tablets 10mg + 5mg was discussed and approved in 316th RB Meeting held on March 15-18, 2022. The inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. The firm have number of HPLC with Empower 3 and DB software having following features: ✓ Have Audit trail ✓ Have backup system ✓ Have Data traceability ✓ Have Data achieving system ✓ Have data integrity ✓ Have Data security ✓ System Security Policy • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are in compliance.		

32.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted Copy of Drug Manufacturing License (DML) no. JI20150076 issued by Hebei Drug Administration. (Valid till 30-08-2025).
33.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.

Batch No.	Invoice No.	Quantity Imported	Date of approval by DRAP
012010134	Y2011ZP50	2 kg	11-11-2020

34.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
35.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.
36.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Remarks OF Evaluator:

Sr.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Justify why the pharmaceutical equivalence was studied against comparator product instead of using innovator / reference product.	Firm submitted the reply in which it is stated that "As per DRAP guidelines "Guidance document for submission of application on Form 5-F (CTD) for registration of pharmaceutical Drug products for human use", to perform Pharmaceutical Equivalence '*The comparison of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted and discussed'.* We have established Pharmaceutical Equivalence of Acetaget Solution for IV Infusion 1g/100ml (manufactured by Getz Pharma) with Bofalgan Infusion 1g/100ml (manufactured by Bosch Pharmaceuticals (Pvt.) Ltd.) as innovator brand is currently not available in Pakistan".
2.	As per the CTD guidance document the minimum batch size for injectable should be at least 2 batches of minimum 2000 batch size OR At least 3 batches having scientifically rational batch size, sufficient enough to perform complete testing till the claimed shelf life, while you have manufactured three trial batches with batch size of 120 vial each. Justify, the batch size of trial batches in light of guidance document approved by DRAP. Firm in their reply submitted following information: This is to inform you that the batch size of 120 vials is sufficient for complete testing of stability studies of Acetaget Solution for IV Infusion 1g/100ml till 24 months. Please note that for each interval i.e. initial, 3, 6, 9, 12, 18 & 24 month, **2 vials** will be required for complete physical and chemical testing. For microbial testing **22 vials** are required for batch release.	

	For container closure integrity testing during accelerated and real time stability conditions **20 vials** are required. Details are as follows: For initial testing: 1 x 2 vials = 2 vials For accelerated studies at 3 & 6 month: 2 x 2 vials = 4 vials For real time studies at 3, 6, 9, 12, 18 & 24 month: 6 x 2 vials = 12 vials For Bacterial Endotoxin Test, Sterility Test and Particulate Matter Test at the time of Release: 1 x 22 vials = 22 vials For container closure integrity testing at initial testing: 1 x 10 vials = 10 vials For container closure integrity testing at 6 month accelerated studies: 1 x 10 vials = 10 vials For container closure integrity testing at 12 and 24 month real time studies: 2 x 10 vials = 20 vials **Total: 80 vials**	
3.	Scientific justification is required for not performing test of osmolality while batch release of trial batches of drug product, since the test has included in drug product specification of innovator brand.	Firm submitted the reply in which it is stated that "This is to inform you that during trial and development of Acetaget Solution for IV Infusion 1g/100ml, we have performed the osmolality test. Please refer to Annex – 1 for "Procedure for the determination of Osmolarity / Osmolality" for your record. However, said test was not incorporated in Finished Product Specifications of trial batches. We hereby commit that we will incorporate the test of osmolality in Finished Product Specifications of Acetaget Solution for IV Infusion 1g/100ml before commercialization".
4.	BMR formulation sheet and COA of drug product manufacturer reflect that you have used injectable grade paracetamol but the COA of API did not reveal that the paracetamol is of injectable grade, clarification is required in this regard.	This is to inform you that Paracetamol API used for our product Acetaget Solution for IV Infusion 1g/100ml is of injectable grade, API manufacturer has performed test for Bacterial Endotoxin test, Aerobic bacterial test & E. Coli test to ensure the sterility / quality of injectable grade material. Please refer to Annex - 2 for Certificate of Analysis of API manufacturer.

Decision: Approved.

- **The manufacturer shall incorporate the Osmolality test in finished product specifications and shall submit the results before issuance of registration letter.**
- **The manufacturer shall submit the applicable fee that is Rs. 7,500/- for revision of specifications as per reference product as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

14.	Name, Address Of Applicant / Marketing Authorization Holder	M/s Bio-Labs (Pvt). Ltd Plot No. 145industrial Triangle Kahuta road Islamabad.
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt). Ltd Plot No. 145industrial Triangle Kahuta road Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 2811 dated 28-01-22
	Details of fee submitted	PKR 30,000/-: dated 26-11-2021
	The proposed proprietary name / brand name	Cetol 100ml infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Paracetamol ……..10mg
	Pharmaceutical form of applied drug	Infusion
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	In-House
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	US FDA
	For generic drugs (me-too status)	Provas infusion by sami Pharma.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 23-4-2019, valid upto 22-04-2022.
	Name and address of API manufacturer.	**Hebei jiheng (Group) Pharmaceutical Co.,Ltd** Xijingming Village Donganzhuang Township Shenzhou Country Hengshui City,Hebei Province,053800 China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data of drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data

		is conducted at 30^{O}C ± 2 ^{O} C / 65% ± 5% RH for 60 months. (31106015,31106016,31106017)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Provas 100ml infusion.
	Analytical method validation/verification of product	Firm has submitted report of validation of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	**Hebei jiheng(Group) Pharmaceutical Co., Ltd** Xijingming Village Donganzhuang Township Shenzhou Country Hengshui City, Hebei Province,053800 China.		
API Lot No.	W32002004		
Description of Pack (Container closure system)	Glass vial filled with clear colorless sterile solution, with blue colored flip-off seal.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	CET 21 -41	CET 21 -42	CET 21 -43
Batch Size	250 Vials	250 Vials	250 Vials
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	05-05-21	05-05-21	05-05-21
No. of Batches	03		

Administrative Portion		
37.	Reference of previous approval of applications with stability study data of the firm (if any)	Empaglif 10mg tablet
38.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP Certificate.

39.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis. The license was issued on 20-03-20 with Invoice No. 2002ZP26.
40.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
41.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail and HPLC CFR Compliance record.
42.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr.no.	**Observations/Deficiencies/ Short-comings**	**Reply of the Firm**
1	Justify why the pharmaceutical equivalence was studied against comparator product instead of using innovator / reference product.	Firm in their reply stated that "As that Paracetamol infusion is short in the pharma market due to current pandemic situation of COVID-1& Dengue. So,innovator packs wasn't available in the local market of Pakistan. That is the reason the comparative study has been done against local leading brand".
2.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2. S.5.	The requisite documents regarding reference standard are attached.
3	Scientific justification is required for not using antioxidant in the applied formulation since the innovator brand used cysteine as an antioxidant because paracetamol is susceptible to degradation by oxidation.	In order to avoid degradation, bio-oxidation and to purging was done during manufacturing that reduces the oxidation and stabilize the formulation. However the executed BMR did not mentioned any kind of purging while filling of vials.
4	Scientific justification is required for not performing test of osmolality while batch release of trial batches of drug product, since the test has included in drug product specification of innovator brand. Justify the acceptance limit of pH below 5.5. ,since the innovator brand describe the pH value of infusion solution about 5.5.	Osmolarity test has been performed on the finished formulation, however, as it was additional test to check the stability of product. So it wasn't included in the final report.
5	As per the CTD guidance document the minimum batch size for injectable should be atleast 2 batches of minimum 2000 batch size OR At least 3 batches having scientifically rational batch size, sufficient enough to perform complete testing till the claimed shelf life, while you have manufactured three trial batches with batch size of 250 vial each. Justify, the batch size of trial batches in light of guidance document approved by DRAP.	The batch size was design to perform the stability testing as the batch size 250 infusion fulfil the requirement of samples for stability testing. So this was selected.

6	BMR formulation sheet reflect that you have used injectable grade paracetamol but the COA of API did not reveal that the paracetamol is of injectable grade, clarification is required in this regard.	The injectable grade of Paracetamol has been used in the formulation. However, it wasn't mentioned on the COA.

Decision: Deferred for;

- **Justification for the acceptance limit of pH below 5.5 for the applied product, since the innovator brand describe the pH value of infusion solution about 5.5.**
- **Submission of finished product specification mentioning Osmolality test.**
- **Scientific justification is required for not using antioxidant in the applied formulation since the innovator brand used cysteine as an antioxidant because paracetamol is susceptible to degradation by oxidation.**

15.	Name, address of Applicant / Marketing Authorization Holder	M/s World Biz Pharmaceutical Company, Plot No. 340, Multan Industrial Estate, Multan.
	Name, address of Manufacturing site.	M/s World Biz Pharmaceutical Company, Plot No. 340, Multan Industrial Estate, Multan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of DML number 000942 issued on 13-09-2021.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of DML dated 17-09-2021 specifying Oral liquid syrup section (General).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22536: 10-08-2022
	Details of fee submitted	PKR 30,000/-: 09-06-2022
	The proposed proprietary name / brand name	**Para Biz Suspension 120mg/5ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Paracetamol ……120mg
	Pharmaceutical form of applied drug	Oral suspension
	Pharmacotherapeutic Group of (API)	Analgesic / antipyretic
	Reference to Finished product specifications	BP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Junior Paracetamol Suspension (**MHRA** Approved)
	For generic drugs (me-too status)	Calpol suspension of M/s GSK Pakistan (Reg # 000354)

	Name and address of API manufacturer.	M/s Zenith Chemical Industries (Pvt) Limited. 16 Kilometer off Ferozepur-Road, Behind Wapda Grid station,1 kilometer of Chandrai Road Lahore - Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product i.e. PANADOL suspension of GSK Pakistan (Pvt) Ltd.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Zenith Chemical Industries (Pvt) Limited. 16 Kilometer off Ferozepur-Road, Behind Wapda Grid station,1 kilometer of Chandrai Road Lahore - Pakistan
API Lot No.	ZPAR20-350
Description of Pack (Container closure system)	Amber color glass bottle

Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-AS-001	RD-AS-002	RD-AS-003
Batch Size	2000 Bottle	2000 Bottle	2000 Bottle
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	15-11-2021	15-11-2021	15-11-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate of M/s Zenith Chemical Industries is issued by DRAP on 22-05-2019. The certificate is issued based on the inspection dated 06-12-2018.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with UV spectra, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable. Our HPLC systems are not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."
- Provide verification studies of drug substance from drug product manufacturer.
- Specifications are mentioned as BP in some sections and USP in other sections.
- Assay method is based on HPLC while verification studies are conducted on UV method.
- Analytical method specifies HPLC method, while assay testing in stability studies is conducted on UV
- Provide copy of commercial invoice for evidence of purchase of the drug substance.

Decision: Deferred for;

- **Submission of data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."**
- **Submission of verification studies of drug substance from drug product manufacturer.**

• **Clarification since specifications are mentioned as BP in some sections and USP in other sections.** • **Clarification regarding the assay method which is based on HPLC while verification studies are conducted on UV method.** • **Clarification since analytical method specifies HPLC method, while assay testing in stability studies is conducted on UV** • **Submission of copy of commercial invoice for evidence of purchase of the drug substance.**		
16.	Name, address of Applicant / Marketing Authorization Holder	M/s Magns Pharmaceutical. Plot No. 7B, Value Addition City, Sahianwala Road, Khurrianwala, Faisalabad.
	Name, address of Manufacturing site.	M/s Magns Pharmaceutical. Plot No. 7B, Value Addition City, Sahianwala Road, Khurrianwala, Faisalabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of GMP certificate dated 22-03-2019 issued on the basis of inspection dated 01-03-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of issuance of Drug Manuacturing License (DML) dated 25-11-2016 specifying Tablet (General) Section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11697: 14-05-2022
	Details of fee submitted	PKR 30,000/-: 15-02-2022
	The proposed proprietary name / brand name	**CETAMOL 500mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol ……500mg
	Pharmaceutical form of applied drug	white color round uncoated tablet
	Pharmacotherapeutic Group of (API)	Analgesic / antipyretic
	Reference to Finished product specifications	BP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Paracetamol IPCA 500mg Tablet by IPCA Laboratories (**MHRA** Approved)
	For generic drugs (me-too status)	Panadol Tablet of M/s GSK Pakistan (Reg # 000817)
	Name and address of API manufacturer.	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40ºC ± 2ºC / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30ºC ± 2ºC / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product i.e. CALPOL tablet of GSK. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. CALPOL tablet of GSK.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	Pharmagen Limited. Kot Nabi Bukshwala, 34 Km, Ferozepur Road, Lahore.
API Lot No.	Not submitted
Description of Pack (Container closure system)	Alu-PVC blister
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-006	T-007	T-008
Batch Size	5000 Tablet	3000 Tablet	3000 Tablet
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	12-02-2021	12-02-2021	18-02-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable since testing method was UV based
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Evaluation by PEC:

- Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."
- Provide verification studies of drug substance from drug product manufacturer.
- Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.
- Justify why qualitative composition is different from the reference product.
- Provide reference of previous approval of applications with stability study data of the firm (if any)
- Provide evidence of approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.
- Provide copy of commercial invoice for evidence of purchase of the drug substance.
- Provide record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Decision: Deferred for the following;

- **Submit data in section 3.2.S.4.1 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."**
- **Provide verification studies of drug substance from drug product manufacturer.**
- **Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.**
- **Justify why qualitative composition is different from the reference product.**

• **Provide reference of previous approval of applications with stability study data of the firm (if any)** • **Provide evidence of approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.** • **Provide copy of commercial invoice for evidence of purchase of the drug substance.** • **Provide record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)**		
17.	Name, address of Applicant / Marketing Authorization Holder	M/s SAMI Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Name, address of Manufacturing site.	M/s SAMI Pharmaceuticals (Pvt) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted copy of GMP certificate of the firm issued dated 11-08-2020 based on the inspection dated 28-08-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of regularization of existing facility under DML number 000072 of M/s Sami Pharma which specifies Tablet (General / General antibiotic) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4785: 21-02-2022
	Details of fee submitted	PKR 75,000/-: 17-02-2022
	The proposed proprietary name / brand name	**PROVAS ACTIFAST 500mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Paracetamol ……500mg
	Pharmaceutical form of applied drug	white to off white uncoated tablet
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	USP
	Proposed Pack size	10’s, 20’s, 30’s, 50’s and 100’s.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Panadol ActiFast 500mg Tablet by GlaxoSmithKline Consumer Healthcare (**MHRA** Approved)
	For generic drugs (me-too status)	NA
	Name and address of API manufacturer.	Hebei Jiheng (Group) Pharmaceutical Co. Ltd. Shenzhou Plant Southeast Xijingming Village Donganzhuang Township, Shenzhou County Henshui City, Hebei Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 75% ± 5% RH for 60 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against the reference product i.e. PANADOL Actifast tablet of GSK Ireland. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. PANADOL Actifast tablet of GSK Ireland.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	Hebei Jiheng (Group) Pharmaceutical Co. Ltd. Shenzhou Plant Southeast Xijingming Village Donganzhuang Township, Shenzhou County Henshui City, Hebei Province, China.
API Lot No.	31709016
Description of Pack (Container closure system)	Alu-PVC blister
Stability Storage Condition	Real time : 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	1000 Tablet	1000 Tablet	1000 Tablet
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	21-12-2020	21-12-2020	21-12-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted reference of last onsite panel inspection for instant dosage form conducted during last two years i.e. EMPOLI (Empagliflozin) 10mg & 25mg Tablets which was presented in 290th meeting of the registration board & hence approved & registered by registration board Date of inspection: 13th June 2019. The inspection report confirms following points • The HPLC software is 21CFR Compliant. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. HE20180054 issued by China Food And Drug Administration valid till 08/07/2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice (Invoice# 1708ZP03 dated 19th October 2017 with received quantity i.e. 5000 kgs) for the purchase of Paracetamol from M/s Hebei Jiheng Shenzhou Pharmaceutical Co., Ltd. China with attestation of DRAP dated 01-11-2017
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete analytical record of product testing of all batches.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

- Qualitative composition is different from the reference product, since reference product has not used potassium sorbate and pregelatinized starch.
- Justify the use of preservative i.e. potassium sorbate in the applied formulation as tablet.
- Dissolution acceptance in USP is NLT 80% in 30 minutes while the firm has set acceptance criteria NLT 80% in 10 minutes.
- Disintegration test acceptance criteria is NMT 30 minutes, while dissolution criteria is NLT 80% in 10 minutes.

Decision: Deferred for the following;

- **Qualitative composition is different from the reference product, since reference product has not used potassium sorbate and pregelatinized starch.**
- **Justify the use of preservative i.e. potassium sorbate in the applied formulation as tablet.**
- **Dissolution acceptance in USP is NLT 80% in 30 minutes while the firm has set acceptance criteria NLT 80% in 10 minutes.**
- **Disintegration test acceptance criteria is NMT 30 minutes, while dissolution criteria is NLT 80% in 10 minutes.**

B: PACLITAXEL ALBUMIN BOUND:

Applications submitted on Form 5F:

18.	Name, address of Applicant / Importer	M/s Lab Diagnostic Systems (SMC) Pvt. Ltd. 111 B, Hali Road, Westridge 1, Rawalpindi C Pakistan.
	Details of Drug Sale License of importer	License No: 01-374-0176-041296D Address: 111-B Hali Road Westridge 1 Cantt Dist Rawalpindi. Address of Godown: NA Validity: 07-03-2023. Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s Jiangsu Hengrui Pharmaceuticals Co. Ltd. No. 38, Huanghe Road, Economic and Technolog Development Zone, Lianyungang, Jiangsu 222 P.R.China.
	Name, address of manufacturer(s)	M/s Jiangsu Hengrui Pharmaceuticals Co. Ltd. No. 38, Huanghe Road, Economic and Technolog Development Zone, Lianyungang, Jiangsu 222 P.R.China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** The firm has submitted original, legal copy of CoPP certificate (No. JS20220254) d 2022-07-05 issued by Jiangsu Drug Administra No. 05 Gulou Street Nanjing Jiangsu Province C for Paclitaxel for Injection (Albumin Bound). The CoPP confirms free sale status of the produc the exporting country as well as GMP status of manufacturing site through periodic inspection e year.
	Details of letter of authorization / sole agency agreement	The firm has submitted original letter of distribu certificate from Jiangsu Hengrui Pharmaceuticals Ltd. The letter species that the manufacturer appo M/s Lab Diagnostic Systems (SMC) Pvt. Ltd register their products in Pakistan. The authoriza letter is valid till 15-08-2023.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract give
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for ex purpose only
	Dy. No. and date of submission	Dy. No. 20927 Dated: 25-07-2022
	Details of fee submitted	PKR 150,000/- Dated: 30-06-2022
	The proposed proprietary name / brand name	NAB Paclid 100mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Paclitaxel (albumin bound)……..100mg
	Pharmaceutical form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anti-neoplastic agent
	Reference to Finished product specifications	In-house
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ABRAXANE® for Injectable Suspension (paclit protein-bound particles for injectable suspens (USFDA Approved).
	For generic drugs (me-too status)	Brand name: Nab-Xelpac Importer: Himmel Pharmaceuticals (Pvt) Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS template. Firm has summarized information relate nomenclature, structure, general proper solubilities, physical form, manufacturers, descrip of manufacturing process and controls, impuri specifications, analytical procedures and validation, batch analysis and justification specification, reference standard, container clo system and stability studies of drug substance.
	Name, address of drug substance manufacturer	M/s Shanghai Jinhe Biopharmaceutical Co., Ltd. Address: Maodian Road, Qingpu District, Shang China. Postal Code : 201716
	Module-III Drug Substance:	The firm has submitted detailed drug substance for both sources related to nomenclature, struct general properties, solubilities, physical fo manufacturers, description of manufacturing pro and controls, impurities, specifications, analy procedures and its validation, batch analysis justification of specification, reference stand container closure system and stability studies of substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batche API at accelerated as well as real time conditions. real time stability data is conducted at 5 ± 3 ℃. stability study data is till 12 months. The acceler

		condition is 25 ± 2 ℃ /60 ± 5%RH for 3 commer batches for 6 months. Lot No: ZSC202011174 Lot No: ZSC202011175 Lot No: ZSC202011176
	Module-III Drug Product:	Firm has submitted data of drug product includin description, composition, pharmaceu development, manufacture, manufacturing pro and process control, process validation protoc control of excipients, control of drug prod specifications, analytical procedures, validation analytical procedures, batch analysis, justificatio specifications, reference standard or mater container closure system and stability.
	Pharmaceutical equivalence	The firm has submitted pharmaceutical equivale with reference product Abraxane Injection () peforming Moisture, pH, residual organic solv and osmolality.
	Analytical method validation/verification of product	Firm has submitted analytical method valida studies for the applied product.
	Container closure system of the drug product	50ml Neutral borosilicate glass injection bottle.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 bat The accelerated stability study data is conducte 40℃±2℃/75 %±5%RH for 6 months. The real t stability study data is conducted at 30℃±2 65%±5%RH for 24 months for 3 batches. Lot No: 16033015 Lot No: 16042216 Lot No: 16051016

Evaluation by PEC:

ABRAXANE™ for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) is indic for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse wi 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinic contraindicated.

Sr. No.	Observations	Response by the firm
1.	Clarification is required regarding address of the product license holder since Jiangsu Hengrui Medicine Co., is mentioned on CoPP while Jiangsu Hengrui Pharmaceuticals Co. Ltd is mentioned on Form-5F.	The applicant has submitted that the manufacturer of the product has changed its name from Jiangsu Hengrui Medicine Co., Ltd to Jiangsu Hengrui Pharmaceuticals Co., Ltd. It is therefore requested to change the name of manufacturer in the original registration letter. Change approval statement has been submitted.
2.	Details of reference product including batch number, manufacturing date and expiry dates are required to be submitted.	The firm has submitted details of batch numbers of reference product. Batch no. 6101841 Batch no. 6109816 Batch no. 6109944
3.	Since the final product is lyophilized preparation therefore submit the details of reconstitution diluent alongwith compatibility studies for the dry powder for injection.	The product is first reconstituted with 0.9% sodium chloride solution, then stored in following: • Normal saline infusion bag • Non-PVC five-layer co-polymerized compound membrane infusion bag

		• Non-PVC three-layer co-polymerized compound membrane infusion bag
4.	Clarification is required regarding executive standard (pharmacopoeial standard) and enterprise control standard.	The firm has submitted that executive standard is a pharmacopoeial standard and enterprise control standard is in-house standard. However, the firm has claimed in-house standard.
5.	Submit in-use stability studies for drug product along with proposed in-use storage statement and in-use shelf-life.	The firm has submitted in-use stability studies. Shelf life in infusion bag is for 10 hours and shelf life in vial is for 24 hours.

Decision: Approved with innovator's specifications as per Policy for inspection of Manufacturer abroad verification of local storage facility. Registration Board further decided that registration letter will be iss after submission of applicable fee that is Rs. 7,500/- for revision of specifications as per notification No. 11/2021-B&A/DRAP dated 13-07-2021.

19.	Name, address of Applicant / Importer	Martin Dow Limited., Plot No. 37, Sector 19, Koran Industrial Area, Karachi-74900, Pakistan
	Details of Drug Sale License of importer	License No: 565 Address: Martin Dow Limited, Plot No. 37, Sector 1 K.I.A, Karachi Address of Godown: (1) 1st floor, Plot No. 211 Sec; K.I.A, Kyc (2) Plot No. 32 sec; 16, K.I.A, Kyc Validity: 16-06-2024. Status: License to sell drugs by way of wholesale Renewal: NA
	Name and address of marketing authorization holder (abroad)	M/s Nano Daru Pajuhan Pardis Pharmaceutical Company No.4 & 8, Northern Tak Ave., Attar St., Vanak., Sq., Tehran, Iran Email: Info@nanodaru.com Manufacturing site Address: Behnood Pharmed Incubation Center, No. 110, Behman St., Karafarinan Blvd., Sepehr Industrial Zone, Nazarabad City, Albo Province, Iran. Tel: +98 (21) 88 78 00 28 Fax: +98 (21) 88 78 63 34
	Name, address of manufacturer(s)	M/s Nano Daru Pajuhan Pardis Pharmaceutical Company Address: Behnood Pharmed Incubation Center, No. Behman St., Karafarinan Blvd., Sepehr Industrial Zo Nazarabad City, Alborz Province, Iran.
	Name of exporting country	Islamic Republic of Iran
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted original legalized CoPP certificate (No. 665/59601) dated 15-01-2022 issued Director General Food & Drug Administration (IFD Division of Pharmaceutical and Narcotic Affairs of Ministry of Health, Food and Drug Administration, MOH Iran for Paclinab 100mg (Paclitaxel albumin-bound particles) lyophilized powder for suspension f infusion. The CoPP confirms free sale status of the product in market of exporting country as well as GM status of the manufacturing site through periodic inspection every year.

		The name of importing country on CoPP is mentione as Islamic republic of Pakistan. Firm has also submitted GMP certificate No#665/59 dated 11/01/2022 issued by Director General IFDA. GMP states that the production line was duly inspect and approved in accordance with Good Manufacturi Practices Principles for pharmaceutical products whi are currently in force in I.R of Iran and also states 'T manufacturer plant is subject to regular GMP inspections based on PIC/S regulations by IFDA.
	Details of letter of authorization / sole agency agreement	Firm has submitted original legalized product specifi sole agency agreement No# 00/S/2307 dated 12th September 2021 from M/s Nano Daru Pajuhan Pardi No.4 & 8, Northern Tak St., Attar St., Vanak Sq., Tehran, Iran. The letter species that the manufacture appoints M/s Martin Dow Limited., as sole authorize importer of their product their product Paclinab 100r (Lyophilized Powder for suspension for infusion) (Paclitaxel albumin-bound particles) in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purp only
	Dy. No. and date of submission	Dy. No. 12521: 23-05-2022
	Details of fee submitted	PKR 150,000/-: 29-12-2021 (Slip#2758347150)
	The proposed proprietary name / brand name	Paclinab 100mg (Paclitaxel (albumin-bound particle Powder for suspension for injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Paclitaxel (formulated as albumin bound nanoparticles)……100 mg
	Pharmaceutical form of applied drug	Lyophilized Powder for suspension for injection.
	Pharmacotherapeutic Group of (API)	Antineoplastic agent ATC Code: L01CD01
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	A per DPC
	The status in reference regulatory authorities	Abraxane for injectable suspension 100mg USFDA Approved.
	For generic drugs (me-too status)	Paclixil Injection (Paclitaxel 100mg / 16.7ml) by M/ Mirza Pharma (Pvt) Ltd., (Reg# '045759)

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related nomenclature, structure, general properties, solubiliti physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validatio batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	M/s Mac-Chem Products (India) Pvt. Ltd., N-211/2/1 M.I.D.C, Boisar, District, Thane, Pin - 401 506, Maharashtra, India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data rela to nomenclature, structure, general properties, solubilities, physical form, manufacturers, descriptio manufacturing process and controls, impurities, specifications, analytical procedures, batch analysis a justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches o API at accelerated as well as real time conditions. Th real time stability data is conducted at 25 ºC ± 2ºC / (± 5% RH for 48 months while accelerated stability study is conducted at 40 ºC ± 2ºC / 75 ± 5% RH for (months. Batch No# (PAT0217002, PAT0217003, PAT02170
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical developme manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, conta closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted Pharmaceutical Equivalence aga the innovator product ABRAXANE by Celgene, US (RLD) by performing quality test (identification, pH Water Content, osmolality, Bacterial Endotoxin, Sterility, particle size, Assay).
	Analytical method validation/verification of product	Firm has submitted analytical method validation stud for the applied product including accuracy, precision specificity, linearity, range, robustness.
	Container closure system of the drug product	The finished product is packed into colorless Type I (60ml) , closed by bromobutyl rubber stopper and crimped by an aluminium flip-off system
	Stability study data of drug product, shelf life and storage conditions	Previous manufacturing site: 24 months long term stability studies have been done completely and 6 months accelerated stability have n been done due to experimental problem. New manufacturing site:

		After changing the construction site, accelerated stability studies were performed completely for three batches and long- term stability studies were done un 18th month on batches 20011, 20012 and until 9th month on batch 20038. Recontinue studies will be subjected for 24th month on batches 20011, 20012 a for 12th, 18th and 24th months on batch 20038.

Remarks of Evaluator [XI]:

Section	Observations	Response
	Fee deposited by M/s Martin Dow Limited Drug Manufacture License: 000267 instead by DSL **License No:** 565	
3.2.S.4	• Copies of specifications and the analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug product manufacturer is required • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted. Firm has submitted method validation report of drug product instead of drug substance. Furthermore method validation report is submitted from Sobhan Oncology Co. Iran instead of drug product manufacturer	• Firm has submitted copies of specifications a Analytical procedure used for routine testing of Drug substance /Active Pharmaceutical Ingredient fr Drug Product manufacturer • Firm has submitted Analytical Method Verificat studies including specificity, accuracy and repeatabil (method precision) performed by the Drug Prod manufacturer for drug substance(s)
3.2.P.1.3	• Provide information including type of diluent, its composition, quantity or volume, specifications (as applicable) and regulatory status in Pakistan (as applicable) for the diluent which is to be provided along with the applied drug product.	• Firm submitted that PACLINAB® is supplied as a wh to off-white, sterile, lyophilized powder reconstitution with 20 mL of 0.9% Sodium Chlor Injection, prior to intravenous infusion. Further deta of diluent and its me-too status in Pakistan is provid as; **0.9% Sodium Chloride ampoule in 20ml volu available in Pakistan**

Brand Name	Manufacturer/registration Holder	Registratio Number
Sodium Chloride	Getz Pharma (Pvt) Ltd	050685
Normal Saline	Mehran International	072556
Zeesol NS	Shahzaib Pharmaceuticals (Pvt) Ltd	064326

• The firm submitted declaration that our applied prod is available in the country of origin in the form of v only as finished pack, without diluent. Hence, manufacturer is providing this product without dilu only.

• Moreover, the product will be administered as Infus in the Health care facility under the supervision of hea

		care practitioner. Hence, diluent is not required to provided with the finished product pack.
3.2.P.8	Submit stability study data of drug product till claimed shelf life from the manufacturing site which is provided in CoPP	Firm has submitted stability study data of 3 batches. T accelerated stability study data is conducted at 40°C ±2 / 75% ± 5% RH for 6 months. The real time stability stu data is conducted at 30°C ±2°C / 65% ± 5% RH for Months. ***However, the manufacturing site cannot confirmed from the submitted stability data.***

Batch No.	**Mfg. date**	**Batch size**
N0002	09-2018	900 vial
N0005	11-2018	1140 vial
N0006	01-2019	1140 vial

Stability study data of Batch No# N0005 at accelera and real time conditions and 3rd month time point is provided/performed.

Decision:Approved with Innovator's specifications as per Policy for inspection of Manufacturer abroad verification of local storage facility.

20.	Name, address of Applicant / Importer	M/s Al Habib Pharmaceuticals, Plot No. 81-B Bloc S.M.C.H.S, Karachi.
	Details of Drug Sale License of importer	License No: 1245. Address: 81-B Block B, S.M.C.H.S, Karachi. Address of Godown: 1. Plot No. 10 sector 25 KIA, Karachi. 2. HT – 8, Landhi Industrial Area, Karachi. Validity: 18-05-2022. Status: License to sell, stock & exhibit for sale, distri and sell drugs by way of wholesale by of manufactu importer or indenter.
	Name and address of marketing authorization holder (abroad)	Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. Xingye Road, Economic Development Zone, Cangz China.
	Name, address of manufacturer(s)	Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. Xingye Road, Economic Development Zone, Cangz China.
	Name of exporting country	China.
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized CoPP certifi No. 202103082 dated 12-08-2021 issued by H Province Drug Administration, No. 391 Hongqi St Shi Jiazhuang P.R. of China for Paclitaxel for injec (albumen bound). CoPP has mentioned Hebei D Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye R Economic Development Zone, Cangzhou China as manufacturer. The name of importing country on CoPP is mentione Pakistan. Furthermore, the CoPP was valid for one till 08-2023. ***However, the certificate has mentioned that the al product is not registered in China and not authorize***

		be placed in china. The exportation of the product is restricted. ***The product has been reformulated with a view improving its stability under specific conditions out of china.*** **GMP:** Firm has submitted copy of GMP certificate FT070/MH/001/2019 in the name of M/s Hebei D Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye R Economic Development Zone, Cangzhou China iss by the National Authority of Medicines and He Products, Portugal. Latest inspection was conducted 20-07-2018 and the certificate reflects that the princi and guidelines of Good manufacturing Practice laid d in the Directive 2003/94/EC are complied. The certificate is valid for three years. Furthermore, the certificate has mentioned that certificate only covers the manufacturing activities in building No. 1 (Injection workshop)
	Details of letter of authorization / sole agency agreement	**Letter of Authorization:** Firm has submitted original legalized and notarized le of Authorization dated 11-04-2022 from Hebei D Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye R Economic Development Zone, Cangzhou City, H province China for Paclitaxel (Albumen bound) Injec 100mg wherein M/s Al Habib Pharmaceuticals, Plot 81-B Block B, S.M.C.H.S, Karachi is authorized as agent and distributor for the above said product.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purp only
	Dy. No. and date of submission	Dy. No. 11265: 11-05-2022.
	Details of fee submitted	PKR 150,000/-: 13-04-2022.
	The proposed proprietary name / brand name	Albino 100 mg Lyophilized powder for injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains; Paclitaxel as albumen bound nanoparti ……. 100mg
	Pharmaceutical form of applied drug	Lyophilized powder for injection.
	Pharmacotherapeutic Group of (API)	L01CD01 Antineoplastic Agents.
	Reference to Finished product specifications	In house specifications.

	Proposed Pack size	As per Policy.
	Proposed unit price	As per Policy.
	The status in reference regulatory authorities	Abraxane 100mg vial (paclitaxel protein-bound parti for injectable suspension) (albumin-bound)), USF Approved.
	For generic drugs (me-too status)	Nab-Xelpac Injection 100mg (Lyophilized powd Himmel Pharmaceuticals, Reg. No. 106640.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD temp Firm has summarized information related nomenclature, structure, general properties, solubili physical form, manufacturers, description manufacturing process and controls, impuri specifications, analytical procedures and its validat batch analysis and justification of specification, refere standard, container closure system and stability studie drug substance.
	Name, address of drug substance manufacturer	Fujian South Pharmaceutical Co. Ltd. No.98, Dongxin Road, Xuefeng Town, Mingxi Cour Fuijian Province, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for l sources related to nomenclature, structure, gen properties, solubilities, physical form, manufactu description of manufacturing process and cont impurities, specifications, analytical procedures and validation, batch analysis and justification specification, reference standard, container clo system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batche API at accelerated for 06 months as well as real t conditions for 36 months. The real time stability da conducted at 25 ^{o}C ± 2^{o}C, RH 60% ± 5% and acceler stability data is conducted at 40^{o}C ± 2^{o}C, RH 75% ± (Batch No. 902-1612411, 902-1701401, 902-170140
	Module-III Drug Product:	Firm has submitted data of drug product including description, composition, pharmaceutical developm manufacture, manufacturing process and process con process validation protocols, control of excipie control of drug product, specifications, analy procedures, validation of analytical procedures, b analysis, justification of specifications, refere standard or materials, container closure system stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established aga the reference product **Abraxane 100mg (Paclit Albumin Bound)** by Abraxis Biosciences for the qua test i.e. Identification, pH, Water content, Particu matter, Particle size & particle size distribution, Rel substances, Human albumen content, Paclitaxel bind rate, sterility, Bacterial endotoxin and assay.
	Analytical method validation/verification of product	Firm has submitted analytical method validation stu for the applied product.

	Container closure system of the drug product	Borosilicate glass vial 50ml. Brominated butyl rubber stopper Aluminum plastic combination caps for injection via
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 4 ±2°C / 75% ± 5% RH for 6 months both upright inverted orientation (Batch No. 1210101, 121010 1210103). The real time stability study data is conducted at 3 ±2°C / 75% ± 5% RH for 24 months (Batch No. 1210 1210102 & 1210103).

Evaluation by PEC:

Sr. No.	Section	Observation	Response by the firm
1	1.3.4	Valid and notarized copy of Drug Sale License of the applicant shall be submitted.	Attested copy of Drug Sale License No. 0230 dated 18-05-2022 in the name of Al Habib Pharmaceuticals 81-B Block B, S.M.C.H.S, Karachi is submitted by the firm. Validity is 18-05-2024. ***However, the address of the Godown mentioned on the DSL is changed from the previously submitted.*** ***Plot no. 393/7 & 393/8 Sector 7A KIA, Karachi.***
2		Justification shall be submitted regarding the statement on the CoPP certificate that the product is not registered in China and not authorized to be placed in china.	Firm has submitted a document from M/s Hebei Dawn Pharmaceutical wherein they have declared the following; "We, Hebei Dawn Pharmaceutical Co., Ltd., hereby state that we are exporting Paclitaxel for injection (albumin bound) to following countries as our Plant is exclusively for export to Foreign Countries and EU GMP Certified. i. Austria. ii. Norway. iii. Iran. iv. South Korea. v. Vietnam ***However, the firm has not produced any evidence of registration of their applied formulation in any of the Reference Regulatory Authorities as defined by the Registration Board.***
3		Valid, Notarized and legalized GMP certificate of the finished product manufacturer issued by the relevant regulatory authority shall be submitted.	Firm has submitted a copy of GMP certificate No. HE20170084 in the name of M/s Hebei Dawn Pharmaceutical Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou China issued by the Hebei Drug Administration China dated 25-12-2017 valid till 24-12-2022.
4	3.2.P.1.1	• Innovator product has mentioned approximately 900 mg of human albumin while the applied formulation has mentioned 800 mg	Firm has submitted composition of formulation in different RRA as follows; • FDA 900 mg of Human Albumin. • NMPA 900 mg of Human Albumin. • PMDA 800mg of human albumin.

		of Albumen. Justification shall be submitted. • Qualitative composition of the drug product is changed from the innovator product. Innovator product has used sodium caprylate and sodium acetyl tryptophanate while the applied formulation has chloroform, anhydrous ethanol and WFI. Compatibility studies shall be submitted.	• EMEA 800mg of human albumin. Firm has submitted that applied medicine is developed as per the innovator product following the PMDA and EMEA Abraxane and both are included in RRA. ***However, the review report approved by Japan (Clinical Summary 2.7) has the following description;*** ***The dosage ratio of paclitaxel and human albumin in the original commercial batch prescription is 1:8 but due to the influence of the sterilization filtration process, the ratio of paclitaxel and human albumin become 1:9.*** ***While EPAR has not mentioned any ratio of paclitaxel and Albumin in the public assessment report.*** Firm has submitted that other excipients used in the manufacturing of Paclitaxel albumin bound i.e. chloroform, anhydrous ethanol, WFI will be removed finally and the finished product does not contain these excipients that why the end product is same as reference product. Firm has also submitted new composition for the applied formulation wherein they have included sodium caprylate and sodium acetyl tryptophanate in the composition. **However, these excipients are not mentioned in the original submitted CoPP nor in original dossier submitted.**
5	3.2.P.1.3	Since the final product is lyophilized preparation, therefor, submit the details of reconstitution diluent along with the compatibility studies for the dry powder for injection.	Firm has submitted the following; "Aseptically, reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP. Slowly inject the 20 mL of 0.9% Sodium Chloride Injection, USP, over a minimum of 1 minute, using the sterile syringe to direct the solution flow onto the inside wall of the Vial. The reconstituted suspension should be milky and homogenous without visible particulates. If particulates or settling are visible, the vial should be gently inverted again to ensure complete resuspension prior to use. Discard the reconstituted suspension if precipitates are observed. Discard any unused portion".
	3.2.P.2.2.1	Details of the innovator product including batch number, manufacturing date & Expiry date shall be submitted.	Firm has submitted the following; Batch No. 0F028C Exp. Date. 06-2023.
	3.2.P.8	Submit in use stability studies for drug product along with proposed in -use storage statement and in-use shelf life.	***Not submitted.*** Firm has submitted again the real time and accelerated stability studies that were submitted in the original dossier.

Decision: The Boar deferred the case for clarification of the following points;

- **The applied product is not present in the market of exporting country for free sale.**
- **The qualitative composition of the applied product is different from the innovator's product.**
- **In-use stability of the applied product is not submitted.**

C. ISOFLURANE

The Authority in its 143rd meeting, keeping in view the shortage of Isoflurane (essential medicine) as highlighted by the Government of Punjab through Additional Secretary Drugs Control and Chief Drugs Controller and also various media reports both electronic and print, decided to consider requests of registration of this salt through Registration Board om priority / out of queue.

Applications submitted on Form 5F:

21.	Name, address of Applicant / Importer	M/s AMB HK ENTERPRISES Pvt Ltd, Pakistan
	Details of Drug Sale License of importer	License No: 05-352-0058-066904D Address: 2nd floor plaza 60, commercial block K, phase 1 DHA, distt. Lahore Address of Godown: NA Validity: 24-02-2023. Status: License to sell drugs as distributor Renewal: NA
	Name and address of marketing authorization holder (abroad)	Hebei yipin pharmaceutical co. Ltd. Sanxia road, economy technology area of shijiahuang, china.
	Name, address of manufacturer(s)	Hebei yipin pharmaceutical co. Ltd. Sanxia road, economy technology area of shijiahuang, china.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized **copy** of CoPP certificate (No. 20220295) dated 10-08-2022 issued by CCPIT for isoflurane 100ml The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. **The name of importing country on CoPP is mentioned as Pakistan. Furthermore the CoPP was valid till 09-08-2024.**
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of distribution certificate from Hebei yipin pharmaceutical Co., Ltd. The letter species that the manufacturer appoints **M/s AMB HK ENTERPRISES Pvt Ltd, Pakistan** to register their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 24078: 25-08-2022
	Details of fee submitted	PKR 150,000/-: 23-08-2022
	The proposed proprietary name / brand name	**EVORANE 100ml**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each pack contains: Isoflurane…….100ml
	Pharmaceutical form of applied drug	Liquid for inhalation
	Pharmacotherapeutic Group of (API)	General anaesthesia
	Reference to Finished product specifications	In house
	Proposed Pack size	1's
	Proposed unit price	USP
	The status in reference regulatory authorities	**USFDA** Approved.
	For generic drugs (me-too status)	FORANE liquid by Getz pharma
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Hebei yipin pharmaceutical co. Ltd. Sanxia road, economy technology area of shijiahuang, china.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 30 ℃±2. The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control,

		process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	submitted.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	USP type-I glass ampoule (5ml)
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 75% ± 5% RH. The real time stability study data of 2 batches is for 12 months while the stability study data for 3rd batch is for 9 months only.

Evaluation by PEC:

Section#	Observation	Firm's response
2.3	QOS shall be submitted as per WHO-QOS PD template.	Submitted.
3.2.P.5.1	Justification shall be submitted for claiming Drug product specifications & analytical procedure as per Chinese pharmacopoeia, whereas USP monograph is available for "Isoflurane".	Firm has submitted as under from M/s Hebei Yipin Pharmaceutical: "We would like to request to your good office to grant registration as per USP specification for regarding the below products under AMB HK enterprises (PVT.) Ltd.: "Isoflurane for Inhalation 100ml" We commit to provide product according to USP specifications."
3.2.P.5.4	Justification shall be submitted for performing Drug product batch analysis as per Chinese pharmacopoeia, whereas USP monograph is available for "Isoflurane".	
3.2.P.8.3	Justification shall be submitted for performing Drug product stability studies as per Chinese pharmacopoeia, whereas USP monograph is available for "Isoflurane".	
• Clarification shall be submitted for submitting copy of COPP instead of original Legalized COPP.		• Firm has submitted an undertaking that "original COPP is under legalization process to which copy has been submitted. We will submit original legalized COPP as soon as we will receive it."

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

22.	**Name, address of Applicant / Importer**	**M/s Himmel Pharmaceuticals (Pvt.)Ltd**
	Details of Drug Sale License of the importer	**License No: 05-352-0065-016174D**

		Address: Ground Floor,6- Judicial Colony Phase-I (Ext.) Shahrah Nazaria e Pakistan, Lahore **Validity:** 06.02.2024. **Status:** License to sell drugs as a distributor
	Name and address of marketing authorization holder & manufacturer	**Eskayef Pharmaceuticals Limited** **Registered Office**: 52 Motijheel Commercial Area, Dhaka 1000, Bangladesh. Operational Head Quarter: Plot 82, Road 14, Block B, Banani, Dhaka 1213, Bangladesh. Plant Address: 400 Squibb Road, Tongi Industrial Area, Tongi, Gazipur 1711, Bangladesh.
	Name of exporting country	**Bangladesh**
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** The firm has submitted the original, legalized CoPP certificate (No.DA/6-39/05/3733) dated 14-02-2022 issued by the Government of the people's republic of Bangladesh, Ministry of Health & Family Welfare, Directorate General of Drug Administration Oushad Bhaban, Mohkhali Dhaka-1212, Bangladesh. **GMP:** Firm has submitted Legalized GMP certificate (Certificate No. DA/6-39/05/10970) issued by M/s Eskayef Pharmaceuticals Limited.
	Details of letter of authorization / sole agency agreement	Firm has submitted original letter of distribution certificate from Eskayef Pharmaceuticals Limited. Issue date 06-08-2022, Valid for 6 months from the date of issue
	Status of the applicant	☒ Importer
	Status of application	☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale
	For imported products, specify one the these	☒ Finished Pharmaceutical product import
	Dy. No. and date of submission	Dy. No.24205: 26-08-2022
	Details of fee submitted	PKR 75,000/-: 04-08-2022
	The proposed proprietary name / brand name	**PAXOVIR Film Coated Tablets (2 strips Combipack)**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each strip contains 2 light pink colour film coated tablets of Nirmatrelvir INN 150 mg each and 1 white color film coated tablet of Ritonavir USP 100 mg.)
	Pharmaceutical form of applied drug	Film Coated Tablets
	Pharmacotherapeutic Group of (API)	Anti-retroviral
	Reference to Finished product specifications	Manufacturer's specs

	Proposed Pack size	2 strips (Combipack) Each strip contains 2 light pink colour film coated tablets of Nirmatrelvir INN 150 mg each and 1 white colour film coated tablet of Ritonavir USP 100 mg.
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	PAXLOVID 150 mg/100mg Film-Coated Tablets (UK)
	For generic drugs (me-too status)	PAXLOVID 150 mg/100mg Film-Coated Tablets of M/s Pfizer
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability the studies of the drug substance.
	Nirmatrelvir	
	Name, address of drug substance manufacturer	KAIFENG Pharmaceutical (Group) Company Limited Head Office:No.1, Yunan Street, Kaifeng, Henan Province, China Manufacturing Site: No.1, Yunan Street, Kaifeng, Henan Province, China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 30°C ±2°C / 65% ± 5% The stability study data is till 12 months.
	Ritonavir	
	Name, address of drug substance manufacturer	M/s Arene Life Sciences Private Limited Plot No. 48, 49 &50, 209, 210 & 211 Phase-II, IDA, Pashamylaram Sangareddy PIN code -502 307 Telangana, India

	Module-III Drug Substance:	The firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25^{o}C ±2^{o}C / 60% ± 5% RH. The stability study data is till 24 months.
	Nirmatrelvir Film Coated Tablets	
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	PE and Comparative analysis Studies against the reference product Nirmatrelvir (Paxlovid) of Pfizer Limited have been submitted
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	PAXOVIR Film Coated Tablets Blister Foil Alu Alu Bottom foil 164 mm
	Stability study data of drug product, shelf life and storage conditions	The accelerated stability study data at 40^{o}C ±2^{o}C / 75% ± 5% RH for 6 months and real time stability study data at 30^{o}C ±2^{o}C / 65% ± 5% RH for 12 months.
	Ritonavir Film Coated Tablets	
	Module-III Drug Product:	The firm has submitted data on drug products including its description, composition, pharmaceutical development, manufacture, manufacturing process, and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications,

		reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	PE and Comparative analysis Studies against the reference product Norvir of AbbVie Inc. have been submitted
	Analytical method validation/verification of product	The firm has submitted analytical method validation studies for the applied product.
	The container closure system of the drug product	PAXOVIR Film Coated Tablets Blister Foil Alu Alu Bottom foil 164 mm
	Stability study data of drug product, shelf life, and storage conditions	The firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 6 months. The real-time stability study data is conducted at 30^{o}C ±2^{o}C / 65% ± 5% RH. The real-time stability study data of 3 batches for 12 months.
Evaluation by PEC:		
Decision: Deferred for submission of data regarding comparative pharmaceutical profiling and comparative dissolution with innovator drug product.		

Case No.01. Request of M/s Dynatis Pakistan (Pvt.) Ltd., Plot No. 710, Sundar Industrial Estate, Lahore (DML No. 000891) Lahore Regarding Contract Manufacturing & Analysis of Tofranil (Imipramine Hydrochloride) Tablet 25mg Under Rule 20A of Drugs (L, R, A) Rules, 1976

Registration Board in its 313th meeting held on 16th-18th November, 2021 approved the case regarding change in registration status of Tofranil (Imipramine Hydrochloride) Tablet 25mg from M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi (DML No.000124) to M/s Dynatis Pakistan (Pvt) Ltd., Plot No. 710, Sundar Industrial Estate, Lahore and accordingly registration letter was issued dated 24-06-2022. Detail is as under:

S.No.	Reg. No.	Name of Drug(s) & Composition
1.	112932	Tofranil 25mg Tablets Each sugar coated tablet contains: Imipramine Hydrochloride …….. 25mg (USP Specifications)

M/s Dynatis Pakistan (Pvt) Ltd., Lahore has now informed regarding some operational challenges stating that their coating and packing equipment validation is in process and the delay is caused due to disruption in procurement and supply chain procedures, therefore, Dynatis Pakistan will not be able to completely manufacture the above-mentioned product for a certain period of time.

Since, tofranil is an antidepressant drug used for long-term treatment and also has a withdrawal effect, therefore, timely availability of this product is very crucial.

Keeping in view the above and in order to avoid patient's inconvenience, the firm has submitted fee of Rs 75000/- (Challan No: 1835657890 Dated 20-08-22) and requested under Rule 20A of the Drug (Licensing Registration and Advertising) Rules 1976 regarding grant of permission for 3 months to complete the manufacturing process i.e., coating and packaging (of tablets compressed at manufacturing facility of M/s Dynatis Pakistan) including the final QC release testing at the manufacturing facility of M/s Indus Pharma, Karachi.

Decision: Registration Board acceded to the request of M/s Dynatis Pakistan (Pvt.) Ltd., Plot No. 710, Sundar Industrial Estate, Lahore (DML No. 000891) Lahore as per following detail:

i. **Manufacturing of Tofranil (Imipramine Hydrochloride) Tablet 25mg till compression will be carried out at manufacturing facility of M/s Dynatis Pakistan (Pvt.) Ltd., Plot No. 710, Sundar Industrial Estate, Lahore (DML No. 000891) Lahore.**
ii. **Coating and packaging of compressed tablets and final QC release testing will be carried out on contract basis at the manufacturing facility of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27, Korangi Industrial Area Karachi (DML No.000124) for a period of 3 months under of Rule 20A(1)(d) of Drugs (L, R, A) Rules, 1976.**

B. Biological Drug Division:

ADDITIONAL AGENDA

A: Priority/ Out of Queue consideration of Heparin & Enoxaparin Injections

DRAP Authority in its 144th meeting held on 26-08-2022 while considering the shortage of Heparin & Enoxaparin injections decided as follows:

"The Authority, as a one time exercise, approved out of queue consideration of submitted registration applications of following drugs in order to ensure their smooth and continuous supply in the market:

i. Paracetamol (Tablets, lnfusion and Syrup / Suspension)
ii. Albumin bound Paclitaxel lnjection
iii. Heparin and Enoxaprin lnjection

PE&R and BE&R Divisions are advised to process the cases of abovementioned drugs without waiting for formal approval of minutes."

Accordingly, DBE&R has evaluated all the new registration applications of Heparin & Enoxaparin Injections available in record and prepared the following agenda:

I: Imported Enoxaparin & Heparin Injections

1.	**Name, address of Applicant / Importer**	**M/s Calory Pharma,** **75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi.**
	Details of Drug Sale License of importer	**License No:** 110 **Address:** 75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi. **Validity: 06-07-2023** **Status:** License to sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	M/s Biem Ilac San. Ve Tic. A.S, Turgut Reis Cad. No.: 21 06570 Tandogan/ Ankara, Turkey.
	Name, address of manufacturer(s)	M/s Mefar Ilac San. A.S., Ramazanoglu Mah. Ensar Cad No: 20 Kurtkoy-Pendik/ Istanbul, Turkey
	Name of exporting country	Turkey
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. 2021/1843) dated 10-06-2021 valid till 10-06-2023 issued by Turkish Medicines & Medical Devices Agency. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from General Manager of M/s Biem Ilac Sanayi ve Ticaret A.S. According to the letter, the firm *M/s Biem Ilac* authorizes "Calory Pharma" to promote, market, sell and perform the registration procedures for the product. The letter was issued on 01-12-2021.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale

		☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 3272 (R&I) Dated 03-02-2022
	Details of fee submitted	Rs. 150,000/- dated 04-01-2022
	The proposed proprietary name / brand name	**Biemparin**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Heparin Sodium……5000IU
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	1's Vial (5mL)
	Proposed unit price	As per SRO/DPC
	Shelf Life	02 Years
	Storage Conditions	$\leq 30^0$C
	The status in reference regulatory authorities	Heparin Panpharma of M/s Panpharma, France.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Yino Pharma Ltd., 2 Cuiping Erxiang, Yubei District, Chongqing, 401120, China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of Drug Substance at real time conditions for 18 months. The real time stability data conducted at $25^0C \pm 2^0C/60 \pm 5\%RH$ is for 18 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Heparin Sodium Assay, benzyl Alcohol determination.
	Container closure system of the drug product	5mL Type I Colorless Glass vial, 20 mm gray brombutyl stopper, 20 mm blue flip-of cover.
	Stability study data of drug product	Firm has submitted stability study data of one commercial process validation batch. The accelerated stability study data is conducted at $40 \pm 2^0C/75\%RH \pm 5\%$ for 6 months. The real time stability study data is conducted at $25 \pm 2^oC/60\% \pm 5RH$ for 24 months.
	Remarks of Evaluator	• pH specification limits are different in Finished product specifications (5.5 to 7.0), in stability studies (5.0 to 7.5) and in European Pharmacopoeia (5.5 to 8.0) • Benzyl Alcohol specification limits are different in Finished product specifications (90% to 110%) and in stability studies (80% to 110%) • The firm has submitted stability study data of only one commercial Process Validation batch. • Non- clinical and Clinical trial data are not submitted by the firm. Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product, hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin.
Decision:	**Registration Board deferred the case fo submission of following by the firm:** **i. Clarification of different pH specification limits in Finished product specifications (5.5 to 7.0), in stability studies (5.0 to 7.5) and in European Pharmacopoeia (5.5 to 8.0)** **ii. Clarification of different Benzyl Alcohol specification limits in Finished product specifications (90% to 110%) and in stability studies (80% to 110%)** iii. **Real time & Accelerated Stability study data of three commercial batches.**	
2.	**Name, address of Applicant / Importer**	**M/s Calory Pharma,** **75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi.**
	Details of Drug Sale License of importer	License No: 110 Address: 75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi. Validity: 06-07-2023 Status: License to sell drugs by way of whole sale.

	Name and address of marketing authorization holder (abroad)	M/s 8161429 Venipharm, 422, Bureaux de la Colline F-92213 Saint-Cloud, France.
	Name, address of manufacturer(s)	M/s Centre Specialites Pharmaceutiques ZAC des Suzots 35 rue de la Chapelle F-63450 Saint-Ament Tallende, France.
	Name of exporting country	France
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. VEN/270521/10) dated 23-06-2021 issued by Authority for Justice and Consumer Protection of the Free and Hanseatic City of Hamburg. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from Qualified Person of M/s Venipharm. According to the letter, the firm M/s Venopharm authorizes "Calory Pharma Private Limited" to register, renew and to get the registration certificate for the product. The letter was issued on 17-12-2021 and valid for five years.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 3894 (R&I) Dated 10-02-2022
	Details of fee submitted	Rs. 150,000/- dated 04-01-2022
	The proposed proprietary name / brand name	Enoxaparin Ledraxen 4000IU (40mg)/0.4mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each PFS (0.4ml) contains: Enoxaparin Sodium……4000IU (equivalent to 40mg)
	Dosage form of applied drug	Solution for Injection in PFS
	Pharmacotherapeutic Group of (API)	Anticoagulant

	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	10's PFS
	Proposed unit price	As per SRO/DPC
	Shelf Life	24 Months
	Storage Conditions	$\leq 25^0$C
	The status in reference regulatory authorities	The product is itself approved in Germany.
	For generic drugs (me-too status)	Noxane of M/s BF Biosciences (Reg. No. 107948).
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd (NKF), China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 7 batches of Drug Substance at real time conditions for 36 months, 01 batch for 12 months, 01 batch for 09 months & 01 batch for 03 months. The real time stability data conducted at 25^0C$\pm 2^0$C/60±5%RH is for 18 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Anti-factor Xa activity, Anti-factor IIa Activity, Free sulfate content, Protein content, Bacterial Endotoxin, Sterility.
	Container closure system of the drug product	• A pre-filled syringe consisting of a 1-mL long barrel of type I glass with a fixed 27-gauge ½ inch stainless steel needle and a needle shield made of bromobutyl rubber • A 1-mL plunger rod made of polypropylene (which does not come directly in contact with the finished product)

		• A plunger stopper consisting of bromobutyl rubber
	Stability study data of drug product	Firm has submitted stability study data of 03 batches of 2000IU & 02 batches of 10000IU at real time, intermediate (Zone IVB) & conditions. The accelerated stability study data is conducted at 40 ± 2^0C/75%RH±5% for 6 months. The real time stability study data is conducted at 25 ± 2^0C/60%±5RH. The intermediate stability study data is conducted at 30 ± 2^0C/65%±5RH.
3.	**Name, address of Applicant / Importer**	**M/s Calory Pharma,** **75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi.**
	Details of Drug Sale License of importer	License No: 110 Address: 75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi. Validity: 06-07-2023 Status: License to sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	M/s 8161429 Venipharm, 422, Bureaux de la Colline F-92213 Saint-Cloud, France.
	Name, address of manufacturer(s)	M/s Centre Specialites Pharmaceutiques ZAC des Suzots 35 rue de la Chapelle F-63450 Saint-Ament Tallende, France.
	Name of exporting country	France
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. VEN/270521/11) dated 23-06-2021 issued by Authority for Justice and Consumer Protection of the Free and Hanseatic City of Hamburg. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from Qualified Person of M/s Venipharm. According to the letter, the firm M/s Venopharm authorizes "Calory Pharma Private Limited" to register, renew and to get the registration certificate for the product. The letter was issued on 17-12-2021 and valid for five years.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 3895 (R&I) Dated 10-02-2022
	Details of fee submitted	Rs. 150,000/- dated 04-01-2022

	The proposed proprietary name / brand name	Enoxaparin Ledraxen 6000IU (60mg)/0.6mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each PFS (0.6ml) contains: Enoxaparin Sodium……6000IU (equivalent to 60mg)
	Dosage form of applied drug	Solution for Injection in PFS
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	10's PFS
	Proposed unit price	As per SRO/DPC
	Shelf Life	24 Months
	Storage Conditions	$\leq 25^0$C
	The status in reference regulatory authorities	The product is itself approved in Germany.
	For generic drugs (me-too status)	Noxane of M/s BF Biosciences (Reg. No. 107949).
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd (NKF), China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 7 batches of Drug Substance at real time conditions for 36 months, 01 batch for 12 months, 01 batch for 09 months & 01 batch for 03 months. The real time stability data conducted at 25^0C±2^0C/60±5%RH is for 18 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures,

		validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Anti-factor Xa activity, Anti-factor IIa Activity, Free sulfate content, Protein content, Bacterial Endotoxin, Sterility.
	Container closure system of the drug product	• A pre-filled syringe consisting of a 1-mL long barrel of type I glass with a fixed 27-gauge ½ inch stainless steel needle and a needle shield made of bromobutyl rubber • A 1-mL plunger rod made of polypropylene (which does not come directly in contact with the finished product) • A plunger stopper consisting of bromobutyl rubber
	Stability study data of drug product	Firm has submitted stability study data of 03 batches of 2000IU & 02 batches of 10000IU at real time, intermediate (Zone IVB) & conditions. The accelerated stability study data is conducted at 40 ± 2^0C/75%RH±5% for 6 months. The real time stability study data is conducted at 25 ± 2^0C/60%±5RH. The intermediate stability study data is conducted at 30 ± 2^0C/65%±5RH.
4.	**Name, address of Applicant / Importer**	**M/s Calory Pharma,** **75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi.**
	Details of Drug Sale License of importer	License No: 110 Address: 75-B, Circular Street No. 13, Central Lane, Phase-II, DHA, Karachi. Validity: 06-07-2023 Status: License to sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	M/s 8161429 Venipharm, 422, Bureaux de la Colline F-92213 Saint-Cloud, France.
	Name, address of manufacturer(s)	M/s Centre Specialites Pharmaceutiques ZAC des Suzots 35 rue de la Chapelle F-63450 Saint-Ament Tallende, France.
	Name of exporting country	France
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. VEN/270521/12) dated 23-06-2021 issued by Authority for Justice and Consumer Protection of the Free and Hanseatic City of Hamburg. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from Qualified Person of M/s Venipharm. According to the letter, the firm M/s Venopharm authorizes "Calory Pharma Private Limited" to register, renew and to get the registration certificate for the product. The letter was issued on 17-12-2021 and valid for five years.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 3896 (R&I) Dated 10-02-2022
	Details of fee submitted	Rs. 150,000/- dated 04-01-2022
	The proposed proprietary name / brand name	Enoxaparin Ledraxen 8000IU (80mg)/0.8mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each PFS (0.8ml) contains: Enoxaparin Sodium……8000IU (equivalent to 80mg)
	Dosage form of applied drug	Solution for Injection in PFS
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	10's PFS
	Proposed unit price	As per SRO/DPC
	Shelf Life	24 Months
	Storage Conditions	$\leq 25^0$C
	The status in reference regulatory authorities	The product is itself approved in Germany.
	For generic drugs (me-too status)	Noxane of M/s BF Biosciences (Reg. No. 107950).
	Module-II (Quality Overall Summary)	Firm has submitted ICH QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd (NKF), China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities,

		specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 7 batches of Drug Substance at real time conditions for 36 months, 01 batch for 12 months, 01 batch for 09 months & 01 batch for 03 months. The real time stability data conducted at $25^0C \pm 2^0C/60 \pm 5\%RH$ is for 18 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Anti-factor Xa activity, Anti-factor IIa Activity, Free sulfate content, Protein content, Bacterial Endotoxin, Sterility.
	Container closure system of the drug product	• A pre-filled syringe consisting of a 1-mL long barrel of type I glass with a fixed 27-gauge ½ inch stainless steel needle and a needle shield made of bromobutyl rubber • A 1-mL plunger rod made of polypropylene (which does not come directly in contact with the finished product) • A plunger stopper consisting of bromobutyl rubber
	Stability study data of drug product	Firm has submitted stability study data of 03 batches of 2000IU & 02 batches of 10000IU at real time, intermediate (Zone IVB) & conditions. The accelerated stability study data is conducted at $40 \pm 2^0C/75\%RH \pm 5\%$ for 6 months. The real time stability study data is conducted at $25 \pm 2^0C/60\% \pm 5RH$. The intermediate stability study data is conducted at $30 \pm 2^0C/65\% \pm 5RH$.

The firm has submitted the following data as per requirements of 289th meeting of Registration Board:

Sr. No.	Required Documents	Documents Provided by the Firm
1.	Equivalence of physicochemical properties, such as:	
	a. Molecular weight distribution using size exclusion chromatography	i. Molecular mass distribution and proportion ii. %1, 6-anhydro derivatives iii. Free sulphate content iv. Ratio of sulfate ions to carboxylate ions v. UV Absorption and specific absorbance at 231 nm
	b. Chain mapping by cetyltrimethylammonium-coated strong anion exchange chromatography matrix-assisted laser desorption ionization mass spectrometry (MALDIMS), gel permeation chromatograph—electro spray ionization mass spectroscopy (GPC-ESI-MS), or reverse phase ion	i. Chain mapping by Gel Filtration Chromatography (GFC) ii. Chain mapping by strong anion exchange HPLC (SAX-HPLC) iii. Proton nuclear magnetic resonance (1H-NMR) iv. Heteronuclear single quantum coherence (HSQC) v. Intact chain mapping by LCMS

	pair—electro spray ionization mass spectroscopy (RPIPESI-MS).	
2.	Equivalence of heparin source material (i.e. heparin that is derived from porcine intestinal mucosa and that meets USP monograph standards for heparin sodium USP) and mode of depolymerization (i.e. cleavage by alkaline b-elimination of the benzyl ester derivative of heparin). The equivalent heparin source material should have at least a similar distribution of natural disaccharide building block sequences (within the context of itsvariability). If an equivalent mode of depolymerization is used, the generic drug products should be at least similar.	• Fresh pig's small intestine is collected and squeezed to get porcine intestinal mucosa. Porcine intestinal mucosa is then digested and heparin is adsorbed on an ion exchange resin (Intermediate A). • After the washing and elution of the resin, further steps of precipitation and drying lead to crude heparin (Intermediate B). • Crude heparin (Intermediate B) is dissolved in water, submitted to enzymolysis and then purified on resins. Heparin sodium (Intermediate C) is obtained after several steps including oxidation, ultra-filtration, fractionation and a final precipitation in ethanol. • Enoxaparin sodium is manufactured in three stages, starting from the heparin sodium which undergoes a step of salification to get the quaternary ammonium salt of heparin (Intermediate I). The salification step is followed by an esterification step to form the ester salt of heparin (Intermediate II). Enoxaparin sodium is finally isolated after depolymerization and purification steps.
3.	Equivalence in disaccharide building blocks, fragment mapping, and sequence of oligosaccharide species. This can be achieved by exhaustive digestion of enoxaparin with purified heparin digesting enzymes (heparinases I, II, and III) and nitrous acid, among other means, to yield the constituent disaccharide building blocks comprising enoxaparin. These individual disaccharide building blocks can be quantified by following: a. Capillary Electrophoresis (CE) b. Reverse phase high-performance liquid chromatography (RP-HPLC) c. Strong anion exchange HPLC (SAX-HPLC) d. Mass spectroscopy e. Nuclear magnetic resonance (NMR) spectroscopy. f. Chemical approaches such as analysis with modifying reagents (e.g. sodium borohydride, nitrous acid) or modifying enzymes (eg, 2-0-sulfatase, 6-0-sulfatase, and 5-glucuronidase) can be included.	i. Disaccharide building block by strong anion exchange HPLC (SAX-HPLC) ii. Fragment mapping (Heparinase I/II/III) by strong anion exchange HPLC (SAX-HPLC) iii. Fragment mapping (heparinase I/II/III) by liquid chromatography – mass spectrometry (LC-MS) iv. Dp6 mapping (heparinase I/II/III) by liquid chromatography – mass spectrometry (LC-MS) v. Dp8 mapping (heparinase I/II/III) by liquid chromatography – mass spectrometry (LC-MS) vi. Dp10 mapping (heparinase I/II/III) by liquid chromatography – mass spectrometry (LC-MS) vii. Nitrous acid (HONO) depolymerisation disaccharide mapping by liquid chromatography – mass spectrometry (LC-MS) iii. Tetrasaccharides (dp4) analysis by strong anion exchange HPLC (SAX-HPLC) ix. Tetrasaccharides (dp4) sequences by reversed-phase ion-pair liquid chromatography- electrospray ionization - mass spectrometry (RPIP-ESI-MS and RPIP-ESI-MS/MS) x. Oligosaccharide mapping by liquid chromatography – mass spectrometry (LC-MS) (dp6/8/10)

4.	Equivalence of in vitro biological and biochemical assay results using activated partial thromboplastin time (aPTT) and Heptest prolongation time. The equivalence in anti-Xa activity, anti-IIa activity, and anti-Xa/anti-IIa ratio between the generic LMWHs should be provided.	i. Anti-factor Xa & Anti-factor IIa activity by using Biophen Heparin Anti-Xa (2 Stages) and Biophen Heparin Anti-IIa (2 Stages) commercial kits. ii. The anticoagulant activity of the biosimilar enoxaparin drug product is analysed and compared with Lovenox®/Clexane® based on aPTT (Activated Partial Thromboplastin Time) and Heptest prolongation time iii.
5.	Equivalence of ex vivo pharmacodynamic (PD) profile in human volunteers. The comparison of in vivo PD profiles is based on measurements of in vivo anti-Xa and anti-IIa profiles.	A monocentric, randomized, open-label, single-dose, two-period, crossover study to assess the pharmacokinetic and pharmacodynamic equivalence of Reference Product Lovenox® 10000 IU/1 mL solution for injection in prefilled syringe and test formulation of Enoxaparin Ledraxen 10.000 IE (100 mg)/1 ml Injektionslösung in einer Fertigspritze following subcutaneous administration in healthy subjects in fasting conditions

Remarks of Evaluator	• The address of product license holder is different on CoPP from SmPC available on official website of Germany & letter of authorization. • The batch release site is different in dossier from Public Assessment Report available on official website of Germany & from Form-5F. • The manufacturer as per submitted CoPP is **M/s Centre Specialites Pharmaceutiques ZAC des Suzots 35 rue de la Chapelle F-63450 Saint-Ament Tallende, France** while as per submitted dossier manufacturer is **M/s Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd (NKF), No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China**. • Firm has not submitted the verification of compendial analytical methods of drug product. • Firm has not submitted the real time and accelerated stability data of applied strengths. However, stability data of lower (2000IU) & higher strengths (10000IU) is provided. • Stability study data of only 02 batches of higher strength i.e. 10000IU is provided. • Related substances are not tested in real time, intermediate & accelerated stability data while 1,6-anhydro derivatives, Average Mass & Sodium content are only tested for 01 batch of each strength. • **The provided intermediate/ Zone IVB stability data is for 36 months for two batches of lower strength & one batch of higher strength and 12 months of one batch each of lower & higher strength**. • **All the batches of both strengths get out of specifications after 12 months at intermediate/ Zone IVB conditions.**

Decision:

Registration Board deferred the products at S.No. 2,3 & 4 for submission of following by the firm:

i. Difference in address of product license holder on CoPP from SmPC available on official website of Germany & letter of authorization.

ii. Difference in batch release site in dossier from Public Assessment Report available on official website of Germany & from Form-5F.

iii. Any legalized evidence issued by regulatory authority of country of origin indicating that the manufacturer of product registered in Germany is M/s Nanjing King-Friend Biochemical

		Pharmaceutical Co., Ltd (NKF), No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China while M/s Centre Specialites Pharmaceutiques ZAC des Suzots 35 rue de la Chapelle F-63450 Saint-Ament Tallende, France is only batch release site. iv. Verification reports of compendial analytical methods of drug product. v. Real time & Accelerated stability data of three commercial batches of 2000IU & 10000IU upto the shelf life including all parameters as per finished product specification. vi. Clarification is required as all the batches of both strengths get out of specification after 12 months of storage at 30±2^{0}C/65%±5RH.
5.	**Name, address of Applicant / Importer**	**M/s Safemed Technologies,** **APT, 3, 2nd Floor, Retoon Plaza, Mini Market, Sector G-15/1,** **Islamabad.**
	Details of Drug Sale License of importer	**License No:** DHO-ISB-333 **Address:** APT, 3, 2nd Floor, Retoon Plaza, Mini Market, Sector G-15/1, Islamabad. **Validity: 24-08-2024** **Status:** Distribution License
	Name and address of marketing authorization holder (abroad)	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd., No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Name, address of manufacturer(s)	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd., No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted legalized CoPP (No. Hebei 20210440) dated 15-10-2021 valid till 14-10-2023 issued by Hebei Province Drug Administration. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from Enterprise Legal Person of M/s Hebei Changshan Biochemical Pharmaceutical Co., Ltd., According to the letter, the firm *M/s Hebei Changshan* exclusively authorizes "Safemed Technologies" to register, sale and quote the product. The letter was issued on 06-04-2022 and valid till 30-03-2025.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only

	Dy. No. and date of submission	Dy. No. 14234 (R&I) Dated 13-06-2022
	Details of fee submitted	Rs. 150,000/- dated 02-06-2022
	The proposed proprietary name / brand name	**Metaparin Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial (5ml) contains: Heparin Sodium……25000IU
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	5's Vials
	Proposed unit price	Rs. 1600/Vial
	Shelf Life	03 Years
	Storage Conditions	25±2℃/60±5% RH
	The status in reference regulatory authorities	Heparin Panpharma of M/s Panpharma, France.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd., No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance	Firm has submitted stability study data of 3 batches of Drug Substance at real time conditions for 36 months and accelerated conditions for 06 months. The real time stability data conducted at $25^0C \pm 2^0C/60 \pm 5\%RH$.

	(Conditions & duration of Stability studies)	
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Anti-factor IIa Activity, Anti-factor Xa activity, Benzyl Alcohol determination & Sterility test. Firm has submitted verification of Analytical methods of Related substances & Bacterial Endotoxin test.
	Container closure system of the drug product	EP Type I Colorless Glass vial, Grey Halogenated Butyl Rubber stopper, Aluminum & Plastic combined caps.
	Stability study data of drug product	Firm has submitted stability study data of 03 batches. The accelerated stability study data is conducted at 40 ± 2^0C/75%RH±5% for 6 months. The real time stability study data is conducted at 25 ± 2^oC/60%±5RH for 36 months.
	Remarks of Evaluator	• Non- clinical and Clinical trial data are not submitted by the firm. Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product, hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin.

Decision:

Keeping in view the availability of product in country of origin as per submitted CoPP and Heparin Injection being non-rDNA pharmacopoeial product; Registration Board approved the product as per current Import Policy for finished drugs.

6.	**Name, address of Applicant / Importer**	**Lab Diagnostic Systems (SMC) Pvt. Ltd. plot 36-A, PSIC SIE, Taxila Rawalpindi**
	Details of Drug Sale License of importer	License No: 01-374-0006-96845D **Address:** 36-A,PSIC,SIE,Taxila Rawalpindi Validity: 04/08/2024
	Name and address of marketing authorization holder (abroad)	NANJING KING-FRIEND BIOCHEMICAL PHARMACEUTICAL CO., LTD located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061 Telephone Number: +86-25-86990701 Fax Number: +86-25-86990701 D-U-N-S Number: 421297554 FEI Number: 3010625707 Last FDA Inspection Date: March 26 to April 3, 2018
	Name, address of manufacturer(s)	NANJING KING-FRIEND BIOCHEMICAL PHARMACEUTICAL CO., LTD located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted copy of CoPP issued by USFDA and copy of COPP from China. The COPP specifies that the product is licensed for sale in country of origin and US. The COPP also specifies the GMP status of manufacturer.

	Details of letter of authorization / sole agency agreement	Firm has submitted Pakistan notarized copy of distribution certificate from **M/s** Nanjing King-Friend Biochemical Pharmaceutical co., ltd According to the letter, the firm **M/s** Nanjing King-Friend Biochemical Pharmaceutical Co., LTD**.** authorizes "M/s Lab Diagnostic Systems (SMC) Pvt. Ltd. for the purpose of registration, distribution and marketing of the product. The letter was issued on 15/08/2022 valid up to 14/08/2023
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Form -5F Dy. No.23288 dated: 17/08/2022, Dy. No.23946 dated: 24/08/2022
	Details of fee submitted	Rs: 1,50,000 dated: 17/08/2022
	The proposed proprietary name / brand name	**Hepalid** 5000IU/5ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Heparin sodium: 5000 USP units
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulants
	Reference to Finished product specifications	USP
	Proposed Pack size	2's
	Proposed unit price	As per SRO
	Shelf Life	24 months
	Storage Conditions	Store at 20°C -- 25°C, excursions permitted between 15°C -- 30°C
	The status in reference regulatory authorities	Heparin Sodium Injection, USP FDA Approved
	For generic drugs (me-too status)	REGISTRATION NO: 066083 Brand Name: HEPARIN RAGALAB 5000 I.U. 5ML VIAL Importer Name: Kurative Pharma International
	Module-II (Quality Overall Summary	**QOS is not as per WHO**. Firm has summarized only information related to general properties, name of manufacturers for drug substance part. Composition of Drug product, description of manufacturing process and controls, specifications analytical procedures and justification of specification, reference standard, container closure system of drug product.
	Name, address of drug substance manufacturer	Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd.MA010-1, Nanjing High & Ne Technology Development Zone, Nanjing, China, 210061 Tel: 86-25-86992106 Fax: 86-25-86990701

	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis an justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches at long term conditions. The real time stability data is conducted at 5 ℃ ±3 ℃ RH 60%±10% for 12 months of 03 batches and 25 ± 2 ℃ /60% ± 5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	A proposed container closure system including Glass meeting the requirements of "Type I glass" as defined in the USP <660> was deemed to be adequate for the product. USP Type I Borosilicate glass container. **In packaging configuration & sizes only following packing are mentioned; 1000 IU/ ml (2ml vial), 10,000/ 10ml (10ml vial), 30,0000 IU/ 30ml (30ml), 5000 IU/ ml (2ml vial), 50,000 IU/ 10ml, 10,000 IU/ 1ml, 40,000 IU/ 4ml (5ml vial)**
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches at real time conditions. The real time stability data is conducted at 30± 2C & 60 ±5% RH for 6 months. A statement for availability of 24 months data is provided. The accelerated stability data provided is of 03 batches and is conducted at 40± 2C & 75 ±5% RH for 06 months.
	Module-IV Non-Clinical	N/A
	Module-V Clinical	N/A
	Remarks of Evaluator	i. For point No. 3.2.S.2.2, 3.2.S.2.3, 3.2.S.2.4, 3.2.S.2.5 & 3.2.S.2.6 of CTD, the firm referred to DMF but DMF has not been provided. ii. The product is from China but the firm has submitted copy of CoPP from USFDA. And regarding China CoPP it has been mentioned that product is under registration in China. And the firm has also submitted statement from their manufacturer that legalized CoPP will be submitted by end of October, 2022. iii. In the copy of USFDA-CoPP , **the importing country Israel has been mentioned.** iv. The firm has submitted copy of CoPP issued by USFDA which can be verified by the QR code mentioned on the CoPP. However, CoPP only mentioned "***Active Ingredient (s) and amount (s) per unit dose: heparin sodium usp 5000 Units***" total number of ml (volume) is not mentioned. The same was searched on USFDA official website wherein under the **Abbreviated New Drug Application (ANDA)**: 211007 (mentioned on the submitted CoPP), three products are mentioned HEPARIN SODIUM (1,000 UNITS/ML) HEPARIN SODIUM (5,000 UNITS/ML)

		HEPARIN SODIUM (10,000 UNITS/ML) But total number of ml (volume) was not mentioned there as well, and no other information is available on USFDA website. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=211007 v. The firm has mentioned (demanded) 5000Units/5ml vial packing in their CTD dossier i.e. covering letter, labeling information, fee receipt, QOS, point no. 1.5.2 of Module-I in all these document the firm has demanded 5000 Units/5ml but in distribution agreement, the firm has been authorized for 5000Units/mL (5ml vial). vi. In CTD dossiers under the packaging & container closure system neither 5000units/5ml vial nor 25000units/5mL vial is mentioned. (Already described in container closure system) vii. The firm has submitted stability study data (real time stability data) for 5000units/ml (5ml vial) is conducted at 30± 2C & 60 ±5% RH for 6 months. A statement from their manufacturer that they will submit complete stability study data once completed.
Decision: **Registration Board deferred the case for submission of following by the firm:** **i. Data related to Section 3.2.S.2.2, 3.2.S.2.3, 3.2.S.2.4, 3.2.S.2.5 & 3.2.S.2.6 of Form 5F.** **ii. Valid legalized CoPP issued by USFDA indicating demanded strength & pack size.** **iii. Clarification regarding difference in strength in dossier and distribution agreement.** **iv. Real time stability study data up to the demanded shelf life.**		
7.	**Name, address of Applicant / Importer**	**Lab Diagnostic Systems (SMC) Pvt. Ltd. plot 36-A, PSIC SIE, Taxila Rawalpindi**
	Details of Drug Sale License of importer	License No: 01-374-0006-96845D **Address:** 36-A, PSIC, SIE, Taxila Rawalpindi Validity: 04/08/2024
	Name and address of marketing authorization holder (abroad)	Nanjing King-Friend Biochemical Pharmaceutical Co., ltd., located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name, address of manufacturer(s)	NANJING KING-FRIEND BIOCHEMICAL PHARMACEUTICAL CO., LTD located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted copy of CoPP issued by USFDA (certificate no. 6HJ2-64TA issued June 04, 2021). The COPP specifies that the product is licensed for sale in country of origin and US. The COPP also specifies the GMP status of manufacturer.(Risk based Inspection)
	Details of letter of authorization / sole agency agreement	Firm has submitted Pakistan notarized copy of distribution certificate from **M/s** Nanjing King-Friend Biochemical Pharmaceutical co., ltd According to the letter, the firm **M/s** Nanjing King-Friend Biochemical Pharmaceutical Co., LTD**.** authorizes "M/s Lab Diagnostic Systems (SMC) Pvt. Ltd. for the purpose of registration, distribution and marketing of the product. The letter was issued on 15/08/2022 valid up to 14/08/2023

	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Form -5F Dy. No.1150 dated: 18/08/2022, Dy. No.23945 dated: 24/08/2022
	Details of fee submitted	Rs: 1,50,000 Dated: 17/08/2022
	The proposed proprietary name / brand name	**VINOX 40mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 0.4ml syringe contains: 40mg enoxaparin sodium injection
	Dosage form of applied drug	IV/SC Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant (Low molecular weight heparins.)
	Reference to Finished product specifications	USP
	Proposed Pack size	2's
	Proposed unit price	As per SRO
	Shelf Life	36 months
	Storage Conditions	Store at Below 30°C
	The status in reference regulatory authorities	Lovenox (enoxaparin sodium injection) for subcutaneous and intravenous USFDA approved
	For generic drugs (me-too status)	Clexane 40mg
	Module-II (Quality Overall Summary	**QOS is not as per WHO**. Firm has summarized only information related to general properties, name of manufacturers & & justification of specification for drug substance part. Composition of Drug product, description of manufacturing process and controls, specifications analytical procedures and justification of specification, reference standard, container closure system of drug product.
	Name, address of drug substance manufacturer	Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd.MA010-1, Nanjing High & Ne Technology Development Zone, Nanjing, China, 210061
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis an justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability	Firm has submitted stability study data of 3 batches at long term conditions. The real time stability data is conducted at 25 ± 2°C 60 ± 5% R for 36 months of 03 batches and 40±2 °C 75 ± 5% RH for 06 months for accelerated conditions.

	studies)	
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	A proposed container closure system including one mL syringe-BD Hypak SCF (sterile clean and ready-to-fill) including barrel one mL USP type I class , needle stainless steel 304, rigid needle shield rubber, rubber stopper, plunger rod, and safety device.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches at real time conditions. The real time stability data is conducted at 30± 2C & 60 ±5% RH for 36 months (by applying bracketing principle on 30mg/0.3ml and 100mg/1ml strengths). The accelerated stability data provided is of 03 batches and is conducted at 40± 2C & 75 ±5% RH for 06 months.
	Module-IV Non-Clinical	N/A
	Module-V Clinical	N/A
8.	**Name, address of Applicant / Importer**	**Lab Diagnostic Systems (SMC) Pvt. Ltd.** **plot 36-A, PSIC SIE, Taxila Rawalpindi**
	Details of Drug Sale License of importer	License No: 01-374-0006-96845D **Address:** 36-A, PSIC, SIE, Taxila Rawalpindi Validity: 04/08/2024
	Name and address of marketing authorization holder (abroad)	Nanjing King-Friend Biochemical Pharmaceutical Co., ltd., located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name, address of manufacturer(s)	NANJING KING-FRIEND BIOCHEMICAL PHARMACEUTICAL CO., LTD located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted copy of CoPP issued by USFDA (certificate no. CE9E-AHA6 issued June 07, 2021). The COPP specifies that the product is licensed for sale in country of origin and US. The COPP also specifies the GMP status of manufacturer.(Risk based Inspection)
	Details of letter of authorization / sole agency agreement	Firm has submitted Pakistan notarized copy of distribution certificate from **M/s** Nanjing King-Friend Biochemical Pharmaceutical co., ltd According to the letter, the firm **M/s** Nanjing King-Friend Biochemical Pharmaceutical Co., LTD**.** authorizes "M/s Lab Diagnostic Systems (SMC) Pvt. Ltd. for the purpose of registration, distribution and marketing of the product. The letter was issued on 15/08/2022 valid up to 14/08/2023
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Form -5F Dy. No.1149 dated: 18/08/2022, Dy. No.23945 dated: 24/08/2022
	Details of fee submitted	Rs: 1,50,000 Dated: 17/08/2022
	The proposed proprietary name / brand name	**VINOX 60mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 0.6ml syringe contains: 60mg enoxaparin sodium injection
	Dosage form of applied drug	IV/SC Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant (Low molecular weight heparins.)
	Reference to Finished product specifications	USP
	Proposed Pack size	2's
	Proposed unit price	As per SRO
	Shelf Life	36 months
	Storage Conditions	Store Below 30°C
	The status in reference regulatory authorities	Lovenox (enoxaparin sodium injection) for subcutaneous and intravenous USFDA approved
	For generic drugs (me-too status)	Clexane 40mg
	Module-II (Quality Overall Summary	**QOS is not as per WHO**. Firm has summarized only information related to general properties, name of manufacturers & & justification of specification for drug substance part. Composition of Drug product, description of manufacturing process and controls, specifications analytical procedures and justification of specification, reference standard, container closure system of drug product.
	Name, address of drug substance manufacturer	Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd.MA010-1, Nanjing High & Ne Technology Development Zone, Nanjing, China, 210061 Tel: 86-25-86992106 Fax: 86-25-86990701
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis an justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches at long term conditions. The real time stability data is conducted at 25 ± 2°C 60 ± 5% R for 36 months of 03 batches and 40±2 °C 75 ± 5% RH for 06 months for accelerated conditions.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	A proposed container closure system including one mL syringe-BD Hypak SCF (sterile clean and ready-to-fill) including barrel one mL USP type I class , needle stainless steel 304, rigid needle shield rubber, rubber stopper, plunger rod, and safety device.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches at real time conditions. The real time stability data is conducted at 30± 2C & 60 ±5% RH for 36 months (by applying bracketing principle on 30mg/0.3ml and 100mg/1ml strengths). The accelerated stability data provided is of 03 batches and is conducted at 40± 2C & 75 ±5% RH for 06 months.
	Module-IV Non-Clinical	N/A
	Module-V Clinical	N/A
	Remarks of Evaluator	
9.	**Name, address of Applicant / Importer**	**Lab Diagnostic Systems (SMC) Pvt. Ltd. plot 36-A, PSIC SIE, Taxila Rawalpindi**
	Details of Drug Sale License of importer	License No: 01-374-0006-96845D **Address:** 36-A, PSIC, SIE, Taxila Rawalpindi Validity: 04/08/2024
	Name and address of marketing authorization holder (abroad)	Nanjing King-Friend Biochemical Pharmaceutical Co., ltd., located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name, address of manufacturer(s)	NANJING KING-FRIEND BIOCHEMICAL PHARMACEUTICAL CO., LTD located at No. 16 Xuefu Road, Nanjing High & New Technology Development Zone, Nanjing, China 210061
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted copy of CoPP issued by USFDA (certificate no. PYCS-KTDV issued June 07, 2021). The COPP specifies that the product is licensed for sale in country of origin and US. The COPP also specifies the GMP status of manufacturer.(Risk based Inspection)
	Details of letter of authorization / sole agency agreement	Firm has submitted Pakistan notarized copy of distribution certificate from **M/s** Nanjing King-Friend Biochemical Pharmaceutical co., ltd According to the letter, the firm **M/s** Nanjing King-Friend Biochemical Pharmaceutical Co., LTD**.** authorizes "M/s Lab Diagnostic Systems (SMC) Pvt. Ltd. for the purpose of registration, distribution and marketing of the product. The letter was issued on 15/08/2022 valid up to 14/08/2023
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Form -5F Dy. No.1152 dated: 18/08/2022, Dy. No.23945 dated: 24/08/2022
	Details of fee submitted	Rs: 1,50,000 Dated: 17/08/2022
	The proposed proprietary name / brand name	VINOX 80mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 0.8ml syringe contains: 80mg enoxaparin sodium injection
	Dosage form of applied drug	IV/SC Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant (Low molecular weight heparins.)
	Reference to Finished product specifications	USP
	Proposed Pack size	2's
	Proposed unit price	As per SRO
	Shelf Life	36 months
	Storage Conditions	Store Below 30°C
	The status in reference regulatory authorities	Lovenox (enoxaparin sodium injection) for subcutaneous and intravenous USFDA approved
	For generic drugs (me-too status)	Clexane 40mg
	Module-II (Quality Overall Summary	**QOS is not as per WHO**. Firm has summarized only information related to general properties, name of manufacturers & & justification of specification for drug substance part. Composition of Drug product, description of manufacturing process and controls, specifications analytical procedures and justification of specification, reference standard, container closure system of drug product.
	Name, address of drug substance manufacturer	Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd.MA010-1, Nanjing High & Ne Technology Development Zone, Nanjing, China, 210061
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis an justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches at long term conditions. The real time stability data is conducted at 25 ± 2°C 60 ± 5% R for 36 months of 03 batches and 40±2 °C 75 ± 5% RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of

		specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	A proposed container closure system including one mL syringe-BD Hypak SCF (sterile clean and ready-to-fill) including barrel one mL USP type I class , needle stainless steel 304, rigid needle shield rubber, rubber stopper, plunger rod, and safety device.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches at real time conditions. The real time stability data is conducted at 30± 2C & 60 ±5% RH for 36 months (by applying bracketing principle on 30mg/0.3ml and 100mg/1ml strengths). The accelerated stability data provided is of 03 batches and is conducted at 40± 2C & 75 ±5% RH for 06 months.
	Module-IV Non-Clinical	N/A
	Module-V Clinical	N/A
	Remarks of Evaluator	i. The product is from China but the firm has submitted copy of CoPP from USFDA. And regarding China CoPP it has been mentioned that product is under registration in China. And the firm has also submitted statement from their manufacturer that legalized CoPP will be submitted by end of October, 2022. ii. In the copy of USFDA-CoPP , **the importing country Israel has been mentioned.** iii. The firm has submitted copy of CoPP issued by USFDA which can be verified by the QR code mentioned on the CoPP. However, the same was searched on USFDA official website wherein the products are available. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=211007 iv. Data as per guideline approved in 289th meeting of Registration Board as regulatory requirements for registration of Enoxaparin Injections, not submitted.
Decision: **Registration Board deferred the case for submission of following by the firm:** **i. Valid legalized CoPP issued by USFDA.** **ii. Data of Enoxaparin Sodium equivalence in light of guidelines of 289th meeting of Registration Board.**		
10	**Name, address of Applicant / Importer**	**M/s Medipak pvt. Limited,132/1, Industrial Estate, Kot Lakhpat, Lahore, 54770, Pakistan**
	Details of Drug Sale License of importer	License No: 05-352-0070-079516D Validity: 06th October, 2023
	Name and address of marketing authorization holder (abroad)	Laboratories Pablo Cassara S.R.L. Carhue 1096 (C1408GBV) La Rosa W/Nº, between Av. Gral. Paz and Saladillo (C1439BVJ) Autonomous City of Buenos Aires, Republic of Argentina.
	Name, address of manufacturer(s)	As above
	Name of exporting country	Republic of Argentina
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted Legalized CoPP issued by The National Institute of Drugs, (ANMAT), Republic of Argentina. The COPP specifies that the product is licensed for sale in country of origin. The COPP also specifies the GMP status of manufacturer.

	Details of letter of authorization / sole agency agreement	Firm has submitted Pakistan notarized copy of distribution certificate from **M/s** Laboratories Pablo Cassara; According to the letter, the firm **M/s** Laboratories Pablo Cassara., authorizes "M/s Medipak Limited. for the purpose of registration, distribution and marketing of the product. The letter was issued on 14th May, 2021.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Form -5F Dy. No.21015 dated: 26th July, 2022,
	Details of fee submitted	Rs: 150,000/- dated: 14th June, 2022
	The proposed proprietary name / brand name	**Synteparin Injection 5000IU**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose contains: Sodium Heparin….5000 IU
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulants
	Reference to Finished product specifications	USP
	Proposed Pack size	1's x 5ml 10's x 5ml
	Proposed unit price	As per SRO
	Shelf Life	24 months
	Storage Conditions	Store at 20°C -- 30°C
	The status in reference regulatory authorities	Heparin Sodium Injection, USP FDA Approved
	For generic drugs (me-too status)	Brand Name: Heparin Injection 5000 IU/ ml, 1's Pack Importer Name: M/s Leo/ Zam Zam Pharma
	Module-II (Quality Overall Summary	Firm has submitted QOS as per WHO. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, Characterization (Elucidation of Structure and Other Characteristics), impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Laboratories Pablo Cassara Carhue 1096 (C1408GBV) Autonomous City of Buenos Aires 54770, Republic of Argentina

	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis an justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches at long term conditions. The real time stability data is conducted at 25 ℃ RH 60%±10% for 48months and at 40℃ ± 2 ℃ /60% ± 5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	Type-I glass ampoule vial (5mL), injection-type opening, colorless. Bromobutyl stopper for injection-type vial, gray color with seal composed of an aluminum capsule with an aluminum cap that allows opening of its central section.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data: 3 **pilot scale batches** (1500 units each) at 25± 2C & 60 ±5% RH (real time conditions) for 24 months. One production scale batch (109.45 Lt) at 25± 2C & 60 ±5% RH (real time conditions) for 12 months. (ongoing) One production scale batch (109.45 Lt) at 30± 2C & 60 ±5% RH (real time conditions) for 12 months. (ongoing) One production scale batch (109.45 Lt) at 40± 2C & 75 ±5% RH (accelerated conditions) for 06 months.
	Remarks of Evaluator	i. In the submitted stability study data only one commercial scale batch data has been submitted. ii. The firm has submitted legalized CoPP wherein only mentioned "***Active Ingredient (s) and amount (s) per unit dose: sodium heparin 5000 Units***" total number of ml (volume) is one ml. iii. The firm has mentioned (demanded) Synteparin Injection 5000Units & proposed packing is 1's x5ml vial as per CTD dossier & proposed packaging. In stability 5ml vial data has been submitted while in CoPP one ml vial is indicated.
Decision: **Registration Board deferred the case for submission of following by the firm:** **i. Clarification regarding difference in pack size mentioned in dossier and proposed packing.** **ii. Real time stability data of 03 commercial batches up to the demanded shelf life.** **iii. Accelerated stability data of 03 commercial batches up to 06 months.** **iv. Evidence of availability of demanded pack size in country of origin.**		
11	**Name, address of Applicant / Importer**	**M/s Bajwa Sons,** **13-Muslim Street, House No. 3, 1st Floor & 2nd Floor, Mayo Hospital Road, Lahore.**
	Details of Drug Sale License of importer	**License No:** 05-352-0063-037644D **Address:** 13-Muslim Street, House No. 3, 1st Floor, Mayo Hospital Road, Lahore.

		Validity: 17-10-2022 **Status:** Distribution License
	Name and address of marketing authorization holder (abroad)	M/s Secondly Factory of Hainan Pharmaceutical Factory Co., Ltd., Linzohou Industrial Development Zone,
	Name, address of manufacturer(s)	M/s Secondly Factory of Hainan Pharmaceutical Factory Co., Ltd., Linzohou Industrial Development Zone,
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted copy of CoPP (No. Henan20210095) dated 26-05-2021 valid till 31-12-2022 issued by Henan Medical Products Administration. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of 2mL (12500IU) Injection in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted legalized exclusive agency agreement signed by both firms valid for five years. There is no date mentioned on agreement.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 32984, 4795, 11480 (R&I) dated 03-12-2021, 21-02-2022 & 12-05-2022.
	Details of fee submitted	Rs. 150,000/- dated 02-06-2022
	The proposed proprietary name / brand name	**Heparin Sodium Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Heparin Sodium……25000IU
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	5's Ampoule
	Proposed unit price	Not Provided
	Shelf Life	36 months
	Storage Conditions	≤25℃

	The status in reference regulatory authorities	Monoparin of M/s Wockhradt UK Ltd.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, flow of manufacturing process, analytical procedures, justification of specification.
	Name, address of drug substance manufacturer	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd., No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Module-III Drug Substance:	Firm has submitted drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, specifications, analytical procedures, batch analysis and justification of specifications.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Not Submitted.
	Module-III Drug Product:	Firm has summarized data of drug product including its composition, manufacturing process, control of drug product, process verification, specifications, batch analysis, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Anti-factor IIa Activity, Anti-factor Xa activity, Benzyl Alcohol determination & Sterility test. Firm has submitted verification of Analytical methods of Related substances & Bacterial Endotoxin test.
	Container closure system of the drug product	5 mL Low Borosilicate Glass Ampoule.
	Stability study data of drug product	Firm has submitted stability study data of 03 batches. The accelerated stability study data is conducted at 40 ± 2^0C/75%RH±5% for 6 months. The real time stability study data is conducted at 25 ± 2^oC/60%±5RH for 36 months.
	Remarks of Evaluator	• Copy of CoPP is submitted. • Address of manufacturer is different on CTD and submitted CoPP. • Submitted CoPP is for 2ml (25000IU) Heparin Sodium while applied formulation is 25000IU/5mL. • No date is mentioned on Agency Agreement. • Undertakings at section 1.5.19, 1.5.20(a) & 1.5.20 (b) are not submitted. • The firm has not submitted the summaries of Characterization, Impurities, Analytical Procedures, Validation of analytical procedures, Reference Standards or Materials, Container Closure system & stability for drug substance in Modul-II. • The firm has not submitted the summaries of Pharmaceutical Development, manufacturing process control of critical steps & intermediates, Process Validation, Control of Excipients, Characterization of Impurities, Analytical Procedures, Validation of analytical procedures, Batch Analysis, Reference Standards or Materials for drug product in Module-II.

		• Characterization of structure, verification of analytical procedures, COAs of reference standards, Container closure system for drug substance is not submitted by the firm in Module-III. • Stability Data of Drug Substance is not submitted. • Label claim mentioned in Module-III is 125000Units/5ml while applied product is 25000IU/5mL. • Product specifications are mentioned as Chinese Pharmacopoeia in Module-III while in Module-I as BP specifications. • Description, Pharmaceutical Development, In-process Controls, Control of Excipients, Control of finished product, Analytical procedures, verification of analytical procedures and COAs of reference standards for drug product are not submitted by the firm in Module-III. • Non- clinical and Clinical trial data are not submitted by the firm. Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product, hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin.

Decision:

Registration Board deferred the case for submission of following by the firm:

i. **Valid legalized CoPP of applied product.**
ii. **Clarification regarding difference in address of manufacturer in CTD and submitted CoPP.**
iii. **Clarification regarding not mentioning the date on Agency Agreement.**
iv. **Undertakings at section 1.5.19, 1.5.20(a) & 1.5.20 (b).**
v. **Summaries of Characterization, Impurities, Analytical Procedures, Validation of analytical procedures, Reference Standards or Materials, Container Closure system & stability for drug substance in Modul-II.**
vi. **Summaries of Pharmaceutical Development, manufacturing process control of critical steps & intermediates, Process Validation, Control of Excipients, Characterization of Impurities, Analytical Procedures, Validation of analytical procedures, Batch Analysis, Reference Standards or Materials for drug product in Module-II.**
vii. **Characterization of structure, verification of analytical procedures, COAs of reference standards, Container closure system for drug substance in Module-III.**
viii. **Stability Data of Drug Substance.**
ix. **Clarification regarding difference in Label claim mentioned in Module-III (125000Units/5ml) and applied product (25000IU/5mL).**
x. **Clarification regarding difference in Product specifications in Module-III (Chinese Pharmacopoeia) and in Module-I (BP specifications).**
xi. **Description, Pharmaceutical Development, In-process Controls, Control of Excipients, Control of finished product, Analytical procedures, verification of analytical procedures and COAs of reference standards for drug product.**

II. Locally Manufactured Heparin & Enoxaparin Injections.

1.	**Name of Manufacturer**	**M/s Macter International Limited.** **F- 216, S.I.T.E, Karachi 75700, Pakistan.**
	DML and last GMP details	DML No. 000141 Address: F- 216, S.I.T.E, Karachi 75700, Pakistan. **Evidence of section:** Liquid and Lyophilized recombinant DNA technology products (biological) section dated 19th July, 2012

		GMP: Last GMP conducted on 13-08-2020 valid up to 12-08-2022
	Bulk Manufacturer	Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi Town, Huangemei County, Hubei Province, China. (Formulation (**dilution), filling, testing & packing**)
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	For imported products, specify one the these	☐ Finished Pharmaceutical product import ☒ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Form 5 Dy.No.30665 dated 09-11-2021. Fee Submitted: Rs.30,000/- dated 20-10-2021.
	Details of fee submitted	Rs: 30,000/- dated: 20-10-2022
	Brand Name + Dosage Form + Strength	**Hepanox** Solution for Injection
	Composition	One ml of solution for injection contains 5000 IU of heparin sodium. While 1 vial (5 ml) contains 25000 IU of heparin sodium.
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulants
	Reference to Finished product specifications	B.P
	Proposed Pack size Proposed unit price	1's, 2's, 5's, 10's & 25's vialAs per DPC/
	Shelf Life	24 Months
	Storage Conditions	(Store below 25^0C)
	The status in reference regulatory authorities	Heparin Sodium Injection, USP FDA Approved
	For generic drugs (me-too status)	Brand Name: Heparin Injection 25000 IU/ 5ml, 1's Pack Importer Name: M/s Leo/ Zam Zam Pharma
	Module-II (Quality Overall Summary	Firm has submitted QOS as per WHO. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, Characterization (Elucidation of Structure and Other Characteristics), impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis an justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions &	Firm has submitted stability study data of 3 batches at long term conditions at 25 ℃ RH 60%±10% for 48months. The accelerated stability data

	duration of Stability studies)	is conducted at 40ºC ± 2 ℃ /60% ± 5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	USP Type-I glass vial (5mL),13mm slit less butyl grey stopper 133 mm Flip off aluminum caps
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches (two pilot scale & one lab scale) at long term conditions at 25 ℃ RH 60%±10% for 06 months. The accelerated stability data is conducted at 40ºC ± 2 ℃ /75% ± 5%RH for 06 months for accelerated conditions.
	Remarks of Evaluator	The applicant i.e. M/s Macter International Limited. Karachi has section for **Liquid and Lyophilized recombinant DNA technology products (biological**) while the applied product is **non-rDNA Biological product**. The clarification was sought from Licensing division for the section requirement of local manufacturing non-rDNA Biological Drugs (i.e. Heparin) whether **such products can be manufactured in rDNA Biological section as per current rules/regulation/practice of licensing division or not?** But comment has not been received from Licensing division yet.
Decision; **Registration Board referred the case to Licensing Division for confirmation of manufacturing section for production of Heparin Sodium.**		
2.	**Name of Manufacturer**	**M/s Macter International Limited.** **F- 216, S.I.T.E, Karachi 75700, Pakistan.**
	DML and last GMP details	DML No. 000141 Address: F- 216, S.I.T.E, Karachi 75700, Pakistan. **Evidence of section:** Liquid and Lyophilized recombinant DNA technology products (biological) section dated 19th July, 2012 GMP: Last GMP conducted on 13-08-2020 valid up to 12-08-2022
	Bulk Manufacturer	Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi Town, Huangemei County, Hubei Province, China
	Brand Name + Dosage Form + Strength	**Inhixa 0.2ml vial**
	Composition	Each 0.2 ml vial contains Enoxaparin sodium 20 mg.
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Antithrombotic agent
	Shelf life	24 Months (Store below 25^0C)
	International availability	Levenox the product is available in PFS in the said strenght & volume.
	Products already registered in Pakistan	Clexane 20mg/0.2ml but the product is available in PFS

	Type of Form Dy. No. Date of Application, Fee submitted	Form 5 Dy.No.32430 dated 29-11-2021. Fee Submitted: Rs.30,000/- dated 27-10-2021.
	Demanded Price / Pack size	s & 2's vial/As per SRO'1
	General Documentation	The formulation in 0.2ml vial is not available in reference country.
3.	**Name of Manufacturer**	**M/s Macter International Limited.** **F- 216, S.I.T.E, Karachi 75700, Pakistan.**
	DML and last GMP details	DML No. 000141 Address: F- 216, S.I.T.E, Karachi 75700, Pakistan. **Evidence of section:** Liquid and Lyophilized recombinant DNA technology products (biological) section dated 19th July, 2012 GMP: Last GMP conducted on 13-08-2020 valid up to 12-08-2022
	Bulk Manufacturer	Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi Town, Huangemei County, Hubei Province, China
	Brand Name + Dosage Form + Strength	**Inhixa 0.4ml vial**
	Composition	Each 0.4 ml vial contains Enoxaparin sodium 40 mg.
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Antithrombotic agent
	Shelf life	24 Months (Store below 25^0C)
	International availability	Levenox the product is available in PFS in the said strenght & volume.
	Products already registered in Pakistan	Clexane 20mg/0.2ml but the product is available in PFS
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5 Dy.No.32431 dated 29-11-2021. Fee Submitted: Rs.30,000/- dated 27-10-2021.
	Demanded Price / Pack size	s & 2's vial/As per SRO'1
	General Documentation	The formulation in 0.4ml vial is not available in reference country.
4.	**Name of Manufacturer**	M/s Macter International Limited. F- 216, S.I.T.E, Karachi 75700, Pakistan.
	DML and last GMP details	DML No. 000141 Address: F- 216, S.I.T.E, Karachi 75700, Pakistan. **Evidence of section:** Liquid and Lyophilized recombinant DNA technology products (biological) section dated 19th July, 2012 GMP: Last GMP conducted on 13-08-2020 valid up to 12-08-2022
	Bulk Manufacturer	Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi Town, Huangemei County, Hubei Province, China
	Brand Name + Dosage Form + Strength	**Inhixa 0.6ml vial**
	Composition	Each 0.6 ml vial contains Enoxaparin sodium 60 mg.
	Finished product	Ph. Eur.

	specifications	
	Pharmacological Group	Antithrombotic agent
	Shelf life	24 Months (Store below 25^0C)
	International availability	Levenox the product is available in PFS in the said strenght & volume.
	Products already registered in Pakistan	Clexane 20mg/0.2ml but the product is available in PFS
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5 Dy.No.32432 dated 29-11-2021. Fee Submitted: Rs.30,000/- dated 27-10-2021.
	Demanded Price / Pack size	s & 2's vial/As per SRO'1
	General Documentation	The formulation in 0.6ml vial is not available in reference country.
5.	**Name of Manufacturer**	M/s Macter International Limited. F- 216, S.I.T.E, Karachi 75700, Pakistan.
	DML and last GMP details	DML No. 000141 Address: F- 216, S.I.T.E, Karachi 75700, Pakistan. **Evidence of section:** Liquid and Lyophilized recombinant DNA technology products (biological) section dated 19th July, 2012 GMP: Last GMP conducted on 13-08-2020 valid up to 12-08-2022
	Bulk Manufacturer	Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi Town, Huangemei County, Hubei Province, China
	Brand Name + Dosage Form + Strength	**Inhixa 0.8ml vial**
	Composition	Each 0.8 ml vial contains Enoxaparin sodium 80 mg.
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Antithrombotic agent
	Shelf life	24 Months (Store below 25^0C)
	International availability	Levenox the product is available in PFS in the said strenght & volume.
	Products already registered in Pakistan	Clexane 80mg/0.8ml but the product is available in PFS
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5 Dy.No.32433 dated 29-11-2021. Fee Submitted: Rs.30,000/- dated 27-10-2021.
	Demanded Price / Pack size	s & 2's vial/As per SRO'1
	General Documentation	The formulation in 0.8ml vial is not available in reference country.
6.	**Name of Manufacturer**	M/s Macter International Limited. F- 216, S.I.T.E, Karachi 75700, Pakistan.
	DML and last GMP details	DML No. 000141 Address: F- 216, S.I.T.E, Karachi 75700, Pakistan. **Evidence of section:** Liquid and Lyophilized recombinant DNA technology products (biological) section dated 19th July, 2012 GMP: Last GMP conducted on 13-08-2020 valid up to 12-08-2022
	Bulk Manufacturer	Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi

		Town, Huangemei County, Hubei Province, China
	Brand Name + Dosage Form + Strength	**Inhixa 1ml vial**
	Composition	Each ml vial contains Enoxaparin sodium 100 mg.
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Antithrombotic agent
	Shelf life	24 Months (Store below 25^0C)
	International availability	Levenox the product is available in PFS in the said strenght & volume.
	Products already registered in Pakistan	Clexane 100mg/ml but the product is available in PFS
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5 Dy.No.32434 dated 29-11-2021. Fee Submitted: Rs.30,000/- dated 27-10-2021.
	Demanded Price / Pack size	s & 2's vial/As per SRO'1
	General Documentation	The formulation in One ml vial is not available in reference country.

Data as per guidelines of 289th meeting of Registration Board;

i) For Bulk Concentrate Import, Local formulation Filling:

	Documents Required	Documents submitted by the firm
i.	The firms shall provide legalized GMP certificate of biological drug substance manufacturer abroad (who will provide concentrate / ready to fill bulk of biological drug to Pakistani manufacturers for further processing) as an evidence that the manufacturer is an authorized manufacturer of biological drug in the country of origin.	Copy of GMP No.2020-20 dated 07-09-2020 issued by Hubei Provincial Drug Administration, China. Copy of GMP issued by Mo Industry and trade of the Russian Federation. Manufactuerer and its address: Hubei Enoray Biopharmaceutical Co.,Ltd. No.108, Yanjiang Road, Xiaochi Town, Huangemei County, Hubei Province, China
ii.	The firms shall provide legalized free sale certificate/CoPP either from country of origin or by any reference regulatory authority as adopted by Registration Board of finished product as evidence that the final product has been manufactured by same concentrate/ready to fill bulk after submission of data to the concerned regulatory authority.	Not provided.
iii.	The firm shall provide the complete data as adopted for imported Enoxaparin injections in 281st meeting of Registration Board of the finished product of same source (bulk concentrate or ready to fill) manufactured either from country of origin or by any reference regulatory authority as adopted by Registration Board to demonstrate the similar efficacy and safety to innovator product covering following requirements:	
	a) The first criterion for demonstrating sameness of enoxaparin is equivalence of physicochemical properties, such as molecular weight distribution using size exclusion chromatography, chain mapping by cetyltrimethylammonium-coated strong anion exchange chromatography, matrix-assisted laser desorption ionization mass spectrometry (MALDIMS), gel permeation chromatograph—electro spray ionization mass	Heparin sodium is dissolved and through salification, esterification, it is converted to heparin benzyl ester, then, Enoxaparin sodium is formed by alkaline degradation. Following a series of purification process (filtration, oxidization, ultrafiltration, membrane filtration, lyophilization, grinding and mixing), the final product Enoxaparin sodium is obtained.

	spectroscopy (GPC-ESI-MS), or reverse phase ion pair—electro spray ionization mass spectroscopy (RPIPESI-MS).	The structure & quality of Enoxaparin sodium has been compared with reference standard (Eu) & reference product**:**
	b) The second criterion for demonstrating the sameness of enoxaparin is equivalence of heparin source material (ie, heparin that is derived from porcine intestinal mucosa and that meets USP monograph standards for heparin sodium USP) and mode of depolymerization (ie, cleavage by alkaline b-elimination of the benzyl ester derivative of heparin). The equivalent heparin source material should have at least a similar distribution of natural disaccharide building block sequences (within the context of its variability). If an equivalent mode of depolymerization is used, the generic drug products should be at least similar.	**a. Elucidation of Structure and other Characteristics:** i. Molecular weight distribution by LC & eighteen-angle laser scattering instrument, Electronic balance. ii. Quantitative analysis of uronic acid by Microplate reader. iii. Qualitative analysis of amino sugar by Ion chromatograph, ampere pulsed, electronic balance. iv. Qualitative analysis of free anions and combined sulfo groups by Ion chromatograph, Electrical conductivity Dectector. v. Nuclear Magnetic Resonance analysis by NMR analyzer. vi. Infrared analysis by Fourier transform infrared spectrometer. vii. Disaccharide composition analysis by HPLC viii. Reducing end content analysis by HPLC. ix. Oligosaccharide sequence LC-MS analysis by Superhigh pressure liquid chromatograph-mass spectrometer x. Fingerprinting analysis with 2D-LC-Q/Tof-MS
	c) The third criterion for demonstrating the sameness of enoxaparin is equivalence in disaccharide building blocks, fragment mapping, and sequence of oligosaccharide species. This can be achieved by exhaustive digestion of enoxaparin with purified heparin digesting enzymes (heparinases I, II, and III) and nitrous acid, among other means, to yield the constituent disaccharide building blocks comprising enoxaparin. These individual disaccharide building blocks can be quantified by capillary electrophoresis (CE), reverse phase high-performance liquid chromatography (RP-HPLC), strong anion exchange HPLC (SAX-HPLC), mass spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy. Chemical approaches such as analysis with modifying reagents (e.g. sodium borohydride, nitrous acid) or modifying enzymes (eg, 2-0-sulfatase, 6-0-sulfatase, and 5-glucuronidase) can be included.	**b. Equivalence of heparin source material:** Based on USP monograph, the starting material of Enoxaparin sodium is from porcine intestinal mucosa & these are obtained from marketing authorization. CoA of crude Heparin Sodium has been submitted. Equivalence of Heparin degradation by chemical reaction (Benzethonium heparinate, nHeparin benzyl ester)
	d) The fourth criterion for establishing sameness of enoxaparin is equivalence of in vitro biological and biochemical assay results using activated partial thromboplastin time (aPTT) and Heptest prolongation time. The equivalence in anti-Xa activity, anti-IIa activity, and anti-Xa/anti-IIa ratio between the generic LMWHs should be provided.	Invitro Bioequivalence study of Low molecular weight Heparins for comparison of the product on aPTT & FXa activity with that of reference drug by aPTT assay & Anti-FXa assay. Equivalence in Biological & Biochemical assays: Anti-factor Xa activity & Anti-factor IIa activity by potency test method of USP mpnograph.
	e) The fifth criterion for establishing sameness of enoxaparin is equivalence of ex vivo pharmacodynamic (PD) profile in human volunteers. The comparison of in vivo PD profiles is based on measurements of in vivo anti-Xa and anti-IIa profiles.	Single center, open, randomized, single dose, two cycle, two-sequence & cross pharmacodynamics bioequivalence study aims to pre-estimate the effects of subcutaneous injection of test preparation Enoxaparin Sodium Injection & reference preparation Clexane in Chinese healthy subject under fasting.
iv.	The firm shall provide the lot release certificate of the finished product manufactured by same bulk concentrate/ ready to fill from country of export (If applicable).	NA

v.	The firm shall provide the 6 months accelerated and real time stability studies for drug substance.	24months real time stability study data at 25°C±2°C, 60%RH±5% RH & 6 months accelerated stability study at 40°C±2°C, 75%RH ±5% RH of drug substance from API manufacturer.
vi.	The local manufacturer shall perform all the tests on Enoxaparin Sodium bulk as detailed in Pharmacopoeial monograph of Enoxaparin Sodium.	• Identification by Size-Exclusion Chromatography (GPC) • Anti-Factor Xa Activity Chromogenic assay • Anti-Factor Ila activity Chromogenic assay • Color & clarity of solution • Light Absorption • Sodium by Atomic Absorption Spectrophotometry • Related Substances by HPLC
vii.	The local manufacturer shall manufacture three trial batches of the finished biological product to finalize the formulation and then perform the six months stability data on all the batches along with all the tests as detailed in Pharmacopoeial monograph of Enoxaparin Sodium Injection.	The stability study has been submitted for lowest 20mg, middle 60mg & highest 100mg vial (as per bracketing) 6-months real time stability study data at 25°C±2°C, 60%RH±5% RH & 6 months accelerated stability study at 40°C±2°C, 75%RH ±5% RH.
viii.	The local manufacturer shall perform suitable tests to evaluate the product and process related impurities both in their product and in Innovator product e.g. Total proteins, Individual proteins, Lipids and DNA content etc. The following techniques may be used: a. SDS-PAGE for individual proteins b. GC-MS for lipid impurities c. Threshold ® Total DNA Assay System for DNA content.	Related Substances by HPLC: Purity of LMW heparins by using Anion Exchange Chromatography based test. Sodium by Atomic Absorption Spectrophotometry
ix.	The firm shall provide the agreement with the source (of bulk concentrate/ready to fill) that if there shall be any critical change in manufacturing process, biological systems used to manufacture, etc. the firm shall inform DRAP immediately along with relevant documents.	Not submitted
x.	Regular monitoring through pharmacovigilance reporting system shall be observed through proper pharmacovigilance cell of the manufacturer and report will be forwarded to the National Pharmacovigilance Centre, Division of Pharmacy Services and Biological Division of DRAP. In case of any severe adverse event, immediate mandatory reporting procedure shall be followed.	Submitted
xi.	The firm shall inform DRAP if there shall be any adverse event or ADR reporting from the country of manufacture of concentrate/ready to fill bulk and finished product as required vide Rules 30 of Drug (LR&A) Rule.	Not submitted
xii.	If any of the conditions is not fulfilled or public health risk reported at any stage, the drug registration shall stand cancelled with immediate effect.	Not submitted
xiii.	All the provisions as contained in the Drugs Act, 1976 and rules made there under including provisions of Lot	Not submitted

	Release certification from National Control Laboratory for Biologicals shall be strictly adhered to.	

Remarks of Evaluator:

i. **The applied products are in vial packing while in reference regulatory authority, the said formulations are only available in PFS.**

ii. The applicant i.e. M/s Macter International Limited. Karachi has section for **Liquid and Lyophilized recombinant DNA technology products (biological**) while the applied product is **non-rDNA Biological product**. The clarification was sought from Licensing division for the section requirement of local manufacturing non-rDNA Biological Drugs (i.e. Heparin) whether **such products can be manufactured in rDNA Biological section as per current rules/regulation/practice of licensing division or not?** But comment has not been received from Licensing division yet.

Decision:

Registration Board deferred the case for submission of following by the firm:

i. **Evidence of availability of formulations in vials in Reference Regulatory Authorities.**
ii. **Valid legalized Free sale certificate/CoPP either from country of origin or by any reference regulatory authority as adopted by Registration Board of finished product as evidence that the final product has been manufactured by same concentrate/ready to fill bulk after submission of data to the concerned regulatory authority.**
iii. **Agreement with the source manufacturer (bulk concentrate) that if there shall be any critical change in manufacturing process, biological systems used to manufacture, etc. the firm shall inform DRAP immediately along with relevant documents.**
iv. **Referred the case to Licensing Division for confirmation of manufacturing section for production of Heparin Sodium.**
v. **An undertaking that the firm shall inform DRAP if there shall be any adverse event or ADR reporting from the country of manufacture of concentrate/ready to fill bulk and finished product as required vide Rules 30 of Drug (LR&A) Rule.**
vi. **An undertaking that if any of the conditions is not fulfilled or public health risk reported at any stage, the drug registration shall stand cancelled with immediate effect.**
vii. **An undertaking that all the provisions as contained in the Drugs Act, 1976 and rules made there under including provisions of Lot Release certification from National Control Laboratory for Biologicals shall be strictly adhered to.**

7.	**Name of Applicant**	**M/s Genix Pharma Limited** **44, 45-B, Korangi Creek Road, Karachi-75190, Pakistan**
	DSL details	DSL License No.000351 valid upto 22-09-2015.
	Name of Manufacturer	M/s Genix Pharma Limited 44, 45-B, Korangi Creek Road, Karachi-75190, Pakistan
	Brand Name + Dosage Form + Strength	**HEPI** Solution for Injection/ Infusion 25000IU
	Composition	Each 5ml Contains: Heparin Sodium : 25000 IU
	Finished product specifications	British Pharmacopoeia (BP Specs)
	Pharmacological Group	Anti-thrombotic agent (ATC code : B01AB01)
	Shelf life	2 Years Store at 25^0C (after reconstitusion store at 2^oC to 8^oC & use within 24 hours)
	International availability	Multiparin 25000IU/ 5ml (*M/s Wokhardt, UK*)
	Alternate Products already registered in Pakistan	POLIPARIN 25000 IU/5ml Reg. No.089815 M/s Shamco Traders (Pvt) Ltd, Lahore

	Type of Form Dy. No. Date of Application, Fee submitted	Form 5 Dy.No.11970/2019-(R&I)DRAP 06-03-2019 Fee of 50,000/- dated 04-03-2019
	Demanded Price Pack size	As per PRC 5ml
	General documentation	i. Form-5 duly signed dated 04th March, 2019. ii. Photocopy of Licence to Manufacture vide No.000351 having date of renewal w.e.f. 22-09-2015 iii. Copy of section approval dated 23-07-2012. iv. Photocopy of Inspection Report dated 23-07-2018.
	Evaluator Comments	Following product of *M/s Genix Pharma Private Limited*, for Registration of Heparin Sodium on Form 5 for Local Manufacturing has been received from PE&R division on 26-08-2022. The firm has **Liquid Biotech (recombinant DNA technology products (biological**) Liquid section while the applied product is **non-rDNA Biological product**.
	Decision : **Registration Board deferred the case for following:** **i. Evidence of availability of manufacturing facility/ section.** **ii. Realtime & Accelerated stability data of 06 months for locally manufactured product.**	

B: Miscellaneous/ Deferred Cases

1. REQUEST OF M/S MARTIN DOW MARKER LIMITED, KARACHI FOR Transfer Of REGISTRATION OF DRUG - ACTILYSE (ALTEPLASE 50MG) POWDER AND SOLVENT FOR SOLUTION FOR INJECTION AND INFUSION.

M/s Martin Dow Marker Limited, Nice Trade Orbit Building, Shahrah-e-Faisal, Block 6, PECHS, Karachi has submitted an application for Registration of following already registered product from M/s Ali Gohar & Company (Pvt.) Ltd, B-23, SITE, Karachi to their name. Detail of proposed product as under:

Requirement as per SOP	**Document submitted**
Application on Form 5-F with required fee as per relevant SRO.	Application on Form-5-F (Covering letter) & Fee of 150,000/-
Copy of registration letter and last renewal status.	Copy of Registration Letter dated 28-10-2020
Termination letter (original) from manufacturer for previous importer.	Original legalized Termination letter.
Authority letter/sole agent letter (original) from manufacturer.	Original legalized Power of Attorney in the name of applicant.
Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.	Original NOC for transfer of registration from the previous importer i.e. AG&C pvt Ltd Karachi.
Original and legalized Certificate of Pharmaceutical Product as per WHO format for new manufacturer's name OR Original and legalized GMP certificate of new manufacturing site with free sale certificate from regulatory body of country of origin.	Legalized Certificate of Pharmaceutical Product (CoPP)
Undertaking that the provided information/ documents are true/ correct.	Undertaking provided on stamp paper.

	Name, address of Applicant / Importer	M/s Martin Dow Marker Limited, Nice Trade Orbit Building, 44-A, Block 6, P.E.C.H.S, Razi Road, Shahrah-e-Faisal, Karachi
	Details of Drug Sale License of importer	License No: 0188 Validity: 08-12-2023 Status: License to sell drugs by way of Wholesale.
	Name and address of marketing authorization holder (abroad)	M/s Boehringer Ingelheim Pharma GmbH & Co. KG Binger Strasse 173 55216 Ingelheim am Rhein, Germany.
	Name, address of manufacturer(s)	M/s. Boehringer Ingelheim Pharma GmbH & Co. KG **Production Site**: Birkendorfer Strasse 65 88397 Biberach/ Riss, Germany.
	Name of exporting country	Federal Republic of Germany
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	Firm has submitted legalized CoPP (No. 155/2022) dated 30-03-2022 issued by Rheinland Pfalz,Landesamt Fur Soziaies, Jugend Und Verorung, Germany. The CoPP specifies free sale status of the product in Germany with its availability. The CoPP also confirms the GMP status of the firm. Periodicity of routine inspection is 3 years. In CoPP it is mentioned that the applicant for the CoPP is M/s Boehringer Ingelheim Pharma GmbH & Co. Germany (MAH) on behalf of M/s Boehringer Ingelheim International GmbH Binger Strasse 173 55216 Ingelheim am Rhein, Germany. (who authorize M/s Martin Dow Marker Limited Karachi for this product)
	Details of letter of authorization / sole agency agreement	Firm has submitted notarized copy of letter of product specific Power of Attorney issued by ***Boehringer Ingelheim International GmbH Binger Strasse 173 55216 Ingelheim am Rhein, Germany.*** *According to the letter, the firm authorizes* ***"M/s Martin Dow Marker Limited, Nice Trade Orbit Building, Shahrah-e-Faisal, Block 6, PECHS, Karachi"*** to be their wholly owned subsidiary and sole importer in Pakistan and to import, distribute & sale the product. The letter was issued on 25-05-2022.
	Status of applicant	□ Manufacturer □ Importer □ Is involved in none of the above (contract giver)
	Status of application	□ New Drug Product (NDP) □ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	□ Domestic sale. □Export sale. □Domestic and Export sales.
	For imported products, specify one the these	□ Finished Pharmaceutical Product Import. □ Bulk Import and local repacking (specify status of bulk). □ Bulk Import Local Repacking for Export purpose only
	Dy. No., date of submission & details of fee submitted	Dy. No. 17536 15-06-2022, Dy. No. 23154 dated 16-08-2022 PKR 150,000/-: 10-06-2022
	The proposed proprietary name / brand name	**Actilyse (Alteplase 50mg)** Powder and solvent for solution for injection and infusion.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: - Alteplase ……50mg (corresponding to 29,000,000 IU)d **Solvent:** Sterile water for injection (50mL)
	Dosage form of applied drug	Injection and infusion
	Pharmacotherapeutic Group of (API)	**Pharmacologic Class:** a.Tissue plasminogen activator (tPA)

		Therapeutic Class: b.Thrombolytic
	Reference to Finished product specifications	Ph. Eur specifications
	Proposed Pack size	1's (One vial of powder drug plus one vial of 50ml Solvent)
	Proposed unit price	As per DPC/SRO/ 1's
	Shelf Life	3 Years
	Storage Conditions	Store below 30°C
	The status in reference regulatory authorities	**The product is from reference country i.e. Germany**
	For generic drugs (me-too status)	The same product is already registered (AG&C) & the current case is transfer of registration.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to nomenclature, structure, general properties, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non- clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Boehringer Ingelheim Pharma GmbH & Co. KG Birkendorfer Str. 65 88397 Biberach Riss, Germany
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted real time stability study data of 5 batches of drug substance at -20°C & accelerated stability study data of 9 batches at 2-8°C for one months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted method validation studies including linearity, range, accuracy, precision, specificity.
	Container closure system of the drug product	Vial: The primary packaging used for the drug product is a colorless 50/60 mL tubing glass vial for pharmaceutical use" Type I glass container". Rubber Stopper: 20mm Chlorobutyl Formulation 1071 4432-50 grey, Flip-off Seal: 20mm Aluminum / polypropylene, West 3769, blue
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted real time stability study data of 3 production scale batches at 30°C/70%RH for 36 months. The accelerated stability study data is conducted at 40°C/75%RH for 12 months with two production scale batches. The firm has also submitted real time stability study data for four other batches as well which are on going & completed

		upto 30 months (one batch), 18 months (one batch) & 6 months (one batch).
	Module-IV Non-Clinical	The firm has submitted following non-clinical studies: • Comparative pharmacology of small & large scale aleplase in dogs, rabbits and monkeys. **(In vivo Pharmacology**) • Comparative pharmacokinetics of small scale & large scale aleplase in rabbits and primates. **(Pharmacokinetic**) • **SINGLE-DOSE TOXICITY** **SINGLE-DOSE TOXICITY STUDIES IN RATS** Intravenous single-dose toxicity study in rats [U84-0317] Intravenous single-dose toxicity study in rats [U85-0531] **SINGLE-DOSE TOXICITY STUDY IN MONKEYS** Intravenous single-dose toxicity study in monkeys [U84-0319] Intravenous single-dose toxicity study in monkeys [U85-0528] Intravenous single-dose toxicity study in monkeys [U85-0529] • **REPEAT-DOSE TOXICITY** **RODENT TOXICITY STUDIES** Intravenous repeat-dose toxicity studies with alteplase in rats Fourteen-day intravenous toxicity study in rats [U86-0302] Four-week intravenous study in rats [U87-0586, U88-0131] Thirteen-week intravenous toxicity study in rats [U90-0027] **NON-RODENT TOXICITY STUDIES** Intravenous repeat-dose toxicity studies with alteplase in non-rodents Fourteen-day intravenous toxicity study in dogs [U87-0928] Fourteen-day intravenous toxicity study in dogs [U86-0065] Fourteen-day intravenous toxicity study in marmosets [U87-0177, U88-0132] Four-week intravenous toxicity study in marmosets [U87-0201, U88-0132] **GENOTOXICITY** IN VITRO ASSAYS Ames test [U85-0322] Ames test [U86-0331] Chromosome aberration assay [U85-0569] Chromosome aberration assay [U86-0365] Unscheduled DNA synthesis assay [U87-0845] • **IN VIVO TESTS** Mouse bone marrow micronucleus test [U87-1009] **CARCINOGENICITY** ATG treated new-born rat assay [U85-0225] REPRODUCTIVE AND DEVELOPMENTAL TOXICITY **REPRODUCTIVE FUNCTION** Reproductive function intravenous toxicity study in rats [U90-0411] **EMBRYO-FETAL DEVELOPMENT** DRF embryo-foetal development intravenous toxicity study in rats [U86-0895]. Embryo-foetal development intravenous toxicity study in rats [U87-1019] DRF embryo-foetal development intravenous toxicity study in rabbits [U86-0894]

		Embryo-foetal development intravenous toxicity study in rabbits [U87-1020] **PERI- AND POSTNATAL DEVELOPMENT, INCLUDING MATERNAL FUNCTION** Peri- and postnatal toxicity study in rats by infusion [U90-0524] • **LOCAL TOLERANCE** **INTRA-ARTERIAL TOLERANCE** Intra-arterial tolerance study in the rabbit [U84-0916] Intra-arterial tolerance study in the rabbit [U86-0321] Local tolerance after single intra-arterial injection in rabbits [U98-2168] **INTRAVENOUS TOLERANCE** Intravenous tolerance study in rabbits [U84-0910] Intravenous tolerance study in rabbits [U86-0281] Local tolerance after single intravenous injection in rabbits [U98-2167] **PARAVENOUS TOLERANCE** Local tolerance after single paravenous injection in rats [U98-2169] **OCULAR TOLERANCE** Tolerability study after a single dose injection into the anterior chamber of rabbits [U97-2274] **OTHER TOXICITY STUDIES** • HEMOLYSIS • Haemolysis test with human blood • ANTIGENICITY • IMMUNOTOXICITY
	Module-V Clinical	**Phase III Trial:** **ECASS III Study [P08-12177]** **Objective:** To compare the safety and efficacy of alteplase vs. Placebo when administered between 3 and 4 hours 30 minutes after onset of stroke symptoms in patients with acute ischaemic stroke.(Randomized Placebo control) 821 Patients **ECASS III Study [P08-12177]** **Objective:** To compare the safety and efficacy of alteplase vs. Placebo when administered between 3 and 4 hours 30 minutes after onset of stroke symptoms in patients with acute ischaemic stroke. Patient Exposed to Alteplase: 406 Patient Exposed to Placebo: 390 **Pooled Analysis: 3-4.5 hr time window** Patient Exposed to Alteplase: 681 Patient Exposed to Placebo: 674 **Pooled Analysis: 0-6 hr time window** Patient Exposed to Alteplase: 1492 Patient Exposed to Placebo: 1470

Remarks of Evaluator: The firm also requested to grant permission for import of the product in international Export Pack & they will fulfil locally all mandatory packaging requirement as per Drug Labelling & Packaging Rule 1986 at their GMP compliant facility "Martin Dow Marker Limited, 7, Jail Road, Quetta, Pakistan" for 02 years (as already approved via letter F.No-3-175/2018-AD(BD)(M-307) for both registered pack sizes 1's & 2's. The firm has submitted fee of 7500/- & SOP for local printing of the information.
Decision: **Keeping in view valid legalized CoPP indicating product availability in country of origin, approval of Germany (Reference Regulatory Authorities) and NOC from M/s Ali Gohar & Company (Private) Limited, Karachi; Registration Board cancelled the registration of product from the name of M/s Ali Gohar & Company (Private) Limited, Karachi and granted the registration in the name of M/s Martin Dow Marker Limited, Karachi as per current Import policy for finished drugs subject to price confirmation from Costing & Pricing division and verification of cold storage facility.**

The Board deferred the rest of cases due to paucity of time.