MINUTES OF 313th MEETING OF REGISTRATION BOARD
HELD ON 16th ,17th & 18th NOVEMBER, 2021.
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Drug Regulatory Authority of Pakistan
T.F. Complex, Mauve Area, G-9/4
Islamabad

313th meeting of Registration Board was held on 16th to 18th November, 2021 in the Committee Room, Drug Regulatory Authority of Pakistan, G-9/4, Islamabad. The meeting was chaired by Dr. Obaidullah, Director, Pharmaceutical Evaluation & Registration Division, DRAP. The meeting started with recitation of the Holy Verses.

The meeting was attended by the following: -

1.	Dr. Rafeeq Alam Khan, Meritorious Professor, Faculty of Pharmacy, Ziauddin University, Karachi.	Member
2.	Lt. Gen. (R) Prof. Dr. Karamat A. Karamat (HI-M; SI-M), Former Surgeon General Pakistan, Rawalpindi	Member
3.	Maj.Gen. (R) Dr. Tahir Mukhtar Sayed, Inspector General (Hospitals), Fauji Foundation, Rawalpindi	Member
4.	Mr. Iftikhar A. Choudhary, Ex-Chief Pharmacist, Punjab University, Lahore	Member
5.	Dr. Qurban Ali, Former Director General, National Veterinary Laboratories, Islamabad	Member
6.	Dr. Amanullah Khan, Director, Drugs Testing Laboratory, Quetta. Government of Balochistan	Member
7.	Dr. Muhammad Munawar Hayat, Director, Drugs Testing Laboratory, Lahore Government of the Punjab	Member
8.	Mr. Ghulam Mujtaba, Deputy Director, Representative of IPO, Islamabad.	Member
9.	Mr. Muhammad Aslam, Deputy Draftsman-II, Representative of Ministry of Law & Justice, Islamabad	Member
10.	Dr. Noor-us-Saba, Director, Representative of Biological Evaluation & Research Division, DRAP	Member
11.	Mst. Mehwish Ansari, Deputy Director, Representative of QA&LT Division, DRAP	Member
12.	Mr. Abdullah, Additional Director (PE&R), DRAP.	Member/ Secretary
13.	Dr. Muhammad Akram, Dy.Animal Husbandry Commissioner, M/o National Food Security & Research, Islamabad	Co-Opted Member

Mr. Asif Jalil, Incharge PEC and respective Assistant Directors, presented the agenda of PE&R Division. Director, BE&R assisted by respective Assistant Directors to present the agenda of Biological Evaluation & Research Division. Deputy Director, QA&LT was assisted by respective Assistant Directors to present the agenda of QA & LT Division.

Mr. Jalal Ud Din Zaffar; Mr. Ali Raza & Mr. Hamid Raza (PPMA); Mr. Nadeem Alamgir (Pharma Bureau) and Mr. Saif ur Rehman (PC&DA) attended the meeting as observers.

Item No. I: Confirmation of Minutes of 312th meetings of Registration Board.

312th meeting of Registration Board was held on 14th, 15th and 16th September, 2021. The draft minutes of the said meeting were circulated for among the members of Registration Board on 12th October, 2021 for perusal/approval/comments (if any) within five days. None of the members disagreed the draft minutes.

Accordingly, Chairman, Registration Board approved the fair minutes of 312nd meeting of Registration Board which were circulated among concerned divisions/sections for implementation.

Decision: Registration Board confirmed the minutes of 312th meeting.

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.	Mr. Muhammad Umar Latif	Evaluator PEC-VI
6.	Mst. Sidra Khalid	Evaluator PEC-VII
7.	Mr. Haneef Ullah	Evaluator PEC-IX
8.	Mr. Farhadullah	Evaluator PEC-XI
9.	Mr. Shahid Nawaz	Evaluator PEC-XIII
10.	Mr. Ahsan Hafiz	Evaluator PEC-XIV
11.	Mst. Saima	AD PE&R
12.	Mr. Syed Ajwad Bukhari	AD PE&R

MISCELLANEOUS TASKS PERFORMED BY P.E & R DIVISION

1. Cefixime capsule Specifications

Registration Board in various meetings deliberated that the product monograph of cefixime capsule is present in Japanese pharmacopoeia however the dissolution test in JP specifies only 50mg and 100mg strength.

Dissolution test acceptance criteria as per JP monograph is NLT 80% in 90 minutes while as per USFDA review of innovator product cefixime 400mg capsule, the acceptance criteria for dissolution test should be NLT (Q) in 45 minutes. Comparison of dissolution specifications of products approved in FDA and JP is tabulated as below:

Parameter	**USFDA**	**JP**
RPM	100	50
Apparatus	Basket (I)	Paddle (II)
Medium	6.8g/L of monobasic potassium phosphate in water, adjusted with 1N sodium hydroxide	Disodium hydrogen phosphate-citric acid buffer solution
pH of the Medium	7.2	7.5
Time	45 minutes	90 minutes

Since in our scenario, the applied products are cefixime 200mg capsule which is approved in Spain and cefixime 400mg capsule approved in FDA. However, the dissolution specifications of 200mg capsule are not revealed by CIMA Spain.

Decision: **Registration Board deliberated the matter in detail and after thoroughly reviewing the product review documents of innovator product Suprax 400mg capsule and the monograph of cefixime capsule in Japanese Pharmacopeia 17th Edition, decided to approve the following monograph for cefixime capsule. The Board further decided that the monograph shall be notified for information of all manufacturers and regulatory laboratories. The Board further advised the manufacturer's / importers having registration of the said product to revise their specifications in the light of approved monograph within 6 months after its notification.**

CEFIXIME CAPSULES

Cefixime Capsules contain not less than 90.0% and not more than 105.0% of the labeled potency of cefixime ($C_{16}H_{15}N_5O_7S_2$: 453.45).

1. IDENTIFICATION:

Take out the contents of Cefixime Capsules, to a quantity of the contents of Cefixime Capsules, equivalent to 70 mg (potency) of Cefixime Hydrate, add 100 mL of 0.1 mol/L phosphate buffer solution (pH 7.0), shake for 30 minutes, and filter. To 1 mL of the filtrate add 0.1 mol/L phosphate buffer solution (pH 7.0) to make 50 mL. Determine the absorption spectrum of this solution using Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 286 nm and 290 nm.

2. PURITY: **Related substances**—

Take out the contents of Cefixime Capsules, to a quantity of the contents of Cefixime Capsules, equivalent to 0.1 g (potency) of Cefixime Hydrate, add 100 mL of 0.1 mol/L phosphate buffer solution (pH 7.0), shake for 30 minutes, filter, and use the filtrate as the sample solution. Perform the test with 10 mL of the sample solution using Liquid Chromatography according to the following conditions.

Determine each peak area from the sample solution by the automatic integration method, and calculate the amount of them by the area percentage method: the amount of each peak other than cefixime is not more than 1.0%, and the total amount of the peaks other than cefixime is not more than 2.5%.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4 mm in inside diameter and 125 mm in length, packed with octadecylsilanized silica gel for liquid chromatography (4 mm in particle diameter).
Column temperature: A constant temperature of about 40°C.
Mobile phase: To 25 mL of a solution of tetrabutylammonium hydroxide TS (10 in 13) add water to make 1000 mL, adjust to pH 6.5 with diluted phosphoric acid (1 in 10). To 300 mL of this solution add 100 mL of acetonitrile.
Flow rate: Adjust so that the retention time of cefixime is about 10 minutes.
Time span for measurement: About 3 times as long as the retention time of cefixime beginning after the solvent peak.
System suitability—
Test for required detectability:
Pipet 1 mL of the sample solution, and add 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 100 mL, and use this solution as the solution for system suitability test. Pipet 1 mL of the solution for system suitability test, and add 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 10 mL. Confirm that the peak area of cefixime obtained from 10 mL of this solution is equivalent to 7 to 13% of that obtained from 10 mL of the solution for system suitability test.
System performance: When the procedure is run with 10mL of the solution for system suitability test under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of cefixime are not less than 4000 and not more than 2.0, respectively.
System repeatability: When the test is repeated 6 times with 10 mL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak area of cefixime is not more than 2.0%.

3. WATER:
Not more than 12.0% (0.1 g of the contents, volumetric titration, direct titration).

4. UNIFORMITY OF DOSAGE UNITS:
Perform the Mass variation test, or the Content uniformity test according to the following method
Sample solution:
Take out the contents of 1 capsule of Cefixime Capsules, and to the contents and the capsule shells add 7V/10 mL of 0.1 mol/L phosphate buffer solution (pH 7.0), shake for 30minutes, and add 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly V mL so that each mL contains about 1 mg (potency) of Cefixime Hydrate. Centrifuge this solution, pipet 10 mL of the supernatant liquid, add 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 50 mL, and use this solution as the sample solution.
Standard solution
Separately, weigh accurately an amount of Cefixime RS, equivalent to about 20 mg (potency), dissolve in 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 100 mL, and use this solution as the standard solution.
Procedure
Perform the test with exactly 10 mL each of the sample solution and standard solution using Liquid Chromatography according to the following conditions, and determine the peak areas, A_T and A_S, of cefixime in each solution.
Amount [μg (potency)] of $C_{16}H_{15}N_5O_7S_2$

$$= MS \times A_T/A_S \times 10000$$

MS: Amount [mg (potency)] of Cefixime RS taken
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 254 nm).
Column: A stainless steel column 4 mm in inside diameter and 125 mm in length, packed with octadecylsilanized silica gel for liquid chromatography (4 mm in particle diameter).
Column temperature: A constant temperature of about 40°C.

Mobile phase: To 25 mL of a solution of tetrabutylammonium hydroxide TS (10 in 13) add water to make 1000 mL, adjust to pH 6.5 with diluted phosphoric acid (1 in 10). To 300 mL of this solution add 100 mL of acetonitrile.
Flow rate: Adjust so that the retention time of cefixime is about 10 minutes.

System suitability—
System performance:
When the procedure is run with 10 mL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of cefixime are not less than 4000 and not more than 2.0, respectively.
System repeatability:
When the test is repeated 6 times with 10 mL of the standard solution under the above operating conditions, the relative standard deviation of peak areas of cefixime is not more than 2.0%.

5. DISSOLUTION:

Apparatus:	Basket (I)
RPM:	100
Medium:	0.05 M Phosphate Buffer, pH 7.2
Volume:	900ml
Time:	45 minutes

Sample solution:
Start the test with 1 capsule of Cefixime Capsules, withdraw not less than 20 mL of the medium 45 minutes after starting the test, and filter through a membrane filter with a pore size not exceeding 0.5 mm. Discard the first 10 mL of the filtrate, pipet V mL of the subsequent filtrate, add the dissolution medium to make exactly V' mL so that each mL contains about 56 µg (potency) of Cefixime Hydrate,
and use this solution as the sample solution.
Standard solution:
Separately, weigh accurately an amount of Cefixime RS, equivalent to about 28 mg (potency), and dissolve in the dissolution medium to make exactly 100 mL. Pipet 4 mL of this solution, add the dissolution medium to make exactly 20 mL, and use this solution as the standard solution.
Procedure:
Perform the test with exactly 20 µL each of the sample solution and standard solution as directed under Liquid Chromatography according to the following conditions, and determine the peak areas, A_T and A_S, of cefixime in each solution.
Dissolution rate (%) with respect to the labeled amount of cefixime ($C_{16}H_{15}N_5O_7S_2$)
$= M_S \times A_T/A_S \times V'/V \times 1/C \times 180$
MS: Amount [mg (potency)] of Cefixime RS taken
C: Labeled amount [mg (potency)] of Cefixime Hydrate in 1 capsule
Acceptance criteria: Not Less than 80% in 45 minutes

Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 254 nm).
Column: A stainless steel column 4 mm in inside diameter and 125 mm in length, packed with octadecylsilanized silica gel for liquid chromatography (4 mm in particle diameter).
Column temperature: A constant temperature of about 40°C.
Mobile phase: To 25 mL of a solution of tetrabutylammonium hydroxide TS (10 in 13) add water to make 1000 mL, adjust to pH 6.5 with diluted phosphoric acid (1 in 10). To 300 mL of this solution add 100 mL of acetonitrile.
Flow rate: Adjust so that the retention time of cefixime is about 10 minutes.
System suitability—
System performance:

When the procedure is run with 20 µL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of cefixime are not less than 4000 and not more than 2.0, respectively.

***System repeatability*:**

When the test is repeated 6 times with 20 mL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of cefixime is not more than 2.0%.

6. ASSAY:

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4 mm in inside diameter and 125 mm in length, packed with octadecylsilanized silica gel for liquid chromatography (4 mm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: To 25 mL of a solution of tetrabutylammonium hydroxide TS (10 in 13) add water to make 1000 mL, adjust to pH 6.5 with diluted phosphoric acid (1 in 10). To 300 mL of this solution add 100 mL of acetonitrile.

Flow rate: Adjust so that the retention time of cefixime is about 10 minutes.

Sample solution:

Take out the contents of not less than 20 Cefixime Capsules, weigh accurately the mass of the contents, and powder. Weigh accurately a portion of the powder, equivalent to about 0.1 g (potency) of Cefixime Hydrate, add 70 mL of 0.1 mol/L phosphate buffer solution (pH 7.0) and shake for 30 minutes, add 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 100 mL. Centrifuge this solution, pipet 10 mL of the supernatant liquid, add 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 50 mL, and use this solution as the sample solution.

Standard solution:

Separately, weigh accurately an amount of Cefixime RS, equivalent to about 20 mg (potency), dissolve in 0.1 mol/L phosphate buffer solution (pH 7.0) to make exactly 100 mL, and use this solution as the standard solution.

Procedure:

Perform the test with exactly 10 mL each of the sample solution and standard solution using Liquid Chromatography and determine the peak areas, A_T and A_S, of cefixime in each solution.

Amount [mg (potency)] of cefixime ($C_{16}H_{15}N_5O_7S_2$)

$= M_S \times A_T/A_S \times 5$

M_S: Amount [mg (potency)] of Cefixime RS taken

System suitability—

System performance: When the procedure is run with 10 mL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of cefixime are not less than 4000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 10 mL of the standard solution under the above operating conditions, the relative standard deviation of peak areas of cefixime is not more than 2.0%.

Containers and storage Containers—Tight containers.

2. Mecobalamin (injection & tablet) testing method

Registration Board in various meetings deliberated on the testing requirements for various dosage forms of mecobalamin. PE&R Division has reviewed the monograph of all type of dosage forms of mecobalamin and the summary regarding testing requirements is as under.

Official monograph for mecobalamin drug substance and mecobalamin tablet is present in Japanese Pharmacopoeia. The important points regarding the specific testing requirements mentioned in both monographs is as follows:

It decomposes on exposure to light.

Conduct this procedure without exposure to light, using light-resistant vessels.

Column temperature: A constant temperature of about 40◦C.

Since Mecobalamin is light sensitive compound which degrades upon exposure to light therefore, it must not be exposed to light while testing. Adequate measures should be taken during the analysis of the product to protect it from light.

Decision: **Registration Board discussed the matter in detail and deliberated regarding the light sensitive nature of mecobalamin and thoroughly reviewed the monograph of mecobalamin drug substance and mecobalamin tablet in Japanese Pharmacopeia 17th Edition. Registration Board observed that mecobalamin is a light sensitive drug and it decomposes on exposure to light. Thus, keeping in view photolabile nature of the mecobalamin and pharmacopoeial recommendations, the Board advised the manufacturers of mecobalamin containing drug products to protect the drug substance from light during all manufacturing and testing stages taking appropriate measures including use of light-resistant vessels. The Board also decided to issue an advisory in this regard for the information of all pharmaceutical manufacturers/importers having registration of mecobalamin and all other light sensitive/photolabile drug substance containing drug products.**

3. Vitamin D injection equivalency case

Registration Board in various meetings deliberated the matter regarding cholecalciferol injection and its official monograph in British Pharmacopoeia. PE&R Division has reviewed the BP monograph as well as the status of this product in various reference regulatory authorities and the summary is as under.

Majority of the preparations of Cholecalciferol Injection registered in Pakistan contains 200,000IU which is equivalent to 5mg of cholecalciferol. However, the BP monograph under the heading of "Definition" defines this product as:

"Colecalciferol Injection is a sterile solution containing 0.75% w/v of Colecalciferol in Ethyl Oleate".

One gram of cholecalciferol is equal to 40,000,000 ($40x10^6$) IU. OR
One IU of cholecalciferol is equal to 0.025mcg of cholecalciferol. OR
40 IU of cholecalciferol is equal to 1mcg.

Sr. No.	Reference	Strength	Diluent
1	British pharmacopoeia	Colecalciferol injection is a sterile solution containing 0.75% w/v or 7.5mg/ml or 300,000 IU/ml Colecalciferol in ethyl Oleate.	Ethyl Oleate
2	ANSM France	200000 IU or 5mg	Medium chain triglycerides.
3	AIFA Italy	i. XARENEL 100,000 IU/ml (2.5mg/ml) solution for injection ii. XARENEL 300,000 IU/ml (7.5mg/ml) solution for injection	Refined olive oil for injectable use.

Decision: **Registration Board deliberated the matter in detail and thoroughly reviewed the approval status of the product in various reference regulatory authorities as well as BP monograph. Registration Board observed that BP monograph specifies that "Colecalciferol injection is a sterile solution containing 0.75% w/v or 7.5mg/ml or 300,000 IU/ml Cholecalciferol in ethyl Oleate". Registration Board decided that BP specifications for the drug product will be granted in those cases where the applied product meets the criteria specified in the BP monograph while all other strengths of Cholecalciferol injection will be approved with the specifications as per the innovator's drug product or manufacturer's specifications based on product development data as per criteria of 267th meeting.**

4. Recommendations / advisory for compliance to GMP.

Registration Board in its various meetings discussed the data requirements for product development and stability studies and has also issued guidance document for submission of application on Form 5-F (PE&R/GL/AF/004) dated 1st October 2020 (available: https://www.dra.gov.pk/Home/Download?ImageName=Guidance%20Document%20on%20CTD-Doc%20No.%20PE%26R-GL-AF-004.pdf). For aforementioned purpose, Registration Board either conduct onsite audit of pharmaceutical units for verification of authenticity of the submitted product development including stability study data or exempts onsite audit based on past inspection's observations (including but not limited to product development facilities, quality control labs including HPLC systems with 21 CFR compliant systems and stability chambers installed with digital data loggers etc) and documents/data submitted with registration dossiers of drug product.

For further guidance of the manufacturers to demonstrate adequate systems and compliance to GMP, in addition to the applicable requirements & guidelines; the Board decided to issue following recommendations / advisory for guidance of industry. Moreover, auditors during various regulatory inspections of QA&LT/Licensing/PE&R Divisions may review these points and record accordingly in reports.

1. It is preferable to have product development area with requisite facilities for relevant dosage form in each licensed unit endorsed from Central Licensing Board.
2. Pharmaceutical manufacturers shall ensure that they have valid operational qualification (OQ) and performance qualification (PQ) for already installed manufacturing equipment and shall perform installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) for equipment to be installed within their premises.
3. Pharmaceutical manufacturers shall ensure to have written procedures and protocols for all activities to be carried out in the licensed premises under the supervision of qualified personnel.
4. Quality control laboratory should be equipped with necessary equipment required to carry out testing of drug substances and drug products intended to be manufactured within the facility. All tests mentioned in official pharmacopoeia shall be performed as per the pharmacopoeial recommendations without any deviation using the same equipment preferably calibrated from an ISO certified firm and procedure as specified within the latest edition of relevant official pharmacopeia.
5. The drug product manufacturers shall have primary reference standard or secondary reference standards traceable to the primary standards, and the potency of any working standard shall be verified using the primary or secondary standard.
6. For all compendial as well as non-compendial drug substances, the drug product manufacturer shall perform analytical method verification studies including specificity, accuracy and repeatability (method precision) etc.
7. For drug products with non-compendial methods, the drug product manufacturers shall develop the method keeping in view the recommendations and tests specified in general monographs of the official pharmacopoeia and validate the analytical method as per ICH guidelines / pharmacopoeial requirements.
8. For the drug products for which officially recognized compendial methods are available, the drug product manufacturer shall perform verification studies which shall include a demonstration of specificity, repeatability (method precision), accuracy etc.
9. Adequate facilities for microbiological testing to comply the requirements of official pharmacopeia for all type of drug substances, drug products being manufactured within the facility and for the area monitoring, where required.
10. Adequate systems for vendor qualification for purchase of materials including Active Pharmaceutical Ingredient (API) / Drug Substance (DS), excipients and other materials through authorised sources. Active Pharmaceutical Ingredient (API) / Drug Substance shall be procured from pharmaceutical manufacturers having valid Drug Manufacturing License (DML) / Good Manufacturing Practices (GMP) certificate issued by concerned regulatory authority of country of origin.

11. Adequate water treatment facility to ensure that water used in manufacturing, testing operations etc of all drug products is of required quality.
12. Suitable Heating, Ventilation, and Air Conditioning (HVAC) system along with proper controls to ensure environment monitoring and to avoid cross contamination.
13. Manufacturers shall perform product development studies including pharmaceutical equivalence, comparative dissolution profile (where applicable, preferably using dissolution apparatus with 12 basket assembly) against the innovator / reference drug product as approved by reference regulatory authorities. Incase where the innovator / reference drug product is not available in Pakistan, the manufacturer shall get approval from QA&LT Division for import of innovator / reference drug product as per Drugs (Import & Export) Rules, 1976. The Board further advised QA&LT Division, DRAP to permit import of innovator or reference drug product on priority for performing aforementioned studies.
14. Preferable to have 21 CFR compliant High-performance liquid chromatography (HPLC) system with enabled audit trail report system. Such systems need to be reviewed and audited during regulatory inspection by QA&LT/Licensing/PE&R Divisions and the details of such system along with its model including information whether gradient or isocratic, 21 CFR compliance status, audit trail report etc should be made part of the inspection report.
15. Adequate number of stability chambers with digital data logger for temperature and humidity monitoring alongwith backup power supply for conducting accelerated as well as real time stability studies of their products (real time stability for already registered drug products and both real time & accelerated stability studies for trial products). The stability chambers should be reviewed and reported during regulatory inspections by QA&LT/Licensing/PE&R Divisions.

5. Azithromycin testing method (capsule, tablet & Dry suspension) as per BP & USP

Registration Board in various meetings deliberated the matter regarding testing requirements for azithromycin dosage forms in the light of BP and USP pharmacopoeia. PE&R Division has reviewed BP & USP monograph for all dosage forms of azithromycin and the summary is as under.

Following is the comparative table of analytical method of USP and BP for Azithromycin capsule, tablet and dry powder for suspension.

Azithromycin Capsule

USP 43	BP
DEFINITION Azithromycin Capsules contain the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of azithromycin (**C38H72N2O12**).	**DEFINITION** Azithromycin Capsules contain Azithromycin. The capsules comply with the requirements stated under Capsules and with the following requirements. **Content of azithromycin, C38H72N2O12** 95.0 to 105.0% of the stated amount.
IDENTIFICATION •**A.** The retention time of the azithromycin peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay.*	**IDENTIFICATION** A. Shake a quantity of the capsule contents containing 0.5 g of Azithromycin with 50 mL of dichloromethane. Filter (a 0.45-µm nylon filter is suitable) and evaporate the filtrate to dryness under a stream of nitrogen. The infrared absorption spectrum, Appendix II A, is concordant with the reference spectrum of azithromycin (RS 487). B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of principal peak in the chromatogram obtained with solution (2).

DISSOLUTION [NOTE— Use water that has a resistivity of NLT 18 Mohm-cm.] **Medium:** pH 6.0 sodium phosphate buffer (Prepare 6 L of 0.1 M dibasic sodium phosphate. Adjust with about 40 mL of hydrochloric acid to a pH of 6.0 ± 0.05, and add 600 mg of trypsin); 900 mL **Apparatus 2:**100 rpm **Time:**45 min **Mobile phase, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*. **Standard stock solution:**0.3 mg/mL of USP Azithromycin RS in *Medium*. Sonicate briefly to dissolve. **Standard solution:**3.84 µg/mL of azithromycin from the *Standard stock solution* in *Mobile phase* **Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.5-µm or finer pore size. Transfer 2.0 mL of the filtrate to a 25-mL volumetric flask, and dilute with *Mobile phase* to volume. Transfer 4.0 mL of this solution to a second 25-mLvolumetric flask, and dilute with *Mobile phase* to volume. **Analysis** **Samples:** *Standard solution* and *Sample solution* Determine the amount of azithromycin (**C38H72N2O12**) dissolved using the procedure in the *Assay*, making any necessary modifications. Calculate the percentage of azithromycin (CHNO) dissolved: Result = $(r/r) \times (C/L) \times D \times V \times 100$ *r*= peak response from the *Sample solution* *r*= peak response from the *Standard solution* *C*= concentration of USP Azithromycin RS in the *Standard solution* (mg/mL) *L*= label claim (mg/Capsule) *D*= dilution factor of the *Sample solution* *V*= volume of *Medium*, 900 mL **Tolerances:** NLT 75% (*Q*) of the labeled amount of azithromycin (CHNO) is dissolved.	**Dissolution** Comply with the requirements in the dissolution test for tablets and capsules. **TEST CONDITIONS** (a) Use Apparatus 1, rotating the basket at 100 revolutions per minute. (b) Use 900 ml of 0.lM sodium dihydrogen orthophosphate previously adjusted to pH 6.0 with orthophosphoric acid, at a temperature of 37°C, as the dissolution medium**.** **PROCEDURE** Carry out the method for liquid chromatography, Appendix III D, using the following solutions. Solvent A 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 8.0 with orthophosphoric acid, and 60 volumes of acetonitrile Rl. (1) After 45 minutes withdraw a sample of the medium and filter. Dilute a quantity of the filtrate with the dissolution medium to produce a solution expected to contain 0.027% w/v of Azithromycin. (2)0.027% w/v of azithromycin EPCRS in the dissolution medium. (3) 0.05% w/v each of azithromycin EPCRS and azithromycin impurityA EPCRS in solvent A. **CHROMATOGRAPHIC CONDITIONS** (a) Use a stainless-steel column (25 cm x 4.6 mm) packed with octadecyl silyl vinyl polymer for chromatography (5 µm) (Asahipak ODP-50 is suitable). (b) Use isocratic elution and the mobile phase described below. (c) Use a flow rate of 1 mL per minute. (d) Use a column temperature of 40°. (e) Use a detection wavelength of 210 nm. (f) Inject 20 µL of each solution. **MOBILE PHASE** • 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 11.0 with a 56% w/v solution of potassium hydroxide, and 60 volumes of acetonitrile Rl. • When the chromatograms are recorded under the prescribed conditions the retention time of azithromycin is about 10 minutes. **SYSTEM SUIT ABILITY** The test is not valid unless: in the chromatogram obtained with solution (2), the symmetry factor of the peak due to

	azithromycin is between 0.8 and 2.0; in the chromatogram obtained with solution (3), the resolution between the peaks due to impurity A and azithromycin is at least 1.5. **DETERMINATION OF CONTENT** Calculate the total content of azithromycin, C3sH12N2O12, in the medium using the declared content of C38H72N2O12 in azithromycin EPCRS. **LIMITS** Amount of azithromycin, C38H72N2O12, released is not less than 75% (Q) of the stated amount.
ASSAY •**PROCEDURE** [NOTE— Use water that has a resistivity of NLT 18 Mohm-cm.] **Mobile phase:** Dissolve 5.8 g of monobasic potassium phosphate in 2130 mL of water, and add 870 mL of acetonitrile. Adjust with about 6 mL of 10 N potassium hydroxide to a pH of 11.0 ± 0.1, and pass through a suitable filter. **Standard stock solution:** 0.165 mg/mL of USP Azithromycin RS in acetonitrile. Swirl, and sonicate as necessary. **Standard solution:**3.3 µg/mL of USP Azithromycin RS from the *Standard stock solution* in *Mobile phase* **System suitability stock solution:** 0.16 mg/mL of USP Azaerythromycin A RS in acetonitrile and *Mobile phase* (1:9). Dissolve first in acetonitrile, using 10% of the final volume. Swirl, and sonicate to dissolve. Dilute with *Mobile phase* to volume. **System suitability solution:**3.2 µg/mL of azaerythromycin A from the *System suitability stock solution* and 3.3 µg/mL of azithromycin from the *Standard stock solution* in *Mobile phase* **Sample stock solution:** Remove, as completely as possible, the contents of NLT 20 Capsules. Prepare a 1-mg/mL solution of anhydrous azithromycin in acetonitrile. Dissolve a portion of the mixed Capsule contents first in 70% of the final volume of acetonitrile, and shake by mechanical means for 30 min. Dilute with acetonitrile to volume. Place 40 mL of the resulting suspension in a centrifuge tube, and centrifuge. Use the supernatant to prepare the *Sample solution*. **Sample solution:**3.2 µg/mL of azithromycin from the *Sample stock solution* in *Mobile phase* **Chromatographic system** (See *Chromatography* ⟨621⟩, *System Suitability*.) **Mode:** LC **Detector:** Amperometric electrochemical detector	**ASSAY** Carry out the method for liquid chromatography, Appendix III D, -using the following solutions. Solvent C 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 8.0 with orthophosphoric acid and 60 volumes of acetonitrile Rl. (1) Shake a quantity of the mixed contents of 20 capsules containing 0.5 g of Azithromycin with 40 mL of solvent C, dilute to 100 mL with the same solvent and filter (a 0.45-µm nylon filter is suitable). Dilute 1 volume of the filtrate to solution to 10 volumes with solvent C. (2) 0.05% w/v of azithromycin EPCRS in solvent C. (3) 0.05% w/v each of azithromycin EPCRS and azithromycin impurity A EPCRS in solvent C. **CHROMATOGRAPHIC CONDITIONS** The chromatographic conditions described under Dissolution may be used, but with an injection volume of 10 µL. **SYSTEM SUITABILITY** The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between the peaks due to impurity A and azithromycin is at least 1.5. **DETERMINATION OF CONTENT** Calculate the content of azithromycin, C38H72N2012, in the capsules using the declared content of C38H72N2012 in azithromycin EPCRS.

Electrode: Dual glassy carbon electrodes **Mode:** Oxidative screen mode **Electrode 1:** +0.70 ± 0.05 V **Electrode 2:** +0.82 ± 0.05 V **Background current:**85 ± 15 nanoampheres **Columns** **Guard:**4.6-mm × 5-cm; 5-µm packing L29 **Analytical:**4.6-mm × 15-cm; 5-µm packing L29 or 3-µm packing L49 without the guard column **Flow rate:**1.5 mL/min **Injection size:**50 µL **System suitability** **Samples:** *Standard solution* and *System suitability solution* [NOTE— The relative retention times for azaerythromycin A and azithromycin with the L29 column are 0.7 and 1.0, respectively; the relative retention times for azaerythromycin A and azithromycin with the L49 column are 0.8 and 1.0, respectively.] **Suitability requirements** **Resolution:** NLT 2.5 between azaerythromycin A and azithromycin, *System suitability solution* **Column efficiency:** NLT 1000 theoretical plates, *Standard solution* **Tailing factor:**0.9–1.5, *Standard solution* **Relative standard deviation:** NMT 2.0%, *Standard solution* **Analysis** **Samples:** *Standard solution* and *Sample solution* Calculate the percentage of the labeled amount of azithromycin (**C38H72N2O12**) in the portion of Capsules taken: Result = (r/r) × (C/C) × P × F × 100 r= peak response from the *Sample solution* r= peak response from the *Standard solution* C= concentration of USP Azithromycin RS in the *Standard solution* (µg/mL) C= nominal concentration of azithromycin in the *Sample solution* (µg/mL) P= potency of azithromycin in USP Azithromycin RS (µg/mg) F= conversion factor, 0.001 mg/µg **Acceptance criteria:**90.0%–110.0%	
•UNIFORMITY OF DOSAGE UNITS ⟨905⟩**:** Meet the requirements **SPECIFIC TESTS** **•WATER DETERMINATION,** *Method I*⟨921⟩**:** NMT 5.0% **ADDITIONAL REQUIREMENTS** **•PACKAGING AND STORAGE:** Preserve in	

well-closed containers. Where packaged in unit-of-use containers, each container contains six 250-mg Capsules, and the label indicates the intended sequential day of use for each Capsule.	

Azithromycin Tablet

USP 43	BP
DEFINITION Azithromycin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of azithromycin (**C38H72N2O12**).	**DEFINITION** Azithromycin tablet contain Azithromycin. The tablet comply with the requirements stated under tablet and with the following requirements. **Content of azithromycin,** (**C38H72N2O12**) 95.0 to 105.0% of the stated amount.
IDENTIFICATION •**A.** The retention time of the azithromycin peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*. ***Change to read:*** **B. SPECTROSCOPIC IDENTIFICATION TESTS** ⟨197⟩**,** *Infrared Spectroscopy***: 197A** **Standard solution:** 25 mg/mL of USP Azithromycin RS in acetonitrile. Pass the solution through a suitable filter, and remove the solvent by natural evaporation. **Sample solution:** Equivalent to 25 mg/mL of azithromycin from Tablets in acetonitrile. Pass the solution through a suitable filter, and remove the solvent by natural evaporation. **Acceptance criteria:** Meet the requirements.	**IDENTIFICATION** A. Shake a quantity of the powdered tablet containing 0.5 g of Azithromycin with 50 mL of dichloromethane. Filter (a 0.45-µm nylon filter is suitable) and evaporate the filtrate to dryness under a stream of nitrogen. The infrared absorption spectrum, Appendix II A, is concordant with the reference spectrum of azithromycin (RS 487). B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of principal peak in the chromatogram obtained with solution (2).
DISSOLUTION ⟨711⟩ **Medium:** pH 6.0 phosphate buffer; 900 mL **Apparatus 2:**75 rpm **Time:**30 min **Solution A:**4.4 mg/mL of dibasic potassium phosphate and 0.5 mg/mL of sodium 1-octanesulfonate; adjusted with phosphoric acid to a pH of 8.20 ± 0.05 **Mobile phase:** Acetonitrile, methanol, and *Solution A* (9:3:8) **Diluent:** 17.5 mg/mL of dibasic potassium phosphate. Adjust with phosphoric acid to a pH of 8.00 ± 0.05. Prepare a mixture of this solution and acetonitrile (80:20). **Standard stock solution:** Dissolve USP Azithromycin RS in *Medium* to obtain a solution with a known concentration of about (*L*/1000) mg/mL, where *L* is the label claim in mg/Tablet. **Standard solution:** Dilute the *Standard stock solution* with *Diluent* to obtain a solution with a known concentration of about (*L*/2000) mg/mL, where *L* is the label claim in mg/Tablet. **Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute a portion of the filtrate with *Diluent* to obtain a solution with a theoretical concentration of about (*L*/2000) mg/mL, where *L* is the label claim in mg/Tablet, assuming complete dissolution. **Chromatographic system**	**TESTS** **Dissolution** Comply with the requirements in the dissolution test for tablets and capsules, Appendix XII B 1. **TEST CONDITIONS** (a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute. (b) Use 900 mL of 0.lM sodium dihydrogen orthophosphate previously adjusted to pH 6.0 with orthophosphoric acid, at a temperature of 37°C, as the dissolution medium. **PROCEDURE** Carry out, the method for liquid chromatography, Appendix III D, using the following solutions. Solvent A 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 8.0 with orthophosphoric acid, and 60 volumes of acetonitrile Rl. (1) After 45 minutes withdraw a sample of the medium and filter. Dilute a quantity of the filtrate with the dissolution medium to produce a solution expected to contain 0.027% w/v of Azithromycin. (2) 0.027% w/v of azithromycin EPCRS in the dissolution medium. (3) 0.05% w/v each of azithromycin EPCRS and azithromycin impurity A EPCRS in solvent A. **CHROMATOGRAPHIC CONDITIONS** **(a)** Use a stainless-steel column (25 cm x 4.6 mm) packed with octadecylsilyl vinyl polymer for

(See *Chromatography* ⟨621⟩, *System Suitability*.) **Mode:** LC **Detector:** UV 210 nm **Column:**4.6-mm × 15-cm; 5-µm packing L1 **Column temperature:**50° **Flow rate:**1.5 mL/min **Injection volume:**50 µL **System suitability** **Sample:** *Standard solution* **Suitability requirements** **Tailing factor:** NMT 2.0 **Relative standard deviation:** NMT 2.0% **Analysis** **Samples:** *Standard solution* and *Sample solution* Calculate the percentage of the labeled amount of azithromycin (CHNO) dissolved: Result = (*r*/*r*) × (*C*/*L*) × *V* × ▲*D*▲ (USP 1-Dec-2019) × 100 *r*= peak response of azithromycin from the *Sample solution* *r*= peak response of azithromycin from the *Standard solution* *C*= concentration of USP Azithromycin RS in the *Standard solution* (mg/mL) *L*= label claim (mg/Tablet) *V*= volume of *Medium*, 900 mL▲ *D*= dilution factor for the *Sample solution*, if necessary▲ (USP 1-Dec-2019) **Tolerances:** NLT 80% (*Q*) of the labeled amount of azithromycin (CHNO) is dissolved.	chromatography (5 µm) (Asahipak ODP-50 is suitable). (b) Use isocratic elution and the mobile phase described below. (c) Use a flow rate of 1 mL per minute. (d) Use a column temperature of 40°C. (e) Use a detection wavelength of 210 nm. (f) Inject 20 µL of each solution. **MOBILE PHASE** 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 11.0 with a 56% w/v solution of potassium hydroxide, and 60 volumes of acetonitrile Rl. When the chromatograms are recorded under the prescribed conditions the retention time of azithromycin is about 10 minutes**.** **SYSTEM SUITABILITY** The test is not valid unless: in the chromatogram obtained with solution (2) the symmetry factor of the peak due to azithromycin is between 0.8 and 2.0; in the chromatogram obtained with solution (3), the resolution between the peaks due to impurity A and azithromycin is at least 1.5. **DETERMINATION OF CONTENT** Calculate the total content of azithromycin, C38H72N2012, in the medium using the declared content of C38H72N2012 in azithromycin EPCRS. **LIMITS** The amount of azithromycin, C38H72N2O12, released is not less than 75% (Q) of the stated amount.
ASSAY **•PROCEDURE** **Buffer:** Dissolve 4.6 g of monobasic potassium phosphate anhydrous in 900 mL of water. Adjust with 1 N sodium hydroxide to a pH of7.5, and dilute with water to 1 L. **Mobile phase:** Acetonitrile and *Buffer* (65:35) **Standard solution:**1 mg/mL of USP Azithromycin RS in *Mobile phase*. Sonicate and shake as needed to dissolve. **Sample solution:** Nominally 1 mg/mL of azithromycin in *Mobile phase* from NLT 20 Tablets, finely powdered. Sonicate and shake as needed to dissolve. **Chromatographic system** (See *Chromatography* ⟨621⟩, *System Suitability*.) **Mode:** LC **Detector:** UV 210 nm **Column:**4.6-mm × 25-cm; 5-µm packing L1 **Column temperature:**50° **Flow rate:**2 mL/min **Injection volume:**100 µL **System suitability** **Sample:** *Standard solution* **Suitability requirements** **Tailing factor:** NMT 2.0 **Relative standard deviation:** NMT 2.0%	**ASSAY** Weigh and powder 20 tablets. Carry out the method for liquid chromatography, Appendix III D, using the following solutions. Solvent C 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 8.0 with orthophosphoric acid and 60 volumes of acetonitrile Rl. (1) Shake a quantity of the powdered tablets containing 0.5 g of Azithromycin with 40 mL of solvent C, dilute to 100 mL with the same solvent and filter (a 0.45-µm nylon filter is suitable). Dilute 1 volume of the filtrate to 10 volumes with solvent C. (2) 0.05% w/v of azithromycin EPCRS in solvent C. (3) 0.05% w/v each of azithromycin EPCRS and azithromycin impurity A EPCRS in solvent C. **CHROMATOGRAPHIC CONDITIONS** The chromatographic conditions described under Dissolution may be used, but with an injection volume of 10 µL. **SYSTEM SIBT ABILITY** The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between the peaks due to impurity A and azithromycin is at least 1.5. **DETERMINATION OF CONTENT**

Analysis Samples: *Standard solution* and *Sample solution* Calculate the percentage of the labeled amount of azithromycin (CHNO) in the portion of Tablets taken: Result = (r/r) × (C/C) × P × F × 100 r= peak response of azithromycin from the *Sample solution* r= peak response of azithromycin from the *Standard solution* C= concentration of USP Azithromycin RS in the *Standard solution* (mg/mL) C= nominal concentration of azithromycin in the *Sample solution* (mg/mL) P= potency of USP Azithromycin RS (µg/mg) F= conversion factor, 0.001 mg/µg **Acceptance criteria:**90.0%–110.0%	Calculate the total content of azithromycin, C38H72N2012 in the tablets using the declared content of C38H72N2012 in azithromycin EPCRS.

Azithromycin Oral Suspension

USP	BP
DEFINITION Azithromycin for Oral Suspension is a dry mixture of Azithromycin and one or more buffers, sweeteners, diluents, anticaking agents, and flavors. It contains NLT 90.0% and NMT 110.0% of the labeled amount of azithromycin (CHNO)	**DEFINITION** Azithromycin Oral Suspension is a suspension of Azithromycin in a suitable vehicle. It is prepared by dispersing the dry ingredients in the specified volume of Water just before issue for use. The dry ingredients comply with the requirements for Powders and Granules for Oral Solutions and Oral Suspensions stated under Oral Liquids. For the following tests prepare the Oral Suspension as directed on the label. The suspension, examined immediately after preparation unless otherwise indicated, complies with the requirements stated under Oral Liquids and with the following requirements. **Content of azithromycin, C38H72N2012** When freshly constituted not more than 120.0% of the stated amount. When stored at the temperature and for the period stated on the label during which the Oral Suspension may be expected to be satisfactory for use, not less than 80.0% of the stated amount.
IDENTIFICATION **A.** The retention time of the azithromycin peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.	**IDENTIFICATION** A. Shake a quantity of the oral suspension containing 0.5 g of Azithromycin with 50 mL of dichloromethane, allow to separate and retain the lower layer. Filter (a 0.45-µm nylon filter is suitable) and evaporate the filtrate to dryness under a stream of nitrogen. The infrared absorption spectrum, Appendix II A, is concordant with the reference spectrum of azithromycin (RS 487). B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of principal peak in the chromatogram obtained with solution (2).
ASSAY ***Change to read:*** **•PROCEDURE** [NOTE— Solutions containing azithromycin are stable up to 12 h at 10°.] **Solution A:** Dissolve 8.7 g of dipotassium hydrogen phosphate anhydrous in 1000 mL of water and adjust	**ASSAY** Carry out the method for liquid chromatography, Appendix III D, using the following solutions. Solvent B 1590 volumes of a 0.138% w/v solution of - potassium dihydrogen orthophosphate, 600 volumes of isopropanol, 480 volumes of methanol and 330

with potassium hydroxide or dilute orthophosphoric acid to a pH of 8.2. **Solution B:** Acetonitrile **Mobile phase:** *Solution A* and *Solution B* (30:70) **Diluent:** Acetonitrile, methanol, and water (40:40:20) **Standard solution:** 0.6 mg/mL of USP Azithromycin RS in *Diluent*. Sonicate in cool water to dissolve as needed. **Sample solution:** Nominally 0.6 mg/mL of azithromycin in *Diluent* prepared as follows. Transfer an accurately measured portion of the constituted suspension to a suitable volumetric flask. Add *Diluent* equal to 50% of the volume of the flask, and sonicate for 20 min with shaking in cool water. Dilute with *Diluent* to volume. Pass a portion of this solution through a suitable filter of 0.45-µm pore size. **Chromatographic system** (See *Chromatography* ⟨621⟩, *System Suitability*.) **Mode:** LC **Detector:** UV 210 nm **Column:**4.6-mm × 25-cm; 5-µm packing L1 **Temperatures** **Autosampler:**10° **Column:**30° **Flow rate:**2 mL/min **Injection volume:**50 µL **Run time:** NLT 2 times the retention time of azithromycin **System suitability** **Sample:** *Standard solution* **Suitability requirements** **Tailing factor:** NMT 2.0 **Relative standard deviation:** NMT 2.0% **Analysis** **Samples:** *Standard solution* and *Sample solution* Calculate the percentage of the labeled amount of azithromycin (CHNO) in the portion of Azithromycin for Oral Suspension taken: Result = (*r*/*r*) × (*C*/*C*) × *P* × *F* × 100 *r*= peak response of azithromycin from the *Sample solution* *r*= peak response of azithromycin from the *Standard solution* *C*= concentration of USP Azithromycin RS in the *Standard solution* (mg/mL) *C*= nominal concentration of azithromycin in the *Sample solution* (mg/mL) *P*= potency of USP Azithromycin RS (µg/mg) *F*= conversion factor, 0.001 mg/µg▲ (USP 1-May-2019) **Acceptance criteria:** 90.0%–110.0%	volumes of acetonitrile, adjusted to pH 8.4 with l0M potassium hydroxide. (1) Shake a weighed quantity of the oral suspension containing 0.2 g of Azithromycin with 300 mL of solvent B, dilute to 500 mL with the same solvent and filter (a 0.45-µm nylon filter is suitable). (2) 0.04% w/v of azithromycin EPCRS in solvent B. (3) 0.04% w/v each of azithromycin EPCRS and azithromycin impurity A EPCRS in solvent B. **CHROMATOGRAPHIC CONDITIONS** (a) Use a stainless-steel column (25 cm x 4.6 mm) packed with octadecyl silyl vinyl polymer for chromatography (5 µm) (Asahipak ODP-50 is suitable). (b) Use isocratic elution and the mobile phase described below. (c) Use a flow rate of 1 mL per minute. (d) Use a column temperature of 40°. (e) Use a detection wavelength of 210 nm. (f) Inject 10 µL of each solution. **MOBILE PHASE** 40 volumes of a 0.67% w/v solution of dipotassium hydrogen orthophosphate adjusted to pH 11.0 with a 56% w/v solution of potassium hydroxide, and 60 volumes of acetonitrile Rl. **SYSTEM SUITABILITY** The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between impurity A and azithromycin is at least 1.5. **DETERMINATION OF CONTENT** Determine the weight per mL of the oral suspension, Appendix V G, and calculate the content of azithromycin, C38H72N2012 in the oral suspension using the declared content of C38H72N2012 in azithromycin EPCRS. Repeat the procedure using a portion of the oral suspension that has been stored at the temperature and for the period stated on the label during which it may be expected to be satisfactory for use.
•**DISSOLUTION** ⟨711⟩ [NOTE— Solutions containing azithromycin are stable up to 12 h at 10°.] **Medium:** Sodium phosphate buffer at a pH of 6.0; 900 mL **Apparatus 2:**50 rpm	**STORAGE** The Oral Suspension should be kept at the temperature and used within the period stated on the label. **Alkalinity** pH, 9.0 to 11.0.

Time:30 min **Solution A:** Dissolve 8.7 g of dipotassium hydrogen phosphate anhydrous in 1000 mL of water and adjust with potassium hydroxide or dilute orthophosphoric acid to a pH of 8.2. **Solution B:** Acetonitrile **Mobile phase:** *Solution A* and *Solution B* (35:65) **Standard stock solution:** 0.55 mg/mL of USP Azithromycin RS prepared as follows. Transfer an accurately weighed amount of USP Azithromycin RS to a suitable volumetric flask. Add acetonitrile to fill 5% of the volume of the flask and sonicate in cool water for 5min to dissolve completely. Dilute with *Medium* to volume. **Standard solution** **For Azithromycin for Oral Suspension labeled to contain 100mg/5mL:** 0.11 mg/mL of USP Azithromycin RS in *Medium* from *Standard stock solution* **For Azithromycin for Oral Suspension labeled to contain 200mg/5mL:** 0.22 mg/mL of USP Azithromycin RS in *Medium* from *Standard stock solution* **Sample solution:** Pass a portion of the solution under test through a suitable filter. **Chromatographic system** (See *Chromatography* ⟨621⟩, *System Suitability*.) **Mode:** LC **Detector:** UV 210 nm **Column:**4.6-mm × 15-cm; 5-µm packing L1 **Temperatures** **Autosampler:**10° **Column:**50° **Flow rate:**2 mL/min **Injection volume:**100 µL **Run time:** NLT 2 times the retention time of azithromycin **System suitability** **Sample:** *Standard solution* **Suitability requirements** **Tailing factor:** NMT 2.0 **Relative standard deviation:** NMT 2.0% **Analysis** **Samples:** *Standard solution* and *Sample solution* Calculate the percentage (*Q*) of the labeled amount of azithromycin (CHNO) dissolved: Result = (*r*/*r*) × (*C*/*L*) × *D* × (*d*/*W*) × *V* × 100 *r*= peak response of azithromycin from the *Sample solution* *r*= peak response of azithromycin from the *Standard solution* *C*= concentration of USP Azithromycin RS in the *Standard solution* (mg/mL) *L*= label claim of Azithromycin for Oral Suspension (mg/5 mL) *D*= dilution factor, necessary only if the *Sample solution* requires dilution (mL/mL)	**Water** Not more than 2.0% w/w, Appendix IX C. Method I. Use 0.5g of the dry ingredients.

d= density of the *Sample solution* (g/mL) *W*= weight of Azithromycin for Oral Suspension taken (g)*V*= volume of *Medium*, 900 mL **Tolerances:** NLT 75% (*Q*) of the labeled amount of azithromycin (CHNO) is dissolved.	
SPECIFIC TESTS **•PH** ⟨791⟩ **For a solid packaged in single-unit containers** **Sample:** The suspension constituted as directed in the labeling **Acceptance criteria:**9.0–11.0 **For a solid packaged in multiple-unit containers** **Sample:** The suspension constituted as directed in the labeling **Acceptance criteria:**8.5–11.0 **ADDITIONAL REQUIREMENTS** **•PACKAGING AND STORAGE:** Preserve in tight containers.	

In USP Amperometric electrochemical detector is only used for the assay of azithromycin capsule, while for the assay of tablet and dry powder suspension UV detector is used in the chromatographic system. As for BP, UV detector is used for the assay of azithromycin tablet, capsule and dry powder for suspension.

Decision: Registration Board deliberated the matter in detail and thoroughly reviewed the official monographs i.e. BP and USP for azithromycin containing drug products. The Board deliberated that as per the USP monograph for azithromycin capsule Amperometric electrochemical detector is required for carrying out assay and dissolution test. The Board further observed that amperometric electrochemical detector is not specified for assay and dissolution test in BP monograph for all dosage forms of azithromycin and in USP for tablet, oral suspension and injection dosage forms of azithromycin. The Board decided to advice all registration holders of azithromycin capsule with USP specifications to comply the requirements of pharmacopoeia and perform assay and dissolution testings using Amperometric electrochemical detector.

6. Review of Ciprofloxacin salt form in various dosage forms (tablet, infusion, eye drops)

Registration Board in various meetings deliberated the matter regarding salt form of ciprofloxacin in oral suspension and other dosage forms. PE&R Division has reviewed the salt form of various dosage forms of ciprofloxacin along with its BP and USP monographs and the summary is as under.

Reference	Ciprofloxacin Injection	Ciprofloxacin Ophthalmic Solution	Ciprofloxacin Tablets	Ciprofloxacin for Oral Suspension
USP	Ciprofloxacin Injection is a sterile solution of **Ciprofloxacin** or **Ciprofloxacin Hydrochloride** in Water for Injection, in 5% Dextrose Injection, or in 0.9% Sodium Chloride Injection prepared with the aid of Lactic Acid.	Ciprofloxacin ophthalmic Solution is a sterile, aqueous solution of **Ciprofloxacin Hydrochloride**.	Ciprofloxacin Tablets contain **Ciprofloxacin Hydrochloride** equivalent to NLT 90.0% & NMT 110.0% of labeled amount of ciprofloxacin	Ciprofloxacin for Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of **ciprofloxacin**
BP	INFUSION…. ciprofloxacin Base	Ciprofloxacin Base	Ciprofloxacin HCl	-
USFDA	**CIPRO IV** (ciprofloxacin) injection	**CILOXAN** Ophthalmic Solution	**CIPRO** film-coated tablets	**CIPRO** Oral Suspension
	Ciprofloxacin Base	Ciprofloxacin HCl	ciprofloxacin hydrochloride monohydrate	Ciprofloxacin base
MHRA	1. **Ciproxin solution for**	**CILOXAN 0.3%**	**Ciprofloxacin 250**	**Ciproxin 250**

	infusion 2. Ciprofloxacin 2mg/ml solution for infusion	**w/v eye drops, solution**	**mg film-coated tablets**	**mg/5 mL granules and solvent for oral suspension**
	1. Ciprofloxacin base (lactic acid used in excipients) 2. Ciprofloxacin (as lactate).	Ciprofloxacin 0.3% w/v (as hydrochloride).	Ciprofloxacin (as hydrochloride).	Ciprofloxacin base

Decision: Registration Board deliberated the matter in detail and reiterated its decision taken in 290th meeting in which all registration holders of ciprofloxacin granules for oral suspension were advised to ensure the supply of ciprofloxacin granules along with the solvent/diluent having following composition as per the innovator drug product.

- **Soya lecithin**
- **Medium chain triglycerides**
- **Flavor**
- **Sucrose**
- **Purified water**

The Board observed that all pharmaceutical manufacturers have not yet complied the decision of the Board taken in 290th meeting. Keeping in view the safety, efficacy and quality of the product, the Board decided as follow:

1. **All registration holders of ciprofloxacin granules for oral suspension should comply the decision of 290th meeting within 3 months.**
2. **All registration holders of ciprofloxacin granules for oral suspension to whom registration has been granted with ciprofloxacin hydrochloride, should revise their formulation as per innovator drug product and apply for correction in salt form in the relevant section of PE&R Division within 2 months.**
3. **The Board also directed PE&R Division to issue an advisory in this regard for compliance and also upload on DRAP"s website for information for all stakeholders.**
4. **The matter regarding formulation and salt form of ciprofloxacin injection and extended release tablet will be discussed in forthcoming meeting of Registration Board.**

Case no. 01 Registration applications of CTD cases

a. New cases of Import

1.	Name, address of Applicant / Importer	M/s Mutabbar Pharma Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore.
	Details of Drug Sale License of importer	License No: 05-352-0063-065145D Address: Flat No E1, 1st Floor Agro Squire Shadman Lahore. Address of Godown: NA Validity: 19-02-2023. Status: License to sell drugs as a distributor
	Name and address of marketing authorization holder (abroad)	ADMAC Lifesciences Plot No. 107 A & 107B, EPIP Phase-I, Jharmajri Baddi, Distt Solan, Himachal Pradesh India.
	Name, address of manufacturer(s)	ADMAC Lifesciences Plot No. 107 A & 107B, EPIP Phase-I, Jharmajri Baddi, Distt Solan, Himachal Pradesh India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized CoPP (certificate No. 206/09 Vol-III (21/003) dated 21-01-20121 for CAPCIT-500 Tablet. The certificate confirms the free sale status of the product along with GMP status of the manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted original, legalized exclusive distribution agreement between ADMAC life sciences and Mutabbar pharma dated 01-01-2021. The agreement is valid for 2 years and specifies Benzomide 100mg, Capcit 500mg, Gemlee 1000mg and Paclibenz 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 ☐ Buk import and local repackaging ☐ Buk import & local repackaging for export purpose only
	Dy. No. and date of submission	Dy No 8862: 18-03-2021
	Details of fee submitted	PKR 100,000/-: 09-11-2020
	The proposed proprietary name/brand name	CAPCIT-500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Capecitabine ……..500mg
	Pharmaceutical form of applied drug	Light pink coloured biconvex, elongated film coated tablet
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	USP
	Proposed Pack size	120’s
	Proposed unit price	21250/- per pack 177.08 / tablet
	The status in reference regulatory authorities	**(**USFDA Approved).

	For generic drugs (me-too status)	Mericap 500mg tablet by Merixil pharma (Reg#081801)
	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	Mac Chem Products (India) Pvt Ltd. N-211/2/10 Tarapur MIDC, Boisar, District Thane, Pin-401 506 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 real time stability data is conducted at 25ºC / 60% RH. The stability study data is till 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 pharmaceutical equivalence against the innovator product Xeloda-500 tablet by Roche Products Limited. Firm has also submitted comparative dissolution profile results against the innovator product Xeloda-500 tablet by Roche Products Limited.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Printed aluminium foil and clear PVC film blister packed in a paper board carton having with insert.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability data of 3 batches for 24 months at 30±2°C, 70±5%RH and 6 months at 40°C±75%RH for three batches.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
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.	Firm has submitted revised module 1 as per the guidance document approved by Registration Board.
Revise the label claim in module 1, section 1.5.2 as per the innovator / reference product along with submission of applicable fee, since the submitted label claim does not specify the film coating of the	Firm has revised the label claim in module 1 along with submission of fee 7500/- dated 05-11-2021. The revised label claim is in line with the actual data provided in module 2 and module 3. The revised label

drug product.	claim is as follows: Each film coated tablet contains: Capecitabine ……..500mg
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 validation of analytical procedures of the drug substance by Mac—Chem Products India which is the drug substance manufacturer. The drug product manufacturer has submitted that the drug substance is as per USP and its validation studies have been conducted by the drug substance manufacturer therefore the drug product manufacturer does not need to submit the method validation.

Decision: Deferred for submission of verification studies of the analytical method of drug substance performed by drug product manufacturer.

2.	Name, address of Applicant / Importer	M/s Mutabbar Pharma Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore.
	Details of Drug Sale License of importer	License No: 05-352-0063-065145D Address: Flat No E1, 1st Floor Agro Squire Shadman Lahore. Address of Godown: NA Validity: 19-02-2023. Status: License to sell drugs as a distributor
	Name and address of marketing authorization holder (abroad)	ADMAC Lifesciences Plot No. 107 A & 107B, EPIP Phase-I, Jharmajri Baddi, Distt Solan, Himachal Pradesh India.
	Name, address of manufacturer(s)	ADMAC Lifesciences Plot No. 107 A & 107B, EPIP Phase-I, Jharmajri Baddi, Distt Solan, Himachal Pradesh India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized CoPP (certificate No. 206/09 Vol-III (21/001) dated 21-01-20121 for Gemlee-1000 injection. The certificate confirms the free sale status of the product along with GMP status of the manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of exclusive distribution agreement between ADMAC life sciences and Mutabbar pharma dated 01-01-2021. The agreement is valid for 2 years and specifies Benzomide 100mg, Capcit 500mg, Gemlee 1000mg and Paclibenz 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 ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only

	Dy. No. and date of submission	Dy No 8863: 18-03-2021
	Details of fee submitted	PKR 100,000/-: 09-11-2020
	The proposed proprietary name/ brand name	GEMLEE-1000 INJECTION
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Gemcitabine as hydrochloride ……..1000mg
	Pharmaceutical form of applied drug	A white colored white lyophilized cake filled in a 50ml clear moulded glass vial USP type-I.
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	9500/-
	The status in reference regulatory authorities	**(USFDA** Approved).
	For generic drugs (me-too status)	Gemcit Injection of Al Habib Pharma (Reg#059247)
	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	Mac Chem Products (India) Pvt Ltd. N-211/2/10 Tarapur MIDC, Boisar, District Thane, Pin-401 506 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 real time stability data is conducted at 30ºC / 65% RH. The stability study data is till 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 pharmaceutical equivalence against the reference product Gemcitabine for injection 1000mg by Accord Healthcare Limited.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	50ml clear moulded glass vial USP type-I.

	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability data of 3 batches for 24 months at 30±2°C, 65±5%RH and 6 months at 40°C±75%RH for three batches.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
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.	Firm has submitted revised module 1 as per the guidance document approved by Registration Board.
Revise the label claim in module 1, section 1.5.2 as per the innovator / reference product along with submission of applicable fee, since the submitted label claim is not in line with the innovator product.	Firm has revised the label claim in module 1 along with submission of fee 7500/- dated 05-11-2021. The revised label claim is in line with the actual data provided in module 2 and module 3. The revised label claim is as follows: Each vial Contains: Gemcitabine as hydrochloride ……..1000mg
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 validation of analytical procedures of the drug substance by Mac—Chem Products India which is the drug substance manufacturer. The drug product manufacturer has submitted that the drug substance is as per USP and its validation studies have been conducted by the drug substance manufacturer therefore the drug product manufacturer does not need to submit the method validation.

Decision: Deferred for submission of verification studies of the analytical method of drug substance performed by drug product manufacturer.

3.	Name, address of Applicant / Importer	M/s Mutabbar Pharma Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore.
	Details of Drug Sale License of importer	License No: 05-352-0063-065145D Address: Flat No E1, 1st Floor Agro Squire Shadman Lahore. Address of Godown: NA Validity: 19-02-2023. Status: License to sell drugs as a distributor
	Name and address of marketing authorization holder (abroad)	ADMAC Lifesciences Plot No. 107 A & 107B, EPIP Phase-I, Jharmajri Baddi, Distt Solan, Himachal Pradesh India.
	Name, address of manufacturer(s)	ADMAC Lifesciences Plot No. 107 A & 107B, EPIP Phase-I, Jharmajri Baddi, Distt Solan, Himachal Pradesh India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized CoPP (certificate No. 206/09 Vol-III (21/002) dated 21-01-20121 for Paclibenz 100 injection. The certificate confirms the free sale status of the product along with GMP status of the manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of exclusive distribution agreement between ADMAC life sciences and Mutabbar pharma dated 01-01-2021. The agreement is valid for 2 years and specifies Benzomide 100mg, Capcit 500mg, Gemlee 1000mg and Paclibenz 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 ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy No 8864: 18-03-2021
	Details of fee submitted	PKR 100,000/-: 09-11-2020
	The proposed proprietary name/ brand name	PACLIBENZ-100 INJECTION
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Paclitaxel ……..100mg/16.7ml
	Pharmaceutical form of applied drug	A clear, colourless slightly yellow, viscous solution filled in 20ml amber colour moulded glass vial USP type-I.
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	20325/-
	The status in reference regulatory authorities	**(USFDA** Approved).
	For generic drugs (me-too status)	Biopac Injection of Merixil Pharma (Reg#078127)
	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	Mac Chem Products (India) Pvt Ltd. N-211/1/10 Tarapur MIDC, Boisar, District Thane, Pin-401 506 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 real time stability data is conducted at 25°C / 60% RH. The stability study data is till 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 pharmaceutical equivalence against the innovator brand Taxol Injection of Bristol-Myers Squibb.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	20ml amber coloured glass vials USP type I
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability data of 3 batches for 24 months at 30±2°C, 70±5%RH and 6 months at 40°C±75%RH for three batches.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm**
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.	Firm has submitted revised module 1 as per the guidance document approved by Registration Board.
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 validation of analytical procedures of the drug substance by Mac—Chem Products India which is the drug substance manufacturer. The drug product manufacturer has submitted that the drug substance is as per USP and its validation studies have been conducted by the drug substance manufacturer therefore the drug product manufacturer does not need to submit the method validation.

Decision: Deferred for submission of verification studies of the analytical method of drug substance performed by drug product manufacturer.

b. Deferred cases of Import

4.	Name, address of Applicant / Importer	M/s Pfizer Pakistan Limited B-2, S.I.T.E., Karachi, Pakistan
	Details of Drug Sale License of importer	License No: DHSKDK(Drug)/-1108 Address: B-2, S.I.T.E., Karachi. Address of Godown: 12 Dockyard Road West Wharf Karachi. C-11-D, S.I.T.E., Karachi. Validity: 17-02-2020. Status: Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	Hospira Australia Pty Ltd. 1-5, 7-23 and 25-39, Lexia Place, Mulgrave, Australia.
	Name, address of manufacturer(s)	Hospira Australia Pty Ltd. 1-5, 7-23 and 25-39, Lexia Place, Mulgrave, Australia.
	Name of exporting country	Australia

	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted original, legalized CoPP certificate (No. 18/0087) dated 15-02-2018 issued by Therapeutic Goods Administration Australia, for ANZATAX Paclitaxel 100mg/16.7ml Injection Vial. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection not less than every two years.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of authorization from Hospira Australia Pty Ltd. 1 Lexia Place Victoria 3170 Australia. The letter specifies that their principal place of business located at 1-5, 7-23, and 25-39 Lexia Place, Mulgrave, VIC 3170 Australia as a manufacturer and marketing authorization holder in country of origin authorize Pfizer Pakistan Limited, 12 Dockyard Road, West Wharf Karachi Pakistan to be the marketing authorization holder in Pakistan and be responsible for all matters pertaining to the regulation of this product in Pakistan. Authorization letter was issued on 15-11-2019.
	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 & local repackaging for export purpose only
	Dy. No. and date of submission	Dy No 11863: 28-05-2020
	Details of fee submitted	PKR 100,000/-: 30-01-2020
	The proposed proprietary name / brand name	ANZATAX Concentrate 100mg/16.7ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Paclitaxel…100mg/16.7ml
	Pharmaceutical form of applied drug	Clear to pale yellow solution, free from visible particulates, presented in clear Type I glass vials
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Paclitaxel 6 mg/ml Concentrate for Solution for Infusion (MHRA Approved).
	For generic drugs (me-too status)	Paclitaxel Ebewe 100mg/16.7ml by Novartis (Reg #083094)
	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	• Python Biotech LLC 1527 Cliveden Avenue Canada-V3M 6P7 Delta, British Colombia. • Hospira Boulder Inc. 4876 Sterling Drive Boulder, CO 80301, USA.
	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. Firm has submitted open part of DMF for both sources.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has not submitted stability study data of each drug substance but referred to CEP certification
	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 initially 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	20 mL, 20 mm clear Type I glass vial with rubber stopper and aluminium seal
	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 40ºC ±2ºC / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30ºC±2ºC/75%±5%RH for 36 months.

Evaluation by PEC:

Shortcomings communicated	Response by the firm
Justify the application for import along with fee (PKR 100,000/-) submitted on the basis of "Drug Manufacturing License" instead of "Drug Sale License".	Firm has submitted that application was submitted on Drug Sale License (DSL address: B-2 SITE Karachi). However, DML number was mentioned on the submitted fee challan.
Provide valid drug sale license since the submitted DSL was valid till 17-02-2020.	Firm has submitted valid DSL with following details: License No: DHSKDK(Drug)/-1222 Address: B-2, S.I.T.E., Karachi. Address of Godown: 12 Dockyard Road West Wharf Karachi. C-11-D, S.I.T.E., Karachi. Validity: 21-04-2022. Status: Drug License by way of Wholesale
Provide complete label claim in section 1.5.2 as per the innovator / reference product.	Required information (i.e. Paclitaxel 100mg/16.7ml) has been provided in Section 1.5.2 of Form 5F.
Provide pharmacopoeial reference and status of	Paclitaxel (Anzatax) is available in USP. Drug product

applied formulation in official pharmacopoeia in section 1.5.6 instead of referring to module 3.	will comply to USP.
Submit batch manufacturing records in section 2.3.R.1.1 as per the decision of 293rd meeting of Registration Board which states that "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."	Firm has submitted batch manufacturing record of the stability batches.
Submit complete data of drug substance in module 3 section 3.2.S for both sources as per the guidance document of 293rd meeting of Registration Board instead of referring to CEP certificate issued by EDQM.	The entire (as per CTD Section) Drug substance information for Phyton Biotech LLC is enclosed. Further, with this response we would like to inform you that we are removing Hospira Boulder Inc. as the site has been divested and confirming that for Pakistan only drug substance manufactured by Phyton will be used for Anzatax commercial batches.
You have mentioned two different sources of drug substance, but the drug product part does not specify the exact source of drug substance which was used to develop the formulation and for which stability studies were provided. Clarification is required in this regard.	We would like to clarify regarding the sources of drug substance used in the development of Anzatax Injection. Paclitaxel (drug substance) manufactured by Boulder was used for the development of Anzatax Injection. Data contained with the 3.2.P.2 section of the dossier, submitted herein, utilized Boulder drug substance material. Since Boulder has been divested, the proposed DS site for commercial batches of Anzatax Injection for Pakistan will only be Phyton. Additional stability studies utilizing only Phyton drug substance have also been submitted by the firm
Submit data of pharmaceutical equivalence in section 3.2.P.2.2.1. as per 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*."	Anzatax has been developed as a generic equivalent of Taxol marketed in Europe by Bristol Myers Squibb (BMS). Pharmaceutical equivalence data is submitted by the firm in which equivalence was conducted against Taxol.
Accelerated stability study data of 3 batches needs to be submitted for both sources of the drug substance in section 3.2.P.8.3.	Firm has submitted that stability data of three (3) batches at the proposed storage conditions to the proposed shelf life has been included. Accelerated data can be used to help determine the proposed shelf-life when full term data is unavailable. However 3 batches to the proposed shelf life (18 months) using the drug substance manufactured by Phyton are included in this response thus accelerated data will not be provided. Firm has not submitted accelerated stability study data.
Real time stability study data of 3 batches of drug product conducted as per Zone IV-A conditions needs to be submitted for both drug substances in section 3.2.P.8.3 since the submitted stability study data is not for 3 batches and is not conducted as per zone IV-A conditions. Furthermore a declaration from the Hospira Australia Pty Ltd dated 11.03.2020 is submitted which specifies that they have	Additional long term stability studies have been provided in Section 3.2.P.8.3. The stability studies provided are conducted at Zone IV-B conditions which is considered to be worst case. As Paclitaxel Injection 6 mg/mL is not supported at the proposed storage conditions for 24 months, a revised 3.2.P.8 section is provided herein which details the proposed shelf-life at 18 months. Further, it is confirmed that the batches provided herein are manufactured with drug substance from Phyton using the

performed stability studies as per zine IV-B conditions but the stability data showed an upward trend for related substances at 24 months' time point, but that particular stability study data is not submitted.	proposed commercial batch size and manufacturing process.

Decision of 297th meeting of Registration Board:
Deferred for submission of complete data of drug product in section 3.2.P in which the data of drug product manufactured by the revised drug substance source i.e. Phyton Biotech LLC British Colombia is used.

Response by the firm:

- Firm has submitted complete data of drug product (section 3.2.P) using drug substance manufactured by Phyton Biotech LLC British Colombia.
- Firm has changed the source of drug substance without submission of fee.

The details of the drug product are summarized in the table below:

Pharmaceutical form of applied drug	Clear to pale yellow solution, free from visible particulates, presented in clear Type I glass vials
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	20 mL, 20 mm clear Type I glass vial with rubber stopper and aluminium seal
Stability study data of drug product, shelf life and storage conditions	Firm has only submitted real time stability study data conducted at 30ºC ±2ºC / 75% ± 5% RH for 1 batch till 18 months for the applied fill volume (i.e. 16.7ml). Accelerated and real time stability study data of three batches is not provided.

Decision of 307th meeting of Registration Board:
Deferred for following submissions:

- Data of pharmaceutical equivalence against the innovator / reference / comparator product, as per the requirements of Form 5F (CTD) as explained in the guidance document issued by Registration Board.
- Accelerated stability study data of 3 batches of the drug product (i.e. Paclitaxel 100mg/16.7ml).
- Real time stability study data as per zone IV-A conditions till the claimed shelf life of 3 batches of the drug product (i.e. Paclitaxel 100mg/16.7ml).

Response by the firm:

Reason for deferment	**Response by the firm**
Data of pharmaceutical equivalence against the innovator / reference / comparator product, as per the requirements of Form 5F (CTD) as explained in the guidance document issued by Registration Board.	Firm has submitted pharmaceutical equivalence of their product from both Boulder and Phyton drug substance source against the innovator product Taxol.
Accelerated stability study data of 3 batches of the drug product (i.e. Paclitaxel 100mg/16.7ml).	Firm has submitted accelerated and real time stability study data of 3 batches of Paclitaxel 100mg/16.7ml from Phyton drug substance. The real time stability studies are conducted till 18.75 months while only sterility and bacterial endotoxin test for 2 batches and particulate matter, sterility and bacterial endotoxin test for 1 batch is performed at 24 months time point.
Real time stability study data as per zone IV-A conditions till the claimed shelf life of 3 batches of the drug product (i.e. Paclitaxel 100mg/16.7ml).	Firm has submitted accelerated and real time stability study data of 3 batches of Paclitaxel 100mg/16.7ml from Phyton drug substance. The real time stability studies are conducted till 18.75 months while only sterility and bacterial endotoxin test for 2 batches and particulate matter, sterility and bacterial endotoxin test

	for 1 batch is performed at 24 months time point.

Decision: Approved with a shelf life of 18 months as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

5.	Name, address and contact details of Applicant / Marketing Authorization Holder	M/s Novartis Pharma (Pakistan) Limited, 15 West Wharf, Karachi
	Name, address and contact details of Manufacturing site	Product License Holder: Sandoz GmbH BiochemiestraBe 10 6250 Kundle Austria Manufacturer: M/s Ebewe Pharma Ges.m.b.H. Nfg. KG Mondseestrasse 11, 4866 Unterach am Attersee, Austria
	Dy No and fee details	Dy. No. 530 Dated 13-03-2019 (Rs. 100,000/- Dated 13-03-2019)
	Brand Name	Fulvestrant Sandoz
	Composition	Each pre-filled syringe Contains: Fulvestrant 250mg/5mL

FORM 5-F

MODULE 1: ADMINISTRATIVE

Section	Sub-Section	Heading
1.1		Covering Letter and Fee Deposit Slip Submitted Dy. No. 530 Dated 13-03-2019 (Rs. 100,000/- Dated 13-03-2019)
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 Novartis Pharma (Pakistan) Limited, 15 West Wharf, Karachi
	1.3.2	Name, address and contact details of Manufacturing site. Product License Holder: Sandoz GmbH BiochemiestraBe 10 6250 Kundle Austria Manufacturer: M/s Ebewe Pharma Ges.m.b.H. Nfg. KG Mondseestrasse 11, 4866 Unterach am Attersee, Austria
	1.3.3	Specify whether the Applicant is: Importer will import from Austria.
	1.3.4	Drug Sale License Drug License by way of Wholesale No. 0488 valid upto 26-Nov-2019 apply for renewed receipt dated 29-11-2019
	1.3.8	Manufacturer's Site Master File and Credential (for importer)
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 and Export 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. Brand (Proprietary) name: Fulvestrant Sandoz Chemical name: Fulvestrant
	1.5.2	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit Each pre-filled syringe Contains: Fulvestrant 250mg/5mL
	1.5.3	The proposed proprietary name / brand name under which the drug is intended to be sold with trademark certification / clearance. Fulvestrant Sandoz
	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 pack of 1PFS, 1 pack of 2PFS & As per DPC
	1.5.5	Pharmacotherapeutic Group of Active Pharmaceutical Ingredient (API)

		Anti-cancer
	1.5.6	Pharmacopoeial reference / Status of applied formulation Firm claim Innovator's specification
	1.5.7	Route of administration Parentral
	1.5.8	For Generic Drug Product, reference of other similar approved medicines with information pertaining to Manufacturer name, brand name, strength, composition, registration number & dosage form, Pack size and Price. Not available
	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. USFDA Approved
	1.5.10	Dosage form of applied drug Pre-filled syringe
	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 Submitted
	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

1.6		Miscellaneous Information Submitted
	1.6.5	Drug Substance related Document including following: Name and address of API manufacturer: M/s Sicor S.R.L. Via Terrazzano 77 Italy 20017 rho, Milano
	• Original Legalized CoPP (No. 11787402) dated 21st Feb. 2019 issued by federal office for security in health care Traisengasse 5 1200 vienna, Austria declaring the not-free sale of applied product in exporting country but confirm the GMP compliant status of the manufacturer. • Original Legalized CoPP (No. 19001494) dated 01-03-2019 issued by Swissmedic declaring the free sale of applied product in Switzerland and the GMP compliant status of the manufacturer. • Copy of Sole agency agreement with product license holder is submitted.	

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

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 Not 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
	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 Submitted
	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 (24 months) at 5±3^{0}C and 6 months at 25^{0}C±60%RH for three batches.

Remarks of Evaluators:

i. Copy of Letter of authorization from product license holder is submitted.
ii. QOS as per Form-5F format?
iii. Submitted application is not as per Form-5F format.

Decision of 296th meeting of Registration Board: Deferred for following:

- Submission of complete Form 5F as per the guidelines of 293rd meeting of Registration Board.
- QOS as per WHO QOS-PD Template.

Response of the firm:

Decision of 296th meeting of Registration Board:

Submission of complete Form 5F as per the guidelines of 293rd meeting of Registration Board

- Firm has submitted CoPP of the swissmedic which is of different dosage form, the firm submitted that we have provided this CoPP only to establish that the product is available in Switzerland which is RRA.
- Firm has further submitted a letter from Sandoz specifying the product is not in Austria due to intellectual property reasons
- Firm has submitted copy of DSL Drug License by way of Wholesale No.47 valid upto 14-Jan-2022
- Firm has submitted QOS as per WHO template.
- Firm has submitted original sole agency agreement between the Sandoz GmbH Austria and Novartis Pharma Pakistan dated 20 December 2019.
- Firm has submitted complete module 3 including drug substance and drug product information
- Firm has submitted data of pharmaceutical equivalence with Faslodex® (Lot HR577)
- Firm has submitted three batches long term stability data (24 months) at 5±3^{0}C and 6 months at 25^{0}C±60%RH for three batches.

Decision of 297th meeting of Registration Board:

Deferred for submission of product specific Certificate of Pharmaceutical Product (CoPP) from the country of origin or from any reference regulatory authority which were adopted by Registration Board in its 275th meeting.

Response by the firm:

- Firm has submitted original, legalized CoPP (No. 21003574) dated 13-08-2021 issued by Swissmedic for Fulvestrant Sandoz 250mg/5ml. As per the details of CoPP the product License holder in Switzerland is *Sandoz Pharmaceuticals 6343 Risch Schweiz* and the manufacturer is *EBEWE Pharma Ges.m.b.H Nfg.KG Mondseestrasse 11 4866 Unterach Austria*. The CoPP declares the free sale status of the product as well as GMP status of the manufacturer.
- Firm has submitted sole agency agreement / letter of authorization dated 20-12-2019 between Sandoz GmbH Austria and Novartis Pharma Pakistan where the manufacturer of the product has been specified as *EBEWE Pharma Ges.m.b.H Nfg.KG Mondseestrasse 11 4866 Unterach Austria.*
- The previously submitted CoPP (No. 11787402) dated 21-02-2019 issued by Austria specifies that the product license holder is *Sandoz GmbH Biochemiestrabe 10 6250 Kundl Austria* and the manufacturer is *EBEWE Pharma Ges.m.b.H Nfg.KG Mondseestrasse 11 4866 Unterach Austria.* However, this CoPP does not confirm the free sale status of the product in Austria due to intellectual property reasons.
- Firm has submitted that the exporting country for their product is Austria and that the product license holder is *Sandoz GmbH Biochemiestrabe 10 6250 Kundl Austria.*

Decision: Approved with Innovator's specifications as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

6.	Name, address of Applicant / Importer	M/s Mutabbar Pharma Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore.
	Details of Drug Sale License of importer	**License No:** 05-352-0063-037381D **Address:** Flat No E1, 1st Floor Agro Squire Shadman Lahore. **Address of Godown:** NA **Validity:** 03-10-2020. **Status:** License to sell drugs as a distributor
	Name and address of marketing authorization holder (abroad)	Health Biotech Ltd Near Dream Hotel Nalagarh Road Baddi 173205 Distt Solan India.
	Name, address of manufacturer(s)	Health Biotech Ltd Near Dream Hotel Nalagarh Road Baddi 173205 Distt Solan India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Not initially submitted **GMP:** copy of GMP certificate (No. HFW-H [Drugs] 185/05) issued by Health and Family Welfare Department Himachal Pradesh, dated 07-03-2020. The certificate is valid till 05-3-2023.
	Details of letter of authorization / sole agency agreement	Not initially 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 36667: 06-11-2018
	Details of fee submitted	PKR 100,000/-: 06-11-2018
	Proposed proprietary name / brand name	CLOMIDE 1g Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Cyclophosphamide eq to anhydrous cyclophosphamide……..1000mg
	Pharmaceutical form of applied drug	Freeze dried powder in amber color glass vial made of USP type I glass.
	Pharmacotherapeutic Group of (API)	Alkylating Agents (L01AA01)
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	458/-
	The status in reference regulatory authorities	Cyclophosphamide 1000 mg Powder for Solution for Injection or Infusion (MHRA Approved).
	For generic drugs (me-too status)	Adriblastine injection by pfizer
	Module-II (Quality Overall Summary)	Not submitted initially as per WHO Template

	Name, address of drug substance manufacturer	Khandelwal Laboratories Pvt Ltd 79/87 D Ladpath Mumbai India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data but complete information is not submitted as per the guidance document
	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 and real time conditions. The accelerated stability is conducted at 40ºC±2 ºC / 75% ±5% RH. The real time stability is conducted at 25ºC±2 ºC / 60% ±5% RH 36 months.
	Module-III Drug Product:	Not submitted initially
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not submitted initially
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	50ml clear colourless USP type I glass vial with 20mm grey butyl rubber stopper & 20mm aluminium flip off seal.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability data of 3 batches for 24 months at 30±2°C, 65±5%RH and 6 months at 4°C±75%RH for three batches.

Evaluation by PEC:

Shortcomings communicated	Response by the firm
Provide valid drug sale license since the submitted DSL was valid till 03-10-2020	Firm has submitted copy of DSL which was valid till 03-10-2020. Firm has also submitted copy of Challan Form for submission of PKR 3000/- in National Bank of Pakistan dated 16-10-2020. The Challan form does not specify the purpose of payment and no evidence of submission of application for renewal of DSL is submitted. Furthermore, the payment is made after the due date.
Provide original, legalized and valid certificate of pharmaceutical product since you have submitted copy of CoPP.	Original, Legalized CoPP (Certificate#. HFW-H[Drugs] 185/05/17-142) dated 24-08-2019 issued by Health and Family Welfare Department Baddi, Himachal Pradesh. The CoPP declares free sale status of the applied product in exporting country. The CoPP also confirms the GMP status of the manufacturer through periodic inspections conducted once an year.
Submit letter of authorization / sole agency agreement from the product license holder (abroad) for the applied product.	Firm has submitted copy of Manufacturing and export agreement dated 7th February 2017. The agreement was valid for three years from the date of agreement. As per the agreement the address of Mutabbar Pharma is mentioned as 25 Taj Arcade 73, Jail Road Lahore, while the address of Mutabbar Pharma mentioned in the application and on DSL is Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore. The agreement does not contains "Annexure A brand products" for which the agreement was made.
Quality overall summary (QOS) in module 2 needs to be submitted as per WHO QOS - PD template or the template approved by Registration Board in its 293rd meeting.	Firm has again submitted QOS which is incomplete and is not as per the WHO template.
Specify the site address of the drug substance manufacturer.	Khandelwal Laboratories Pvt Ltd 79/87 D Ladpath Mumbai India.
Submit data of verification of analytical method	Firm has submitted that the analytical procedures are

for the drug substance in section 3.2.S.4.3 of module 3.	described in USP 40 and have been adopted for the testing. Firm has not submitted verification report of analytical method for the drug substance.
Submit complete information of drug product in section 3.2.P in module 3 as per the numbering system approved as per CTD Form (5-F) promulgated vide SRO 713 (l) 2018 and the data requirement as per guidance document approved by Registration Board in its 296th meeting.	Firm has submitted drug product part of module 3. The drug product part Module 3.2.P submitted by the firm is not as per the CTD Form (5-F) and as per the guidance document.
Submit information in section in 3.2.P.1 regarding 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.	Firm has not submitted any details regarding the diluent to be used along with the drug product.
Submit details of pharmaceutical development in section 3.2.P.2 as per the guidance document approved by Registration Board.	Firm has submitted abstracts from the literature data of various articles.
Submit data of pharmaceutical equivalence in section 3.2.P.2.2.1 as per the guidance document approved by 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 shall be submitted and discussed".*	Firm has not provided results of pharmaceutical equivalence.
Submit data of compatibility in section 3.2.P.6 as per the guidance document approved by Registration Board which states 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".*	Results of compatibility with the diluent is not submitted.
Submit batch analysis certificate of 3 batches of drug product in section 3.2.P.5.4 of module 3.	Firm has submitted COA of 3 batches of the drug product.
Submit verification studies of the analytical method for testing of drug product in section 3.2.P.5.3 of module 3.	Firm has not submitted verification studies of analytical method for testing of drug product.
Submit copy of batch manufacturing record for the three batches for which stability studies have been performed.	Firm has submitted stability study data and process validation report. Firm has not submitted copy of Batch Manufacturing Record (BMR) of the three stability batches.

Based on the response received by the firm and after evaluation, another letter of shortcoming was also issued on 31.12.2020 in which following observations were communicated to the firm. The Firm submitted its reply which was received in DRAP on 11-01-2021. The details of the response of the firm is provided below:

Shortcomings communicated	**Response by the firm**
Provide valid Drug Sale License (DSL) since the submitted DSL was valid till 03-10-2020 and you have only submitted a copy of challan form dated 16.10.2020 without specifying the purpose of challan form. However, no evidence of submission of application for renewal of DSL is submitted. Furthermore, the payment on challan form is also made	Firm has submitted copy of application receipt for renewal of DSL submitted in primary and secondary healthcare department dated 07-01-2021. Firm has also submitted copy of fee challan form 32-A

after the validity date of DSL.	
Provide valid agreement between importer / applicant and manufacturer since the submitted agreement was valid till 6th February 2020. The address of Mutabbar Pharma is mentioned as 25 Taj Arcade 73, Jail Road Lahore, while the address of Mutabbar Pharma mentioned in the application and on DSL is Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore. Furthermore, the agreement does not contains "Annexure A brand products" for which the agreement was made.	Firm has submitted scanned copy of exclusive distribution agreement dated 1 January 2021 between Health BioTech India and M/s Mutabbar Pharma. The newly submitted agreement contains the updated address of Mutabbar Pharma as mentioned in the DSL. The agreement also contains list of 4 products which are applied by Mutabbar Pharma.
Quality Overall Summary (QOS) in module 2 needs to be submitted as per WHO QOS - PD template or the template approved by Registration Board as per the guidance document, since the submitted QOS is incomplete and is not as per WHO template.	Firm has submitted QOS as per WHO QOS-PD template.
Submit data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3, as the USP General chapter Verification of Compendial Procedures <1226> and the CTD guidance document approved by Registration Board recommends verification of compendial analytical methods for the drug substance.	Firm has not submitted data of verification studies of analytical method of the drug substance.
Submit complete information of drug product in section 3.2.P in module 3 as per the numbering system approved as per CTD Form (5-F) promulgated vide SRO 713 (l) 2018 and the data requirement as per guidance document approved by Registration Board since the submitted information in module 3.2.P is not as per CTD format.	Firm has submitted revised drug product part of module 3 in section 3.2.P as per the correct numbering system of CTD.
Submit information in section in 3.2.P.1 regarding 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.	Firm has not submitted information regarding the type of diluent.
Submit pharmaceutical equivalence data in section 3.2.P.2.2.1 as per the guidance document 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 shall be submitted and discussed".	Firm has not submitted data of pharmaceutical equivalence.
Submit data of compatibility of the drug product along with recommended diluents in section 3.2.P.6 as per the guidance document approved by Registration Board which states 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".	Firm has not submitted data of compatibility of drug product along with recommended diluent.
Submit verification studies of the analytical method for testing of drug product in section 3.2.P.5.3 of module 3.	Firm has not submitted data of verification studies of analytical method of the drug product.
Submit copy of batch manufacturing record for the three batches for which stability studies have been performed.	Firm has not submitted copy of batch manufacturing record for the three stability batches

Firm was also advised vide letter dated 31st December, 2020 to appear before Registration Board on 13th January 2021 through authorized person well conversant with registration application(s). Mr. Khawaja Umer CEO along with technical persons appeared before the Board on 13-01-2021. During the proceedings of the Board, firm representatives were asked about the shortcomings which were still present in their registration applications despite of 3 deficiencies letters issued to the applicant. The firm's representatives agreed about deficiencies and responded that they will rectify the shortcomings when they will receive the relevant documents from their principle manufacturer.

Decision of 297th meeting of Registration Board:

Registration Board after hearing the representative of the firm and keeping in view the response submitted by the firm and after thorough delibrations decided to defer the case for following submissions:

- Data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3.
- Information in section in 3.2.P.1 regarding 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.
- Data of pharmaceutical equivalence against the innovator / reference / comparator product, as per the requirements of Form 5F (CTD).
- Data of compatibility of the drug product along with recommended diluents in section 3.2.P.6 of module 3.
- Data of validation / verification of analytical method for the drug product in section 3.2.P.4.3 of module 3.
- Submission copy of batch manufacturing record for the three stability batches.

Response by the firm:

Reason for deferment	Response by the firm
Data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3.	Firm has submitted standard operating procedure for drug substance analysis, certificate of analysis and USP reference monograph. *However, verification studies of the compendial method is not submitted.*
Information in section in 3.2.P.1 regarding 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.	Firm has submitted that the product will be imported without diluent as per the agreement of both firms. Mutabbar Pharma will arrange diluent locally in Pakistan as per patient need basis.
Data of pharmaceutical equivalence against the innovator / reference / comparator product, as per the requirements of Form 5F (CTD).	Firm has submitted results of pharmaceutical equivalence with Endoxan injection of Baxter
Data of compatibility of the drug product along with recommended diluents in section 3.2.P.6 of module 3.	Compatability study with the specified diluent which is listed in packaging inset of product CLOMIDE are performed. The finished product is reconstituted with the specified diluent and kept for 8 hours. After 8 hours the finished product was tested for descrition, identification, pH and assay. The results of above tests were found satisfactory. The results are not provided by the firm.
Data of validation / verification of analytical method for the drug product in section 3.2.P.4.3 of module 3.	Firm has submitted report of validation of analytical procedure of drug product.
Submission copy of batch manufacturing record for the three stability batches.	Firm has submitted copy of BMR of stability batches.

Decision of 312nd meeting of Registration Board:

Deferred for following submissions:

- Verification studies of the analytical method of drug substance performed by drug product manufacturer.
- Results of compatibility studies of the drug product along with recommended diluent.

Response by the firm:

Reason for deferment	Response by the firm
Verification studies of the analytical method of drug substance performed by drug product manufacturer.	Firm has submitted **v**erification studies of the analytical method of drug substance performed by drug product manufacturer i.e. Health Biotech Ltd.

Results of compatibility studies of the drug product along with recommended diluent.	Firm has submitted Results of compatibility studies of the drug product along with recommended diluent sterile water for injection.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

7.	Name, address of Applicant / Importer	M/s Mutabbar Pharma Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore.
	Details of Drug Sale License of importer	**License No:** 05-352-0063-037381D **Address:** Flat No E1, 1st Floor Agro Squire Shadman Lahore. **Address of Godown:** NA **Validity: 03-10-2020.** **Status:** License to sell drugs as a distributor
	Name and address of marketing authorization holder (abroad)	Health Biotech Ltd Near Dream Hotel Nalagarh Road Baddi 173205 Distt Solan India.
	Name, address of manufacturer(s)	Health Biotech Ltd Near Dream Hotel Nalagarh Road Baddi 173205 Distt Solan India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Not initially submitted **GMP:** copy of GMP certificate (No. HFW-H [Drugs] 185/05) issued by Health and Family Welfare Department Himachal Pradesh, dated 07-03-2020. The certificate is valid till 05-03-2023.
	Details of letter of authorization / sole agency agreement	Not initially 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 36666: 06-11-2018
	Details of fee submitted	PKR 100,000/-: 06-11-2018
	Proposed proprietary name / brand name	CEFTAMIDE 1gm Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial Contains: Ifosfamide……..1g
	Pharmaceutical form of applied drug	White cake powder filled in colourless glass vials.
	Pharmacotherapeutic Group of (API)	Alkylating Agents (L01AA06)
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	1200/-
	Status in reference regulatory authorities	Ifex 1gm injection (USFDA Approved).

	For generic drugs (me-too status)	Ifos Injection by A.J.Mirza (Reg#069565)
	Module-II (Quality Overall Summary)	Not submitted initially as per WHO template
	Name, address of drug substance manufacturer	Aarti Drugs Pvt Ltd Mahendra IndustrialEstate, Ground Floor, Road No. 29, Plot No. 109-D Sion (East) Mumbai India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data but complete information is not submitted as per the guidance document
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Not submitted initially
	Module-III Drug Product:	Firm has submitted detailed drug product data but complete information is not submitted as per the guidance document
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has not submitted pharmaceutical equivalence data
	Analytical method validation/ verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	30ml clear colourless glass vials type I
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability data of 3 batches for 24 months at 30±2°C, 65±5%RH and 6 months at 4°C±75%RH for three batches.

Evaluation by PEC:

Shortcomings communicated	**Response by the firm (dated 20-11-2020)**
Provide valid drug sale license since the submitted DSL was valid till 03-10-2020	Firm has submitted copy of DSL which was valid till 03-10-2020. Firm has also submitted copy of Challan Form for submission of PKR 3000/- in National Bank of Pakistan dated 16-10-2020. The Challan form does not specify the purpose of payment and no evidence of submission of application for renewal of DSL is submitted. Furthermore, the payment is made after the due date.
Provide original, legalized and valid certificate of pharmaceutical product since you have submitted copy of CoPP.	Original, Legalized CoPP (Certificate#. HFW-H[Drugs] 185/05/16-143) dated 24-08-2019 issued by Health and Family Welfare Department Baddi, Himachal Pradesh. The CoPP declares free sale status of the applied product in exporting country. The CoPP also confirms the GMP status of the manufacturer through periodic inspections conducted once an year.
Submit letter of authorization / sole agency agreement from the product license holder (abroad) for the applied product.	Firm has submitted copy of Manufacturing and export agreement dated 7th February 2017. The agreement was valid for three years from the date of agreement. As per the agreement the address of Mutabbar Pharma is mentioned as 25 Taj Arcade 73, Jail Road Lahore, while the address of Mutabbar Pharma mentioned in the application and on DSL is Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore. The agreement does not contains "Annexure A brand products" for which the agreement was made.
Quality overall summary (QOS) in module 2 needs to be submitted as per WHO QOS - PD template or the template approved by Registration Board in its 293rd meeting.	Firm has again submitted QOS which is incomplete and is not as per the WHO template.
Specify the site address of the drug substance manufacturer.	Aarti Drugs Pvt Ltd Mahendra IndustrialEstate, Ground Floor, Road No.29, Plot No.109-D Sion (East) Mumbai India.

Submit data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3.	Firm has submitted that the analytical procedures are described in USP 40 and have been adopted for the testing of ifofamide and compliance to specifications as per USP 40. Firm has submitted validation record of analytical method of related substances by HPLC. Firm has not submitted verification report of analytical method for the drug substance.
Submit certificate of analysis of 3 batches of drug substance in section 3.2.S.4.4. of module 3.	Firm has submitted COA of 3 batches of drug substance.
Submit stability study data of 3 batches of drug substance in section 3.2.S.7.3 of module 3.	Firm has submitted real time and accelerated stability study data of 3 batches as per Zone IV-A conditions.
Submit information in section in 3.2.P.1 regarding 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.	Firm has not submitted any details regarding the diluent to be used along with the drug product.
Submit details of pharmaceutical development in section 3.2.P.2 as per the guidance document approved by Registration Board.	Firm has submitted abstracts from the literature data of various articles.
Submit data of pharmaceutical equivalence in section 3.2.P.2.2.1 as per the guidance document approved by 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 shall be submitted and discussed".*	Firm has submitted introductions and details regarding Lyophilization Technology Inc. (LTI) an organization founded in 1992. Moreover the firm has provided details on a webinar related to lyophilized products. Firm has not provided results of pharmaceutical equivalence.
Submit data of compatibility in section 3.2.P.6 as per guidance document approved by Registration Board which states 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".*	Firm has submitted report of compatibility of the drug with excipients instead of providing compatibility of the drug product with the recommended diluent. Results of compatibility with the diluent is not submitted.
Submit batch analysis certificate of 3 batches of drug product in section 3.2.P.5.4 of module 3.	Firm has submitted COA of 3 batches of the drug product.
Justify how the results of stability testing at initial time point for all the batches are different for real time and accelerated stability studies.	Firm has not submitted any justification and again submitted the same results
Submit copy of batch manufacturing record for the three batches for which stability studies have been performed.	Firm has submitted stability study data and process validation protocols and process validation report. Firm has not submitted copy of Batch Manufacturing Record (BMR) of the three stability batches.

Based on the response received by the firm and after evaluation, another letter of shortcoming was also issued on 31.12.2020 in which following observations were communicated to the firm. The Firm submitted its reply which was received in DRAP on 11-01-2021. The details of the response of the firm is provided below:

Shortcomings communicated	**Response by the firm**
Provide valid Drug Sale License (DSL) since the submitted DSL was valid till 03-10-2020 and you have only submitted a copy of challan form dated 16.10.2020 without specifying the purpose of challan form. However, no evidence of submission of	Firm has submitted copy of application receipt for renewal of DSL submitted in primary and secondary healthcare department dated 07-01-2021. Firm has also submitted copy of fee challan form 32-A

application for renewal of DSL is submitted. Furthermore, the payment on challan form is also made after the validity date of DSL.	
Provide valid agreement between importer / applicant and manufacturer since the submitted agreement was valid till 6th February 2020. The address of Mutabbar Pharma is mentioned as 25 Taj Arcade 73, Jail Road Lahore, while the address of Mutabbar Pharma mentioned in the application and on DSL is Flat No. E-1, 1st Floor Agro Squire 47 Shadman Market Lahore. Furthermore, the agreement does not contains "Annexure A brand products" for which the agreement was made.	Firm has submitted scanned copy of exclusive distribution agreement dated 1 January 2021 between Health BioTech India and M/s Mutabbar Pharma. The newly submitted agreement contains the updated address of Mutabbar Pharma as mentioned in the DSL. The agreement also contains list of 4 products which are applied by Mutabbar Pharma.
Quality Overall Summary (QOS) in module 2 needs to be submitted as per WHO QOS - PD template or the template approved by Registration Board as per the guidance document, since the submitted QOS is incomplete and is not as per WHO template.	Firm has submitted QOS as per WHO QOS-PD template.
Submit data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3, as the USP General chapter Verification of Compendial Procedures <1226> and the CTD guidance document approved by Registration Board recommends verification of compendial analytical methods for the drug substance.	Firm has not submitted data of verification studies of analytical method of the drug substance.
Submit information in section in 3.2.P.1 regarding 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.	Firm has not submitted information regarding the type of diluent.
Submit pharmaceutical equivalence data in section 3.2.P.2.2.1 as per the guidance document 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 shall be submitted and discussed".	Firm has not submitted data of pharmaceutical equivalence.
Submit data of compatibility of the drug product along with recommended diluents in section 3.2.P.6 as per the guidance document approved by Registration Board which states 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".	Firm has not submitted data of compatibility of drug product along with recommended diluent.
Justify how the results of stability testing at initial time point for all the batches are different for real time and accelerated stability studies.	Firm has not submitted any justification that how the results of stability testing at initial time point for all the batches are different for real time and accelerated stability studies
Submit copy of batch manufacturing record for the three batches for which stability studies have been performed.	Firm has not submitted copy of batch manufacturing record for the three stability batches

Firm was also advised vide letter dated 31st December, 2020 to appear before Registration Board on 13th January 2021 through authorized person well conversant with registration application(s). Mr. Khawaja Umer CEO along with technical persons appeared before the Board on 13-01-2021. During the proceedings of the Board, firm

representatives were asked about the shortcomings which were still present in their registration applications despite of 3 deficiencies letters issued to the applicant. The firm's representatives agreed about deficiencies and responded that they will rectify the shortcomings when they will receive the relevant documents from their principle manufacturer.

Decision of 297th meeting of Registration Board:

Registration Board after hearing the representative of the firm and keeping in view the responses submitted and after thorough delibrations decided to defer the case for following submissions:

- Data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3.
- Information in section in 3.2.P.1 regarding type of diluent, its composition, quantity or volume, specifications and regulatory status in Pakistan for the diluent which is to be provided along with the applied drug.
- Data of pharmaceutical equivalence against the innovator / reference / comparator product, as per the requirements of Form 5F (CTD).
- Data of compatibility of the drug product along with recommended diluents in section 3.2.P.6 of module 3.
- Justification that how the results of stability testing at initial time point for all the batches are different for real time and accelerated stability studies.
- Submit copy of batch manufacturing record for the three stability batches.

Response by the firm:

Reason for deferment	Response by the firm
Data of verification of analytical method for the drug substance in section 3.2.S.4.3 of module 3.	Firm has submitted standard operating procedure for drug substance analysis, certificate of analysis and USP reference monograph. *However, verification studies of the compendial method is not submitted.*
Information in section in 3.2.P.1 regarding 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.	Firm has submitted that the product will be imported without diluent as per the agreement of both firms. Mutabbar Pharma will arrange diluent locally in Pakistan as per patient need basis.
Data of pharmaceutical equivalence against the innovator / reference / comparator product, as per the requirements of Form 5F (CTD).	Firm has submitted results of pharmaceutical equivalence with Holaxan injection of Baxter Healthcare
Data of compatibility of the drug product along with recommended diluents in section 3.2.P.6 of module 3.	Compatability study with the specified diluent which is listed in packaging inset of product CEFTAMIDE are performed. The finished product is reconstituted with the specified diluent and kept for 8 hours. After 8 hours the finished product was tested for descrition, identification, pH and assay. The results of above tests were found satisfactory. The results are not provided by the firm.
Data of validation / verification of analytical method for the drug product in section 3.2.P.4.3 of module 3.	Firm has submitted report of validation of analytical procedure of drug product.
Justification that how the results of stability testing at initial time point for all the batches are different for real time and accelerated stability studies.	Firm has submitted a letter from manufacturer that there was a typographical error in the initial stability study results.
Submission copy of batch manufacturing record for the three stability batches.	Firm has submitted copy of BMR of stability batches.

Decision of 312nd meeting of Registration Board:

Deferred for following submissions:

- Verification studies of the analytical method of drug substance performed by drug product manufacturer.
- Results of compatibility studies of the drug product along with recommended diluent.

Response by the firm:

Reason for deferment	Response by the firm
Verification studies of the analytical method of drug substance performed by drug product manufacturer.	Firm has submitted **v**erification studies of the analytical method of drug substance performed by drug product manufacturer i.e. Health Biotech Ltd.
Results of compatibility studies of the drug product	Firm has submitted Results of compatibility studies of

along with recommended diluent.	the drug product along with recommended diluent sterile water for injection.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

c. Cases of New License / New Section

Case No. 01: 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)	-	-	01	01	01	01
Tablet (Psychotropic)	-	-	-	-	-	-
Capsule (General)	03	06	01	01	04	07
Cream /ointment/Lotion/Gel	-	-	-	-	-	-

Capsule (General) section: 01 Molecules / 01 Products

8.	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 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.
	Evidence of approval of manufacturing facility	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
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 23180: 25-08-2021
	Details of fee submitted	PKR 30,000/-: 26-07-2021
	Proposed proprietary name/brand name	ITRANAG 100mg Capsule
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Itraconazole (as IR pellets) ……100mg
	Pharmaceutical form of applied drug	Green / white color hard gelatin casule containing white to off white spherical IR pellets
	Pharmacotherapeutic Group of (API)	Antimycotics for systemic use
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Sporanox 100mg capsule (MHRA Approved)
	For generic drugs (me-too status)	Icon capsule of M/s Ferozesons (Reg # 026877)
	Name and address of API manufacturer.	M/s Surge Laboratories (Pvt) Ltd. 10th KM Faisalabad Road Bikhi, District Sheikhupura.
	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 all the quality tests defined in BP for their product against the reference product i.e. Sporanox Capsule of Janssen Cilag UK. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. Sporanox Capsule of Janssen Cilag UK

	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 Surge Laboratories (Pvt) Ltd. 10th KM Faisalabad Road Bikhi, District Sheikhupura.		
API Lot No.	ITC-22-002		
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	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	31-12-2020	31-12-2020	31-12-2020
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)	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 of M/s Surge Laboratories issued by DRAP on 04-07-2019. The certificate is issued based on the inspection dated 03-07-2019.
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 7Kg Itraconazole pellets dated 24-12-2020.
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	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:

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 drug substance specifications and analytical method from both drug substance and drug product manufacturer.

Submit details including Batch number, manufacturing and expiry date of the comparator product against which pharmaceutical equivalence as well as CDP studies were conducted.	Firm has submittd details of the reference product i.e. Sporanox 100mg capsule of Janssen Cilag Limited UK against whch pharmaceutical eqivalence and CDP studies were carried out.
Justify the manufacturing of batches before the issuance of Drug Manufacturing License.	We have submitted an application dated 06-10-2020 for grant of DML as all the required machinery were duly installed and was ready for manufacturing of drugs. DRAP accordingly accepted the request and constituted a panel which inspected our premises on 11-11-2020 and 30-11-2020. The panel was satisfied with the installed facility and gave a go ahead. However the report of the panel was submitted on 03-12-2020 which came for consideration in the forthcoming meeting of CLB held on 11-12-2020. The board accordingly approved the DML however due to non-availability of Director Licensing, the formal DML could not be issued to newly established firms. As such Authority decided to entertain the cases of all such firms in which DML were approved in the meeting dated 11-12-2020. In view of above our firm has already got registration for export purpose only from DAP. Acknowledgment of DML dated 19-02-2021 was obtained only for the purpose of weboc and import of APIs. You are therefore requested that our cases may be considered in upcoming meeting of Registration Board.
Provide detailed method of analysis by which pharmaceutical equivalence and CDP studies were performed.	Firm has submitted detailed method of analysis by which pharmaceutical equivalence and CDP studies were performed.
Provide detailed method including the exact concentration of sample and standard solution preparation for dissolution test.	Firm has submitted detailed method for dissolution test including the details of sample and standard solution preparation as per USP monograph.
Provide valid GMP certificate of the drug substance manufacturer.	Firm has submitted copy of GMP certificate of M/s Surge Laboratories issued by DRAP on 04-07-2019. The certificate is issued based on the inspection dated 03-07-2019.
Provide copy of commercial invoice for evidence of purchase of the drug substance.	Firm has submitted copy of commercial invoice specifying purchase of 7Kg Itraconazole pellets dated 24-12-2020.
Provide Batch Manufacturing Record (BMR) of three stability batches.	Firm has submitted copy of BMR 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.**

Tablet (General) section: 01 Molecules / 01 Products

9.	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 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.
	Evidence of approval of manufacturing facility	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
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24068: 01-09-2021
	Details of fee submitted	PKR 30,000/-: 16-08-2021
	Proposed proprietary name/brand name	NAGDOL 500mg Tablet
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol ……500mg
	Pharmaceutical form of applied drug	white to off white uncoated tablet
	Pharmacotherapeutic Group of (API)	Analgesic / antipyretic
	Reference to finished product specification	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.	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°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.
	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 quality tests defined in BP for their product against the reference product i.e. PANADOL tablet of GSK Pakistan (Pvt) Ltd. Firm has submitted results of CDP in three dissolution medium for their product against the reference product i.e. PANADOL tablet 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.	ZPAR20-340		
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	2500 Tablet	2500 Tablet	2500 Tablet
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	31-12-2020	31-12-2020	31-12-2020
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)	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 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).	Firm has submitted copy of commercial invoice specifying purchase of 25Kg Paracetamol dated 23-12-2020 from Zenith Chemicals.
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 & 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**
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 drug substance specifications and analytical method from both drug substance and drug product manufacturer.
Provide COA of relevant batch of drug substance which is used in the manufacturing of batches of drug product.	Firm has submitted copy of COA of relevant batch ZPAR20-340 whch is used in the manufacturing of batches of drug product.
Provide detailed method of analysis by which pharmaceutical equivalence and CDP studies were performed.	Firm has submitted detailed method of analysis by which pharmaceutical equivalence and CDP studies were performed.
Provide copy of commercial invoice for evidence of purchase of the drug substance.	Firm has submitted copy of BMR 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.**

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 312nd RB meeting**		**Freshly applied**	
	No of molecules	**No of products**	**No of molecules**	**No of products**
Dry Vial section (Cephalosporin)	02	10	-	-
Dry suspension section (Cephalosporin)	01	02	-	-
Capsule section (Cephalosporin)	02	02	-	-
Ampoule Section SVP (General)	05	07	-	-
Capsule section (General)	02	04	-	-
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)	01	02	-	-
Cream section (general)	-	-	02	02

Ointment section (General)	-	-	01	01
Lotion section (General)	-	-	01	01

Cream section (General): 02 Molecules / 02 Products

10.	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 Cream 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. 23544: 27-08-2021
	Details of fee submitted	PKR 20,000/-: 05-05-2021
	Proposed proprietary name/brand name	VALBE 20 gm Cream
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each gram of cream Contains: Betamethasone as valerate……0.1% w/w
	Pharmaceutical form of applied drug	White color viscous cream free from foreign oarticles filled in aluminium tube
	Pharmacotherapeutic Group of (API)	Corticosteroids
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	**MHRA** Approved.
	For generic drugs (me-too status)	Betnovate cream by GSK
	Name and address of API manufacturer.	ENVEE Drugs Pvt. Ltd. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, 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 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 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 USP for their product against the reference i.e. Betnovate cream of M/s 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	ENVEE Drugs Pvt. Ltd. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, Gujrat India.		
API Lot No.	EV/BV-256/20		
Description of Pack (Container closure system)	Aluminium tube		
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.	T097	T098	T099
Batch Size	500 tubes	500 tubes	500 tubes
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	05-08-2020	05-08-2020	05-08-2020
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 Food and Drug Control Administration Gujrat State India. The GMP certificate is valid till 06-07-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice (No. 14, indent No. NXT-119-2020) specifying 3Kg Betamethasone valerate dated 25-05-2020. Firm has also submitted copy of DHL invoice number C0235125 dated 27-05-2020.

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:

- R & I date is 27-08-2021, while the submitted fee is 20,000/-. As per the revised fee SRO, the 30,000/- fee should be submitted.

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 drug substance specifications and analytical method from drug product manufacturer.
Provide evidence of facility of autosampler with 4° for HPLC assay method, since the same is recommended by USP monograph.	Autosampler HPLC was not present at the time of studies so the sample was kept in refrigerator at 4°C. Sample was taken immediately before injecting manually.
Submit valid GMP certificate of the API manufacturer since the submitted certificate was valid till 14-06-2021.	Firm has submitted copy of GMP certificate issued by Food and Drug Control Administration Gujrat State India. The GMP certificate is valid till 06-07-2023.
The submitted copy of commercial invoice is of 02-11-2020 while the batches were manufactured in August 2020. Justification is required in this regard.	Firm has submitted copy of commercial invoice (No. 14, indent No. NXT-119-2020) specifying 3Kg Betamethasone valerate dated 25-05-2020.
Submit evidence of import of the drug substance and also justify why the material was not cleared by Assistant Director (I&E) DRAP.	Firm has also submitted copy of DHL invoice number C0235125 dated 27-05-2020.

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 letter shall be issued after confirmation of separate dispensing booth for steroidal drug substance.**
- **Registration Board further advised the firm to perform validation studies of the analytical method of drug product before manufacturing of commercial batches, since the firm kept the sample in refrigerator at 4°C without using autosampler.**
- **Registration Board further decided that registration letter will be issued after submission of balance fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

11.	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 Cream 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. 19885: 15-07-2021
	Details of fee submitted	PKR 20,000/-: 18-05-2021
	Proposed proprietary name/brand name	FUSIGEN 15gm (2%) Cream
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each gram of cream Contains: Fusidic acid……20mg (2% w/w)
	Pharmaceutical form of applied drug	White to off white coloured cream, filled in pre-printed aluminium tube
	Pharmacotherapeutic Group of (API)	Antibiotics for topical use
	Reference to Finished product specifications	BP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	MHRA Approved.
	For generic drugs (me-too status)	Fucidin cream by Zam Zam coorporation
	Name and address of API manufacturer.	Joyang Laboratories No. 9 Haidu North Road, Sheyang Economic Development Zone Yancheng Jiangsu 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 defined in USP for their product against the reference i.e. Genidic cream of Biogen 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	Joyang Laboratories No. 9 Haidu North Road, Sheyang Economic Development Zone Yancheng Jiangsu China.		
API Lot No.	190713FB		
Description of Pack (Container closure system)	Aluminum tube		
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.	T094	T095	T096
Batch Size	500 packs	500 packs	500 packs
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	06-07-2020	06-07-2020	06-07-2020
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 Drug Manufacturing License of the firm (No. Su20160342) issued by CFDA China and also verified from the official website of NMPA. The certificate is valid till 06-09-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice (No. 00025096) specifying 1.5Kg Fusidic acid dated 02-04-2020. Firm has also submitted copy of DHL invoice number D01135151 dated 04-04-2020.
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 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:

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 27th August 2021.	Firm has submitted that they will submit the fee before issuance of Registration letter.
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 drug product manufacturer.
Submit valid GMP certificate of the API manufacturer, since the submitted copy of GMP certificate is of Chongqing Winbond Shengkai Pharmaceutical Co., Ltd. No. 666 Rongjun Road, Nanjin Street Sub-district Office, Hechuan District, Chongqing.	Firm has submitted copy of Drug Manufacturing License of the firm (No. Su20160342) issued by CFDA China and also verified from the official website of NMPA. The certificate is valid till 06-09-2025.
Submit stability study data of three batches of drug substance as per zone IV-A conditions.	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.
Justify why pharmaceutical equivalence is conducted against comparator product instead of innovator product.	Comparator product was readily available therefore pharmaceutical equivalence was performed against comparator product.
Justify why pH was not tested in pharmaceutical equivalence studies.	pH studies were performed as reflected in the raw data sheets but were not incorporated in the COA. Now updated documents are being submitted.
Provide COA of reference standard / working standard used in the analysis of drug product.	Firm has submitted copy of COA of working reference standard from API manufacturer.
Justify why pH testing was not performed during stability studies.	pH studies were performed as reflected in the raw data sheets but were not incorporated in the COA. Now updated documents are being submitted.
Provide copy of commercial invoice specifying purchase of relevant batch of drug substance.	Firm has submitted copy of commercial invoice (No. 00025096) specifying 1.5Kg Fusidic acid dated 02-04-2020.
Submit evidence of import of the drug substance and also justify why the material was not cleared by Assistant Director (I&E) DRAP.	Firm has also submitted copy of DHL invoice number D01135151 dated 04-04-2020.

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.**
- **The firm shall submit pharmaceutical equivalence data with innovator product before issuance of registration letter.**
- **Registration Board further decided that registration letter will be issued after submission of balance**

fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.		
Ointment section (General): 01 Molecules / 01 Products		
12.	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 Ointment 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. 23543: 27-08-2021
	Details of fee submitted	PKR 20,000/-: 05-05-2021
	Proposed proprietary name/brand name	VALBE 20gm Ointment
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each gram of ointment Contains: Betamethasone as valerate……0.1% w/w
	Pharmaceutical form of applied drug	White color viscous ointment filled in aluminium tube
	Pharmacotherapeutic Group of (API)	Corticosteroids
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	**MHRA** Approved.
	For generic drugs (me-too status)	Betnovate ointment by GSK
	Name and address of API manufacturer.	ENVEE Drugs Pvt. Ltd. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, 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 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 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 USP for their product against the reference i.e. Betnovate ointment of M/s 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	ENVEE Drugs Pvt. Ltd. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, Gujrat India.		
API Lot No.	EV/BV-256/20		
Description of Pack (Container closure system)	Aluminium tube		
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.	T100	T101	T102
Batch Size	500 tubes	500 tubes	500 tubes
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	10-08-2020	10-08-2020	10-08-2020
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 Food and Drug Control Administration Gujrat State India. The GMP certificate is valid till 06-07-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice (No. 14, indent No. NXT-119-2020) specifying 3Kg Betamethasone valerate dated 25-05-2020. Firm has also submitted copy of DHL invoice number C0235125 dated 27-05-2020.
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:

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 27th August 2021.	Firm has submitted that they will submit the fee before issuance of Registration letter.
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 drug product manufacturer.
Provide evidence of facility of autosampler with 4° for HPLC assay method, since the same is recommended by USP monograph.	Autosampler HPLC was not present at the time of studies so the sample was kept in refrigerator at 4°C. The sample was taken immediately before injecting manually.
Submit valid GMP certificate of the API manufacturer since the submitted certificate was valid till 14-06-2021.	Firm has submitted copy of GMP certificate issued by Food and Drug Control Administration Gujrat State India. The GMP certificate is valid till 06-07-2023.
The submitted copy of commercial invoice is of 02-11-2020 while the batches were manufactured in August 2020. Justification is required in this regard.	Firm has submitted copy of commercial invoice (No. 14, indent No. NXT-119-2020) specifying 3Kg Betamethasone valerate dated 25-05-2020.
Submit evidence of import of the drug substance and also justify why the material was not cleared by Assistant Director (I&E) DRAP.	Firm has also submitted copy of DHL invoice number C0235125 dated 27-05-2020.

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 advised the firm to perform validation studies of the analytical method of drug product before manufacturing of commercial batches, since the firm kept the sample in refrigerator at 4°C without using autosampler.**
- **Registration Board further decided that registration letter will be issued after submission of balance fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

Lotion section (General): 01 Molecules / 01 Products

13.	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 Lotion 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. 23545: 27-08-2021
	Details of fee submitted	PKR 20,000/-: 05-05-2021
	Proposed proprietary name/brand name	VALBE 60ml Lotion
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml of lotion Contains: Betamethasone as valerate……0.1% w/v
	Pharmaceutical form of applied drug	White color viscous lotion filled in plastic bottle
	Pharmacotherapeutic Group of (API)	Corticosteroids
	Reference to Finished product specification	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	USFDA Approved.
	For generic drugs (me-too status)	Betnovate lotion by GSK
	Name and address of API manufacturer.	ENVEE Drugs Pvt. Ltd. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, 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 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 & 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 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 USP for their product against the reference i.e. Betnovate lotion of M/s 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	ENVEE Drugs Pvt. Ltd. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, Gujrat India.		
API Lot No.	EV/BV-256/20		
Description of Pack (Container closure system)	Plastic 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.	T103	T104	T105
Batch Size	500 bottles	500 bottles	500 bottles
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	15-08-2020	15-08-2020	15-08-2020
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 Food and Drug Control Administration Gujrat State India. The GMP certificate is valid till 06-07-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice (No. 14, indent No. NXT-119-2020) specifying 3Kg Betamethasone valerate dated 25-05-2020. Firm has also submitted copy of DHL invoice number C0235125 dated 27-05-2020.
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:

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	Firm has submitted that they will submit the fee before issuance of Registration letter.

R&I section of DRAP on 27th August 2021.	
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 drug product manufacturer.
Provide evidence of facility of autosampler with 4° for HPLC assay method, since the same is recommended by USP monograph.	Autosampler HPLC was not present at the time of studies so the sample was kept in refrigerator at 4°C. The sample was taken immediately before injecting manually.
Submit valid GMP certificate of the API manufacturer since the submitted certificate was valid till 14-06-2021.	Firm has submitted copy of GMP certificate issued by Food and Drug Control Administration Gujrat State India. The GMP certificate is valid till 06-07-2023.
The submitted copy of commercial invoice is of 02-11-2020 while the batches were manufactured in August 2020. Justification is required in this regard.	Firm has submitted copy of commercial invoice (No. 14, indent No. NXT-119-2020) specifying 3Kg Betamethasone valerate dated 25-05-2020.
Submit evidence of import of the drug substance and also justify why the material was not cleared by Assistant Director (I&E) DRAP.	Firm has also submitted copy of DHL invoice number C0235125 dated 27-05-2020.

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 advised the firm to perform validation studies of the analytical method of drug product before manufacturing of commercial batches, since the firm kept the sample in refrigerator at 4°C without using autosampler.**
- **Registration Board further decided that registration letter will be issued after submission of balance fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

Case No. 03: Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.

Quaper (Pvt) Ltd Sargodha.has been granted approval of additional section by Licensing division DRAP dated 29-09-2020. specifies following sections:

- Tablet (General) (Revised)
- Capsule (General) section (New)
- R&D Laboratory (New)
- Sachet (General) (New)

Another letter from Secretary Central Licensing Board dated 19-03-2021 states that CLB in its 279th meeting has considered and approved correction in the name / title of section from Tablet (general) section revised to Tablet (General) section new.

Now the firm has submitted following applications as per the details mentioned in the table below:

Name of Section	Already considered		Newly applied		Total	
	No of molecules	No of products	No of molecules	No of products	No of molecules	No of products
Capsule (General) section (New)	03	07	03	03	06	10

Name of Section	No of molecules	No of products
Sachet (General) (New)	02	03

Firm has been granted approval of new section on 29-09-2020, however they have manufactured stability batches in June 2020. Firm has submitted that they have developed R&D lab and capsule general section as per the DRAP approved layout plan. The HVAC was also installed in R&D Lab. The panel inspection for the purpose of grant of additional sections was conducted on 16-06-2020 and 18-06-2020. The panel inspection report also endorse the R&D Lab with following remarks "Firm has established R&D Laboratory as per approved layout plan approved by DRAP. Following production machines and Quality control instruments were provided for small scale

development purpose. HVAC system was installed. It is humbly requested to you to kindly consider our study of these trial batches which we have submitted through CTD application.		
Capsule (General) section (New): 03 (Molecule) / 03 (Products)		
14.	Name, address of Applicant / Marketing Authorization Holder	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Name, address of Manufacturing site.	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm has submitted copy of GMP certificate issued on the basis of inspection dated 28-01-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 29-09-2020. The letter specifies following sections: • Tablet (General) (Revised) • Capsule (General) section (New) • R&D Laboratory (New) • Sachet (General) (New)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19163: 08-07-2021
	Details of fee submitted	PKR 30,000/-: 31-05-2021
	Proposed proprietary name/brand name	LASOMAX 30mg Capsule
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Lansoprazole (as enteric coated pellets)……..30mg
	Pharmaceutical form of applied drug	Red/white color hard gelatin capsule containing white to off white spherical enteric coated pellets
	Pharmacotherapeutic Group of (API)	Proton pump inhibitors
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Lansoprazole capsule 30mg (**MHRA** Approved)
	For generic drugs (me-too status)	Selanz SR capsule by Searle
	Name and address of API manufacturer.	Vision Pharmaceuticals, plot No. 22-23, Industrial Trinagle 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 the quality tests for their product against Q-Pro 30mg capsule of Bosch Pharmaceutical. Firm has submitted results of comparative dissolution profile for their product against -Pro 30mg capsule of Bosch 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	Vision Pharmaceuticals, plot No. 22-23, Industrial Trinagle Kahuta Road Islamabad.		
API Lot No.	LPS0319		
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.	T1/30	T2/30	T3/30
Batch Size	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	27-06-2020	27-06-2020	27-06-2020
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)	Quaper Pharma has been granted approval of new section therefore 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 of M/s Vision Pharmaceuticals issued by Additional Director DRAP. The certificate was 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 copy of commercial invoice dated 18-06-2020 specifying 2.5Kg Lansoprazole pellets from Vision Pharma.
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	The firm submitted that their HPLC system is not 21 CFR compliant therefore the audit trail reports are not applicable.
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[3]:

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 drug substance specifications from drug product manufacturer Quaper Pharmaceuticals
Provide COA of reference standard / working standard used in the analysis of the drug substance and drug product.	Firm has submitted COA of working standard Batch No. LSA/2009150.
Submit detailed method of analysis of drug product in section 3.2.P.5.2.	Firm has submitted detailed method of analysis of drug product which is in line with USP monograph.
Provide copy of BMR of the three stability batches.	Firm has submitted copy of BMR 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.**

15.	Name, address of Applicant / Marketing Authorization Holder	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Name, address of Manufacturing site.	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm has submitted copy of GMP certificate issued on the basis of inspection dated 28-01-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 29-09-2020. The letter specifies following sections: • Tablet (General) (Revised) • Capsule (General) section (New) • R&D Laboratory (New) • Sachet (General) (New)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19162: 08-07-2021
	Details of fee submitted	PKR 30,000/-: 31-05-2021
	Proposed proprietary name/brand name	**ITRAMAX 100mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Itraconazole IR pellets eq to itraconazole..……100mg
	Pharmaceutical form of applied drug	Hard gelatin capsule with gray cap and pink body properly locked filled with white to off white spherical immlediate release pellets
	Pharmacotherapeutic Group of (API)	Antifungal
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Itraconazole 100 mg Capsules Hard (**MHRA** Approved)
	For generic drugs (me-too status)	Icon 100 mg Capsule by Ferozsons Laboratories Ltd
	Name and address of API manufacturer.	Vision Pharmaceuticals, plot No. 22-23, Industrial Trinagle 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	Firm has submitted results of pharmaceutical equivalence for

	Comparative Dissolution Profile	the quality tests for their product against Sporanox 100mg capsule of Janssen Cilag. Firm has submitted results of comparative dissolution profile for their product against Sporanox 100mg capsule of Janssen Cilag.
	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 Trinagle Kahuta Road Islamabad.		
API Lot No.	ICZ1467		
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.	T1/20	T2/20	T3/20
Batch Size	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	24-06-2020	24-06-2020	24-06-2020
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)	Quaper Pharma has been granted approval of new section therefore 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 of M/s Vision Pharmaceuticals issued by Additional Director DRAP. The certificate was 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 copy of commercial invoice dated 18-06-2020 specifying 3.5Kg itraconazole pellets from Vision Pharma.
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	The firm submitted that their HPLC system is not 21 CFR compliant therefore the audit trail reports are not applicable.
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[3]:

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 drug substance specifications from drug product manufacturer Quaper Pharmaceuticals

Provide verification studies of the drug substance by drug product manufacturer in section 3.2.S.4.3.	Firm has submitted verification studies of the drug substance from drug product manufacturer.
Submit detailed method of analysis of dissolution test for the drug product in section 3.2.P.5.2.	Firm has submitted detailed method of dissolution of drug product which is in line with USP monograph.
Submit details including Batch number, manufacturing and expiry date of the comparator product against which pharmaceutical equivalence as well as CDP studies were conducted.	Firm has submitted detail of the reference product Name: Sporanox 100mg Capsule Batch No. N0729 Exp date: 01/2023 Manufacturer: Janssen Cilag & company

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 / Marketing Authorization Holder	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Name, address of Manufacturing site.	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm has submitted copy of GMP certificate issued on the basis of inspection dated 28-01-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 29-09-2020. The letter specifies following sections: • Tablet (General) (Revised) • Capsule (General) section (New) • R&D Laboratory (New) • Sachet (General) (New)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 19161: 08-07-2021
	Details of fee submitted	PKR 30,000/-: 31-05-2021
	Proposed proprietary name/brand name	HICAM 20mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Piroxicam……20mg
	Pharmaceutical form of applied drug	Red/Red color hard gelatin capsule containing white to off white mixed powder
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Feldene capsule (**USFDA** Approved)
	For generic drugs (me-too status)	Feldene Capsule by Pfizer

	Name and address of API manufacturer.	Alcon Biosciences Pvt Ltd. A-1/2104, Phase-III, GIDC, VAPI, 396195, District Valsad, 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 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	Firm has submitted results of pharmaceutical equivalence for the quality tests for their product against Feldene 20mg capsule of Pfizer. Firm has submitted results of comparative dissolution profile for their product against Feldene 20mg capsule 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	Alcon Biosciences Pvt Ltd. A-1/2104, Phase-III, GIDC, VAPI, 396195, District Valsad, Gujrat India.		
API Lot No.	PCM-1011/20		
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.	T1/20	T2/20	T3/20
Batch Size	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	07-2020	07-2020	07-2020

Date of Initiation	15-07-2020	15-07-2020	15-07-2020
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)	Quaper Pharma has been granted approval of new section therefore 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. 20102297) of M/s Alcon Biosciences issued by Food and Drugs Control Administration Gujrat State India. The certificate is valid till 21-10-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice dated 15-06-2020 specifying 25Kg piroxicam from Alcon Bioscience through Decina Pharma Pvt Ltd. The invoice is cleared by AD (I&E) dated 155-06-2020.
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	The firm submitted that their HPLC system is not 21 CFR compliant therefore the audit trail reports are not applicable.
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[3]:

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 drug substance specifications from drug product manufacturer Quaper Pharmaceuticals.
Provide COA of reference standard / working standard used in the analysis of the drug substance and drug product.	Firm has submitted COA of reference standard from API manufacturer for batch number ALC/PCM/WS/20010
Provide detailed method for uniformity of dosage units of the drug product in section 3.2.P.5.2.	Firm has submitted detailed method for the test for uniformity of dosage units as per USP monograph.
Justify why water content is not determined during the stability studies.	Test for water contents was determined at the batch release time and the same has been mentioned in batch analysis report in section 3.2.P.5.4.
Provide raw data sheet and chromatograms for 6th month testing for batch T3/20	Firm has submitted raw data sheet and chromatograms for 6th month testing for batch T3/20.

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.**

Sachet (General) section (New): 02 (Molecule) / 03 (Products)

17.	Name, address of Applicant / Marketing Authorization Holder	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.

	Name, address of Manufacturing site.	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm has submitted copy of GMP certificate issued on the basis of inspection dated 28-01-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 29-09-2020. The letter specifies following sections: • Tablet (General) (Revised) • Capsule (General) section (New) • R&D Laboratory (New) • Sachet (General) (New)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29205: 26-10-2021
	Details of fee submitted	PKR 30,000/-: 12-10-2021
	Proposed proprietary name/brand name	ESOMAX 20mg Sachet of oral suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each sachet contains: Esomeprazole (as esomeprazole magnesium trihydrate enteric coated pellets)…..20mg
	Pharmaceutical form of applied drug	White to off white spherical enteric coated pellets and excipients filled in aluminium foil
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	As per Innovator's product
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Nexium Sachet by AstraZaneca (USFDA Approved)
	For generic drugs (me-too status)	Somezol Sachet by Bosch pharma
	Name and address of API manufacturer.	Vision Pharmaceuticals, plot No. 22-23, Industrial Trinagle 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 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 the quality tests for their product against Nexium 20mg sachet. Firm has submitted results of comparative dissolution profile for their product against Nexium 20mg sachet.
	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 Trinagle Kahuta Road Islamabad.		
API Lot No.	EMZ045640		
Description of Pack (Container closure system)	Aluminium 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.	T1/21	T2/21	T3/21
Batch Size	1500 Sachet	1500 Sachet	1500 Sachet
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	14-01-2021	19-01-2021	21-01-2021
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)	Quaper Pharma has been granted approval of new section therefore 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 of M/s Vision Pharmaceuticals issued by Additional Director DRAP. The certificate was 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 copy of commercial invoice dated 10-12-2020 specifying purchase of 5Kg esomeprazole 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	The firm submitted that their HPLC system is not 21 CFR compliant therefore the audit trail reports are not applicable.
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[3]:

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 drug substance specifications from drug product manufacturer Quaper Pharmaceuticals.
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 verification studies of the analytical procedure of drug substance performed by drug product manufacturer.
Submit complete stability study data of the drug substance, since the submitted data of real time stability study is till 12 months only.	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.
Submit details including Batch number, manufacturing and expiry date of the comparator product against which pharmaceutical equivalence as well as CDP studies were conducted.	Firm has submitted detail of the reference product Name: Nexium 20mg Sachet Batch No. EH1398 Exp date: 01/2024 Manufacturer: Astrazaneca
Provide evidence of purchase including commercial invoice of the drug substance.	Firm has submitted copy of commercial invoice dated 10-12-2020 specifying purchase of 5Kg esomeprazole pellets
Provide copy of BMR of the stability batches.	Firm has submitted copy of BMR 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.**

18.	Name, address of Applicant / Marketing Authorization Holder	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Name, address of Manufacturing site.	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	GMP status of the firm	The firm has submitted copy of GMP certificate issued on the basis of inspection dated 28-01-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 29-09-2020. The letter specifies following sections: • Tablet (General) (Revised) • Capsule (General) section (New) • R&D Laboratory (New) • Sachet (General) (New)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28325: 14-10-2021
	Details of fee submitted	PKR 30,000/-: 12-10-2021
	Proposed proprietary name/brand name	ESOMAX 40mg Sachet of oral suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each sachet contains: Esomeprazole (as esomeprazole magnesium trihydrate enteric coated pellets)…..40mg
	Pharmaceutical form of applied drug	White to off white spherical enteric coated pellets and excipients filled in aluminium foil
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	As per Innovator's product
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Nexium Sachet by AstraZaneca (USFDA Approved)
	For generic drugs (me-too status)	Somezol Sachet by Bosch pharma
	Name and address of API manufacturer.	Vision Pharmaceuticals, plot No. 22-23, Industrial Trinagle 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 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 the quality tests for their product against Nexium 40mg sachet. Firm has submitted results of comparative dissolution profile for their product against Nexium 40mg sachet.
	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 Trinagle Kahuta Road Islamabad.		
API Lot No.	EMZ045640		
Description of Pack (Container closure system)	Aluminium 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.	T1/21	T2/21	
Batch Size	2500 Sachet	2500 Sachet	
Manufacturing Date	01-2021	01-2021	
Date of Initiation	21-01-2021	22-01-2021	
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)	Quaper Pharma has been granted approval of new section therefore 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 of M/s Vision Pharmaceuticals issued by Additional Director DRAP. The certificate was 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 copy of commercial invoice dated 10-12-2020 specifying purchase of 5Kg esomeprazole 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	The firm submitted that their HPLC system is not 21 CFR compliant therefore the audit trail reports are not applicable.
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[3]:

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 drug substance specifications from drug product manufacturer Quaper Pharmaceuticals.
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 verification studies of the analytical procedure of drug substance performed by drug product manufacturer.
Submit complete stability study data of the drug substance, since the submitted data of real time stability study is till 12 months only.	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.
Submit details including Batch number, manufacturing and expiry date of the comparator product against which pharmaceutical equivalence as well as CDP studies were conducted.	Firm has submitted detail of the reference product Name: Nexium 20mg Sachet Batch No. EH1398 Exp date: 01/2024 Manufacturer: Astrazaneca
Justify why stability study data of only 2 batches is submitted.	As per DRAP guidelines for CTD dossier it is recommended for suspensions that if the batch size of a stability batch is of2000 units then 2 batches data is sufficient.
Provide evidence of purchase including commercial invoice of the drug substance.	Firm has submitted copy of commercial invoice dated 10-12-2020 specifying purchase of 5Kg esomeprazole pellets
Provide copy of BMR of the stability batches.	Firm has submitted copy of BMR 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.**

19.	Name, address of Applicant / Marketing Authorization Holder	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Name, address of Manufacturing site.	M/s Quaper (Pvt) Ltd. 26-A, Small Industrial Estate, Lahore Road Sargodha.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm has submitted copy of GMP certificate issued on the basis of inspection dated 28-01-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of grant of additional section dated 29-09-2020. The letter specifies following sections:

		• Tablet (General) (Revised) • Capsule (General) section (New) • R&D Laboratory (New) • Sachet (General) (New)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27302: 04-10-2021
	Details of fee submitted	PKR 30,000/-: 27-09-2021
	Proposed proprietary name/brand name	**Q-Salt ORS Sachet (Lemon Flavor)**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each sachet contains: Sodium chloride…….2.6g Trisodium citrate dihydrate…….2.9g Potassium chloride……..1.5g Glucose anhydrous……13.5g
	Pharmaceutical form of applied drug	White to off white mixed powder filled in sealed specific aluminium foil
	Pharmacotherapeutic Group of (API)	Oral rehydration salt
	Reference to Finished product specifications	BP specs
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	**WHO** Approved, available in international pharmacopoeia
	For generic drugs (me-too status)	Werisol sachet by Werrick pharma
	Name and address of API manufacturer.	**Sodium chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Trisodium citrate dihydrate:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Potassium chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Glucose anhydrous:** Xiwang Pharmaceutical Co. Ltd. No. 237, Tongfu Road, Handian Town, Zouping County, Binzhou City, Shandong 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 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)	**Sodium chloride:** 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. **Trisodium citrate dihydrate:** 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 chloride:** 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. **Glucose anhydrous:** 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 Davisalt ORS Sachet manufactured by Davis 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	**Sodium chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Trisodium citrate dihydrate:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Potassium chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Glucose anhydrous:** Xiwang Pharmaceutical Co. Ltd. No. 237, Tongfu Road, Handian Town, Zouping County, Binzhou City, Shandong Province China.
API Lot No.	**Sodium chloride:** 5234 **Trisodium citrate dihydrate:** 183 **Potassium chloride:** 736 **Glucose anhydrous:** XW20200302
Description of Pack	White to off white mixed powder filled in sealed specific aluminium foil

(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.	T-001	T-002	T-003
Batch Size	2000 Sachet	2000 Sachet	2000 Sachet
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	12-01-2021	12-01-2021	12-01-2021
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)	Quaper Pharma has been granted approval of new section therefore 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.	**Sodium chloride:** Firm has submitted copy of GMP certificate (No. 1037/2020-21) of M/s Nandu Chemicals (Pvt) Ltd. India issued by Drugs Control Department Government of Karnataka. The certificate is valid till 17-11-2021. **Trisodium citrate dihydrate:** Firm has submitted copy of GMP certificate (No. 1037/2020-21) of M/s Nandu Chemicals (Pvt) Ltd. India issued by Drugs Control Department Government of Karnataka. The certificate is valid till 17-11-2021. **Potassium chloride:** Firm has submitted copy of GMP certificate (No. 1037/2020-21) of M/s Nandu Chemicals (Pvt) Ltd. India issued by Drugs Control Department Government of Karnataka. The certificate is valid till 17-11-2021. **Glucose anhydrous:** Firm has submitted copy of GMP certificate (No. SD20170644) of M/s Xiwang Pharmaceutical Co. Ltd. Xiwang Industry zone Zouping County, Shandong Province China issued by CFDA China. The certificate is valid till 11-01-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sodium chloride, Trisodium citrate dihydrate, Potassium chloride:** Firm has submitted copy of commercial invoice No. EXP/00147 dated 16-12-2020 specifying purchase of Potassium chloride, sodium chloride and sodium citrate from Nandu Chemicals. Firm has also submitted copy of DHL invoice number 29 8293 5462 dated 18-12-2020. **Glucose anhydrous:** Firm has submitted copy of commercial invoice number 20YX0090L dated 01-12-2020 specifying purchase of Glucose anhydrous from Xiwang Pharmaceutical Co. Ltd. Firm has also submitted copy of DHL invoice number 29 8293 5462 dated 04-12-2020.
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 raw data sheets, COA and summary data sheets.

	chromatograms, Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm submitted that their HPLC system is not 21 CFR compliant therefore the audit trail reports are not applicable.
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[3]:

Shortcomings communicated	**Response by the firm**
Submit data in section 3.2.S.4.1 for all drug substances 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 all drug substance specifications from drug product manufacturer Quaper Pharmaceuticals.
Submit data of verification of analytical procedure of each 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 verification studies of the analytical procedure of all drug substance performed by drug product manufacturer.
Submit details including Batch number, manufacturing and expiry date of the comparator product against which pharmaceutical equivalence were conducted.	Firm has submitted detail of the reference product Name: Davisalt ORS Batch No. DV5768 Exp date: 12/2022 Manufacturer: Davis Pharmaceutical
Provide evidence of flame photometer which is required for the testing of drug product as per BP monograph.	Firm has submitted copy of invoice for purchase of flame photometer dated 10-11-2020
Provide evidence of purchase / import of each drug substance.	Firm has submitted copy of commercial invoice with following details: Sodium chloride, Trisodium citrate dihydrate, Potassium chloride: Firm has submitted copy of commercial invoice No. EXP/00147 dated 16-12-2020 specifying purchase of Potassium chloride, sodium chloride and sodium citrate from Nandu Chemicals. Firm has also submitted copy of DHL invoice number 29 8293 5462 dated 18-12-2020. Glucose anhydrous: Firm has submitted copy of commercial invoice number 20YX0090L dated 01-12-2020 specifying purchase of Glucose anhydrous from Xiwang Pharmaceutical Co. Ltd. Firm has also submitted copy of DHL invoice number 29 8293 5462 dt: 4-12-2020.

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.**

Case No. 04: M/s Lakhani Pharma Private Limited, Sheikh Zayed Road, Rahim Yar Khan

Firm has submitted copy of issuance of DML by way of formulation to M/s Lakhani Pharma Private Limited dated 07-06-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 279th meeting held on 18th February 2021 has approved the grant of DML in the name of M/s Lakhani Pharma Private Limited for following section:

1. IV Infusion section (General)

Now the firm has submitted following applications as per the details mentioned in the table below:

Name of Section	Previously considered		Freshly applied		Total	
	No of molecules	No of products	No of molecules	No of products	No of molecules	No of products
IV Infusion section (General)	03	15	01	05	04	20

IV Infusion section (General): 01 Molecules / 5 Products

20.	Name, address of Applicant / Marketing Authorization Holder	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Name, address of Manufacturing site.	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	New license granted on 16/03/2021 (Inspection date 03/02/2021) IV Infusion section approved.
	Evidence of approval of manufacturing facility	Firm has submitted copy of issuance of DML by way of formulation to M/s Lakhani Pharma Private Limited dated 07-06-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 279th meeting held on 18th February 2021 has approved the grant of DML in the name of M/s Lakhani Pharma Private Limited for following section: 1. IV 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. 28930: 22-10-2021
	Details of fee submitted	PKR 20,000/-: 24-03-2021 PKR 10,000/-: 09-10-2021
	Proposed proprietary name/brand name	LAKSOL-DS IV Infusion 500ml
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Sodium chloride…… 0.9g Glucose anhydrous….. 5g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolytes & Carbohydrates
	Reference to Finished product specifications	BP
	Proposed Pack size	500ml
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	**MHRA** Approved.

		0.9% Sodium Chloride and 5% Glucose Intravenous Infusion
	For generic drugs (me-too status)	Unisol-DS I.V Infusion BP by M/s Unisa Pharmaceutical Industries Limited.
	Name and address of API manufacturer.	**Glucose Anhydrous** M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county,shandong province, china. **Sodium chloride** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark.
	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)	**Glucose anhydrous** 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. **Sodium chloride** 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 72 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 'Unisol-DS I.V Infusion by M/s Unisa Pharmaceutical Industries Limited.
	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	**(Sodium chloride)**	

	M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark. **(Glucose Anhydrous)** M/s Xiwang Pharmaceutical Co.,Ltd . Xiwang industry park, zouping county,shandong province, china.			
API Lot No.	4102011902 (Sodium chloride) F200303B (Glucose Anhydrous)			
Description of Pack (Container closure system)	Low Density Polyethylene bag			
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 (Months)			
Batch No.	Ex-040	Ex-041	Ex-042	
Batch Size	500 liters	500 liters	500 liters	
Manufacturing Date	02-2021	02-2021	02-2021	
Date of Initiation	14-02-2021	14-02-2021	14-02-2021	
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 applicable since it is a newly established license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Glucose:** Firm has submitted copy of GMP certificate in the name of M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county,shandong province, China valid upto 11-01-2023 issued by China Food and Drug Administration. **Sodium chloride:** Firm has submitted copy of Eudra GMP certificate of API manufacturer issued by Danish Medicine Agency based on inspection dated 07-03-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
4.	Data of stability batches will be supported	Firm has submitted stability study data of 3 batches along with

	by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	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	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:

Shortcomings communicated	**Response by the firm**
Justify the manufacturing of batches before the issuance of Drug Manufacturing License.	Firm has submitted that our firm was ready and we have submitted application for panel inspection on 3rd June 2020. Panel for Inspection was constituted on 22nd October 2020. Panel Inspection of our Plant was conducted on 3rd Feb, 2021, The Panel members appreciated our efforts for approved layout plan compliance as well as documentation. Our DML was approved in 279th meeting of CLB held on 18th February 2021. After the approval of our DML we started to manufacture trial batches. Firm has also submitted copy of panel inspection report.
Justify the label claim containing glucose anhydrous, since the MHRA approved reference product as well as BP monograph specifies that the product contains glucose monohydrate equivalent to glucose anhydrous.	Our Product Claim is Glucose (Glucose Anhydrous) which is as per B.P 2020 (III-1267). Competitors are manufacturing the same product with same label claim. The BP monograph of "Glucose Infusion" specifies the definition as "*Glucose Infusion is a sterile solution containing Glucose or Glucose Monohydrate*".
Justify why pharmaceutical equivalence studies are conducted against a comparator product instead of performing such studies with innovator or reference product.	Firm has submitted that as per the CTD guidance document, pharmaceutical equivalence can also be conducted against comparator product Unisol-DS I.V Infusion by M/s Unisa Pharmaceutical Industries Limited Page No. 21 "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"
Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis. Also specify if the applied product is with Eurocap or not.	We have BFS Machine Bottlepack (Rommelage), Bottle is being Blown, Filled and Sealed in a single cycle of 19 sec under Laminar Air Flow to ensure the Quality of our Product. Injectable grade LDPE is being used for the production of Packaging Material (Bottle). Which is manufactured by the well-known European company (Ineous). We have Eurocap machine (Rommelag Germany) for Eurocap Bottles. But in this particular case we have applied for Simple cap (With out Eurocap).
Provide details regarding the method of sterilization of the drug product, keeping in view the material of construction of LDPE bottle whether it is autoclavable or not.	Low Density Polyethylene LDPE) is being autoclaved worldwide which bears temperature up to 113°C. Principle for Sterilization is reduce the temperature and increase the time to achieve the required Sterility Assurance Level (SAL). Our Sterilizers/ autoclave is PLC controlled with Automatic additional time selection in Sterilization cycle.
Provide details including batch number, and COA of the reference standard / working standard used during the analysis and validation studies of the drug substance and drug product.	Copy of reference standard COA is provided by the firm.

Justify the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Stability study Performed at 30°C ± 2°C at 65% + 5%RH, and at 40°C + 2°C at 75% + 5%RH additional water loss study was performed as per ICH guidelines and the data for water loss was submitted.
Provide raw data sheet for calculation of results of stability studies at each month time point.	Firm has submitted raw data sheets for calculation of results of stability studies at each month time point.
Submit copy of commercial invoice along with evidence of import of the drug substance.	Firm has submitted copy of commercial invoice for both drug substance with following details **Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
Provide Batch Manufacturing Record (BMR) of three stability batches.	Firm has submitted copy of BMR 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.**
- **Furthermore, manufacturer shall submit data of pharmaceutical equivalence and comparative dissolution profile with innovator's/reference product before issuance of registration letter.**

21.	Name, address of Applicant / Marketing Authorization Holder	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Name, address of Manufacturing site.	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	New license granted on 16/03/2021 (Inspection date 03/02/2021) IV Infusion section approved.
	Evidence of approval of manufacturing facility	Firm has submitted copy of issuance of DML by way of formulation to M/s Lakhani Pharma Private Limited dated 07-06-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 279th meeting held on 18th February

		2021 has approved the grant of DML in the name of M/s Lakhani Pharma Private Limited for following section: 1. IV 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. 28931: 22-10-2021
	Details of fee submitted	PKR 20,000/-: 24-03-2021 PKR 10,000/-: 09-10-2021
	Proposed proprietary name/brand name	LAKSOL-DS IV Infusion 1000ml
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Sodium chloride…… 0.9g Glucose anhydrous….. 5g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolytes & Carbohydrates
	Reference to Finished product specifications	BP
	Proposed Pack size	1000ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**MHRA** Approved. 0.9% Sodium Chloride and 5% Glucose Intravenous Infusion
	For generic drugs (me-too status)	Unisol-DS I.V Infusion BP by M/s Unisa Pharmaceutical Industries Limited
	Name and address of API manufacturer.	**Glucose Anhydrous** M/s Xiwang Pharmaceutical Co.,Ltd . Xiwang industry park, zouping county,shandong province, china **Sodium chloride** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark.
	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)	**Glucose anhydrous** 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.

		Sodium chloride 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 72 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 'Unisol-DS I.V Infusion by M/s Unisa Pharmaceutical Industries Limited.
	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	**(Sodium chloride)** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark. **(Glucose Anhydrous)** M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county,shandong province, china.		
API Lot No.	4102011902 (Sodium chloride) F200303B (Glucose Anhydrous)		
Description of Pack (Container closure system)	Low Density Polyethylene bag		
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 (Months)
Batch No.	Ex-037	Ex-038	Ex-039
Batch Size	500 liters	500 liters	500 liters
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	14-02-2021	14-02-2021	14-02-2021
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 applicable since it is a newly established license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Glucose:** Firm has submitted copy of GMP certificate in the name of M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county,shandong province, China valid upto 11-01-2023 issued by China Food and Drug Administration.

		Sodium chloride: Firm has submitted copy of Eudra GMP certificate of API manufacturer issued by Danish Medicine Agency based on inspection dated 07-03-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
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	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:

Shortcomings communicated	**Response by the firm**
Justify the manufacturing of batches before the issuance of Drug Manufacturing License.	Firm has submitted that our firm was ready and we have submitted application for panel inspection on 3rd June 2020. Panel for Inspection was constituted on 22nd October 2020. Panel Inspection of our Plant was conducted on 3rd Feb, 2021, The Panel members appreciated our efforts for approved layout plan compliance as well as documentation. Our DML was approved in 279th meeting of CLB held on 18th February 2021. After the approval of our DML we started to manufacture trial batches. Firm has also submitted copy of panel inspection report.
Justify the label claim containing glucose anhydrous, since the MHRA approved reference product as well as BP monograph specifies that the product contains glucose monohydrate equivalent to glucose anhydrous.	Our Product Claim is Glucose (Glucose Anhydrous) which is as per B.P 2020 (III-1267). Competitors are manufacturing the same product with same label claim. The BP monograph of "Glucose Infusion" specifies the definition as "*Glucose Infusion is a sterile solution containing Glucose or Glucose Monohydrate*".
Justify why pharmaceutical equivalence studies are conducted against a comparator product instead of performing such studies with innovator or reference product.	Firm has submitted that as per the CTD guidance document, pharmaceutical equivalence can also be conducted against comparator product Unisol-DS I.V Infusion by M/s Unisa Pharmaceuical Industries Limited Page No. 21 "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"
Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis. Also specify if the applied product is with Eurocap or not.	We have BFS Machine Bottlepack (Rommelage), Bottle is being Blown, Filled and Sealed in a single cycle of 19 sec under Laminar Air Flow to ensure the Quality of our Product. Injectable grade LDPE is being used for the production of Packaging Material (Bottle). Which is manufactured by the well-known European company (Ineous). We have Eurocap machine (Rommelag Germany) for Eurocap Bottles. But in this particular case we have applied for Simple cap (With out Eurocap).
Provide details regarding the method of sterilization of the drug product, keeping in view the material of construction of LDPE bottle whether it is autoclavable or not.	Low Density Polyethylene LDPE) is being autoclaved worldwide which bears temperature up to 113°C. Principle for Sterilization is reduce the temperature and increase the time to achieve the required Sterility Assurance Level (SAL). Our Sterilizers/ autoclave is PLC controlled with Automatic additional time selection in Sterilization cycle.
Provide details including batch number, and COA of the reference standard / working standard used during the analysis and validation studies of the drug substance and drug product.	Copy of reference standard COA is provided by the firm.
Justify the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Stability study Performed at 30°C ± 2°C at 65% + 5%RH, and at 40°C + 2°C at 75% + 5%RH additional water loss study was performed as per ICH guidelines and the data for water loss was submitted.
Provide raw data sheet for calculation of results of stability studies at each month time point.	Firm has submitted raw data sheets for calculation of results of stability studies at each month time point.
Submit copy of commercial invoice along with evidence of import of the drug substance.	Firm has submitted copy of commercial invoice for both drug substance with following details **Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
Provide Batch Manufacturing Record (BMR) of three stability batches.	Firm has submitted copy of BMR 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.** • **Furthermore, manufacturer shall submit data of pharmaceutical equivalence and comparative dissolution profile with innovator's/reference product before issuance of registration letter.**	
22.	Name, address of Applicant / Marketing Authorization Holder	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Name, address of Manufacturing site.	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	New license granted on 16/03/2021 (Inspection date 03/02/2021) IV Infusion section approved.
	Evidence of approval of manufacturing facility	Firm has submitted copy of issuance of DML by way of formulation to M/s Lakhani Pharma Private Limited dated 07-06-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 279th meeting held on 18th February 2021 has approved the grant of DML in the name of M/s Lakhani Pharma Private Limited for following section: 1. IV 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. 28926: 22-10-2021
	Details of fee submitted	PKR 20,000/-: 24-03-2021 PKR 10,000/-: 09-10-2021
	Proposed proprietary name/brand name	**LAKSOL-DS 1/2 Infusion 500ml**
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Sodium chloride…… 0.45g Glucose anhydrous….. 5g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolytes & Carbohydrates
	Reference to Finished product specifications	BP
	Proposed Pack size	500ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**MHRA** Approved. Sodium Chloride 0.45% and Glucose 5% Intravenous Infusion
	For generic drugs (me-too status)	Unisol-DS$^{1/2}$ I.V Infusion BP by M/s Unisa Pharmaceutical Industries Limited
	Name and address of API manufacturer.	**Glucose Anhydrous** M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county,shandong province, china **Sodium chloride** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark.

	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)	**Glucose anhydrous** 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. **Sodium chloride** 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 72 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 'Unisol-DS$^{1/2}$ I.V Infusion by M/s Unisa Pharmaceutical Industries Limited..
	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	**(Sodium chloride)** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark. **(Glucose Anhydrous)** M/s Xiwang Pharmaceutical Co.,Ltd . Xiwang industry park, zouping county,shandong province, china.
API Lot No.	4102011902 (Sodium chloride) F200303B (Glucose Anhydrous)
Description of Pack (Container closure system)	Low Density Polyethylene bag

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 (Months)		
Batch No.	Ex-055	Ex-056	Ex-057
Batch Size	500 liters	500 liters	500 liters
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	15-02-2021	15-02-2021	15-02-2021
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 applicable since it is a newly established license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Glucose:** Firm has submitted copy of GMP certificate in the name of M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county, shandong province, China valid upto 11-01-2023 issued by China Food and Drug Administration. **Sodium chloride:** Firm has submitted copy of Eudra GMP certificate of API manufacturer issued by Danish Medicine Agency based on inspection dated 07-03-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
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	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:		

Shortcomings communicated	Response by the firm
Justify the manufacturing of batches before the issuance of Drug Manufacturing License.	Firm has submitted that our firm was ready and we have submitted application for panel inspection on 3rd June 2020. Panel for Inspection was constituted on 22nd October 2020. Panel Inspection of our Plant was conducted on 3rd Feb, 2021, The Panel members appreciated our efforts for approved layout plan compliance as well as documentation. Our DML was approved in 279th meeting of CLB held on 18th February 2021. After the approval of our DML we started to manufacture trial batches. Firm has also submitted copy of panel inspection report.
Justify the label claim containing glucose anhydrous, since the MHRA approved reference product as well as BP monograph specifies that the product contains glucose monohydrate equivalent to glucose anhydrous.	Our Product Claim is Glucose (Glucose Anhydrous) which is as per B.P 2020 (III-1267). Competitors are manufacturing the same product with same label claim. The BP monograph of "Glucose Infusion" specifies the definition as "*Glucose Infusion is a sterile solution containing Glucose or Glucose Monohydrate*".
Justify why pharmaceutical equivalence studies are conducted against a comparator product instead of performing such studies with innovator or reference product.	Firm has submitted that as per the CTD guidance document, pharmaceutical equivalence can also be conducted against comparator product Unisol-DS$^{1/2}$ I.V Infusion by M/s Unisa Pharmaceutical Industries Limited Page No. 21 "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"
Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis. Also specify if the applied product is with Eurocap or not.	We have BFS Machine Bottlepack (Rommelage), Bottle is being Blown, Filled and Sealed in a single cycle of 19 sec under Laminar Air Flow to ensure the Quality of our Product. Injectable grade LDPE is being used for the production of Packaging Material (Bottle). Which is manufactured by the well-known European company (Ineous). We have Eurocap machine (Rommelag Germany) for Eurocap Bottles. But in this particular case we have applied for Simple cap (With out Eurocap).
Provide details regarding the method of sterilization of the drug product, keeping in view the material of construction of LDPE bottle whether it is autoclavable or not.	Low Density Polyethylene LDPE) is being autoclaved worldwide which bears temperature up to 113°C. Principle for Sterilization is reduce the temperature and increase the time to achieve the required Sterility Assurance Level (SAL). Our Sterilizers/ autoclave is PLC controlled with Automatic additional time selection in Sterilization cycle.
Provide details including batch number, and COA of the reference standard / working standard used during the analysis and validation studies of the drug substance and drug product.	Copy of reference standard COA is provided by the firm.
Justify the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Stability study Performed at 30°C ± 2°C at 65% + 5%RH, and at 40°C + 2°C at 75% + 5%RH additional water loss study was performed as per ICH guidelines and the data for water loss was submitted.

Provide raw data sheet for calculation of results of stability studies at each month time point.	Firm has submitted raw data sheets for calculation of results of stability studies at each month time point.
Submit copy of commercial invoice along with evidence of import of the drug substance.	Firm has submitted copy of commercial invoice for both drug substance with following details **Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
Provide Batch Manufacturing Record (BMR) of three stability batches.	Firm has submitted copy of BMR 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.**
- **Furthermore, manufacturer shall submit data of pharmaceutical equivalence and comparative dissolution profile with innovator's/reference product before issuance registration of letter.**

23.	Name, address of Applicant / Marketing Authorization Holder	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Name, address of Manufacturing site.	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	New license granted on 16/03/2021 (Inspection date 03/02/2021) IV Infusion section approved.
	Evidence of approval of manufacturing facility	Firm has submitted copy of issuance of DML by way of formulation to M/s Lakhani Pharma Private Limited dated 07-06-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 279th meeting held on 18th February 2021 has approved the grant of DML in the name of M/s Lakhani Pharma Private Limited for following section: 1. IV 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. 28927: 22-10-2021
	Details of fee submitted	PKR 20,000/-: 24-03-2021 PKR 10,000/-: 09-10-2021
	Proposed proprietary name/brand name	**LAKSOL-DS 1/3 Infusion 500ml**
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Sodium chloride…… 0.3g Glucose anhydrous….. 3.3g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolytes & Carbohydrates
	Reference to Finished product specifications	BP
	Proposed Pack size	500ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	BAXTER 0.3% SODIUM CHLORIDE and 3.3% GLUCOSE 500mL injection AHB1033 by Baxter Healthcare Pty Ltd (**TGA** Australia Approved)
	For generic drugs (me-too status)	Medisol 3.3% / 0.3% infusion by Medipak (Reg#024300)
	Name and address of API manufacturer.	**Glucose Anhydrous** M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county,shandong province, china **Sodium chloride** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark.
	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)	**Glucose anhydrous** 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. **Sodium chloride** 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 72 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 against Medisol infusion 0.3%/3.3% of Medipak
	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	**(Sodium chloride)** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark. **(Glucose Anhydrous)** M/s Xiwang Pharmaceutical Co.,Ltd . Xiwang industry park, zouping county,shandong province, china.		
API Lot No.	4102011902 (Sodium chloride) F200303B (Glucose Anhydrous)		
Description of Pack (Container closure system)	Low Density Polyethylene bag		
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 (Months)		
Batch No.	Ex-094	Ex-095	Ex-096
Batch Size	500 liters	500 liters	500 liters
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	16-02-2021	16-02-2021	16-02-2021
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 applicable since it is a newly established license.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Glucose:** Firm has submitted copy of GMP certificate in the name of M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county, shandong province, China valid upto 11-01-2023 issued by China Food and Drug Administration. **Sodium chloride:** Firm has submitted copy of Eudra GMP certificate of API manufacturer issued by Danish Medicine Agency based on inspection dated 07-03-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of	**Glucose:** Firm has submitted copy of commercial invoice (No. F200907B)

	import).	dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
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	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:

Shortcomings communicated	**Response by the firm**
Justify the manufacturing of batches before the issuance of Drug Manufacturing License.	Firm has submitted that our firm was ready and we have submitted application for panel inspection on 3rd June 2020. Panel for Inspection was constituted on 22nd October 2020. Panel Inspection of our Plant was conducted on 3rd Feb, 2021, The Panel members appreciated our efforts for approved layout plan compliance as well as documentation. Our DML was approved in 279th meeting of CLB held on 18th February 2021. After the approval of our DML we started to manufacture trial batches. Firm has also submitted copy of panel inspection report.
Justify the label claim containing glucose anhydrous, since the MHRA approved reference product as well as BP monograph specifies that the product contains glucose monohydrate equivalent to glucose anhydrous.	Our Product Claim is Glucose (Glucose Anhydrous) which is as per B.P 2020 (III-1267). Competitors are manufacturing the same product with same label claim. The BP monograph of "Glucose Infusion" specifies the definition as "*Glucose Infusion is a sterile solution containing Glucose or Glucose Monohydrate*".
Provide evidence of approval of applied formulation in reference regulatory authorities which were adopted by the Board in its 275th meeting, since the submitted evidence could not be verified.	BAXTER 0.3% SODIUM CHLORIDE and 3.3% GLUCOSE 500mL injection AHB1033 by Baxter Healthcare Pty Ltd (**TGA** Australia Approved)
Provide evidence of generic status, since the submitted reference could not be verified.	Medisol 3.3% / 0.3% infusion by Medipak (Reg#024300)
Justify why pharmaceutical equivalence studies are conducted against a comparator product instead of performing such studies with innovator or	Firm has submitted that as per the CTD guidance document, pharmaceutical equivalence can also be conducted against comparator product Medisol infusion

reference product.	0.3%/3.3% of M/s Medipak Page No. 21 "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"
Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis. Also specify if the applied product is with Eurocap or not.	We have BFS Machine Bottlepack (Rommelage), Bottle is being Blown, Filled and Sealed in a single cycle of 19 sec under Laminar Air Flow to ensure the Quality of our Product. Injectable grade LDPE is being used for the production of Packaging Material (Bottle). Which is manufactured by the well-known European company (Ineous). We have Eurocap machine (Rommelag Germany) for Eurocap Bottles. But in this particular case we have applied for Simple cap (With out Eurocap).
Provide details regarding the method of sterilization of the drug product, keeping in view the material of construction of LDPE bottle whether it is autoclavable or not.	Low Density Polyethylene LDPE) is being autoclaved worldwide which bears temperature up to 113°C. Principle for Sterilization is reduce the temperature and increase the time to achieve the required Sterility Assurance Level (SAL). Our Sterilizers/ autoclave is PLC controlled with Automatic additional time selection in Sterilization cycle.
Provide details including batch number, and COA of the reference standard / working standard used during the analysis and validation studies of the drug substance and drug product.	Copy of reference standard COA is provided by the firm.
Justify the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Stability study Performed at 30°C ± 2°C at 65% + 5%RH, and at 40°C + 2°C at 75% + 5%RH additional water loss study was performed as per ICH guidelines and the data for water loss was submitted.
Provide raw data sheet for calculation of results of stability studies at each month time point.	Firm has submitted raw data sheets for calculation of results of stability studies at each month time point.
Submit copy of commercial invoice along with evidence of import of the drug substance.	Firm has submitted copy of commercial invoice for both drug substance with following details **Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
Provide Batch Manufacturing Record (BMR) of three stability batches.	Firm has submitted copy of BMR 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.**
- **Furthermore, manufacturer shall submit data of pharmaceutical equivalence and comparative dissolution profile with innovator's/reference product before issuance of registration letter.**

24.	Name, address of Applicant / Marketing Authorization Holder	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Name, address of Manufacturing site.	M/s Lakhani Pharma Private Limited Sheikh Zayed Road, Rahim Yar Khan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	New license granted on 16/03/2021 (Inspection date 03/02/2021) IV Infusion section approved.
	Evidence of approval of manufacturing facility	Firm has submitted copy of issuance of DML by way of formulation to M/s Lakhani Pharma Private Limited dated 07-06-2021 from Secretary Central Licensing Board. The letter specifies that CLB in its 279th meeting held on 18th February 2021 has approved the grant of DML in the name of M/s Lakhani Pharma Private Limited for following section: 1. IV 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. 28925: 22-10-2021
	Details of fee submitted	PKR 20,000/-: 24-03-2021 PKR 10,000/-: 09-10-2021
	Proposed proprietary name / brand name	LAKSOL-Peads IV Infusion 500ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Sodium chloride…… 0.18g Glucose anhydrous….. 4.3g
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Electrolytes & Carbohydrates
	Reference to Finished product specifications	BP
	Proposed Pack size	500ml
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Could not be confirmed
	For generic drugs (me-too status)	Medisol infusion 4.3% and 0.18% by Medipak (Reg#009695)
	Name and address of API manufacturer.	**Glucose Anhydrous** M/s Xiwang Pharmaceutical Co.,Ltd . Xiwang industry park, zouping county,shandong province, china **Sodium chloride** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark.

	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)	**Glucose anhydrous** 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. **Sodium chloride** 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 72 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 'Medisol Peads I.V Infusion by M/s Medipak Limited.
	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	**(Sodium chloride)** M/s Dansk Salt A/S. Hadsundvej 17, Mariager, 9550, Denmark. **(Glucose Anhydrous)** M/s Xiwang Pharmaceutical Co.,Ltd . Xiwang industry park, zouping county,shandong province, china.
API Lot No.	4102011902 (Sodium chloride) F200303B (Glucose Anhydrous)
Description of Pack (Container closure system)	Low Density Polyethylene bag

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 (Months)		
Batch No.		Ex-064	Ex-065	Ex-066
Batch Size		500 liters	500 liters	500 liters
Manufacturing Date		02-2021	02-2021	02-2021
Date of Initiation		17-02-2021	17-02-2021	17-02-2021
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 applicable since it is a newly established license.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Glucose:** Firm has submitted copy of GMP certificate in the name of M/s Xiwang Pharmaceutical Co.,Ltd. Xiwang industry park, zouping county, shandong province, China valid upto 11-01-2023 issued by China Food and Drug Administration. **Sodium chloride:** Firm has submitted copy of Eudra GMP certificate of API manufacturer issued by Danish Medicine Agency based on inspection dated 07-03-2019.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.		
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	NA		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.		

	accelerated)	

Evaluation by PEC:

<table>
<tr><th>Shortcomings communicated</th><th>Response by the firm</th></tr>
<tr><td>Justify the manufacturing of batches before the issuance of Drug Manufacturing License.</td><td>Firm has submitted that our firm was ready and we have submitted application for panel inspection on 3rd June 2020. Panel for Inspection was constituted on 22nd October 2020. Panel Inspection of our Plant was conducted on 3rd Feb, 2021, The Panel members appreciated our efforts for approved layout plan compliance as well as documentation. Our DML was approved in 279th meeting of CLB held on 18th February 2021. After the approval of our DML we started to manufacture trial batches. Firm has also submitted copy of panel inspection report.</td></tr>
<tr><td>Justify the label claim containing glucose anhydrous, since the MHRA approved reference product as well as BP monograph specifies that the product contains glucose monohydrate equivalent to glucose anhydrous.</td><td>Our Product Claim is Glucose (Glucose Anhydrous) which is as per B.P 2020 (III-1267). Competitors are manufacturing the same product with same label claim.
The BP monograph of “Glucose Infusion” specifies the definition as “Glucose Infusion is a sterile solution containing Glucose or Glucose Monohydrate”.</td></tr>
<tr><td>Provide evidence of approval of applied formulation in reference regulatory authorities which were adopted by the Board in its 275th meeting, since the submitted evidence could not be verified.</td><td>As per RRA formulation (Glucose 4% and Sodium Chloride 0.18% whereas comparator’s Product in Pakistan contains Glucose 4.3% and Sodium Chloride 0.18%. Following is detail for me-too status and RRA reference.
<table>
<tr><th></th><th>Reg No.</th><th>Composition</th></tr>
<tr><td>RRA
(Baxter U.K)</td><td>PL
00116/0342</td><td>4% Glucose with
0.18%Sodium Chloride</td></tr>
<tr><td>RRA
(Baxter
Australia)</td><td>ABH-1253</td><td>4% Glucose with
0.18%Sodium Chloride</td></tr>
<tr><td>Otsuka</td><td>018364</td><td>4.3% Glucose with
0.18%Sodium Chloride</td></tr>
<tr><td>Medipak</td><td>009695</td><td>4.3% Glucose with
0.18%Sodium Chloride</td></tr>
<tr><td>Frontier
Dextrose</td><td>049286</td><td>4.3% Glucose with
0.18%Sodium Chloride</td></tr>
<tr><td>Mediflow</td><td>079597</td><td>4.3% Glucose with
0.18%Sodium Chloride</td></tr>
</table></td></tr>
<tr><td>Provide evidence of me-too status, since the submitted reference could not be verified.</td><td>Medisol infusion 4.3% and 0.18% by Medipak (Reg#009695)</td></tr>
<tr><td>Justify why pharmaceutical equivalence studies are conducted against a comparator product instead of performing such studies with innovator or reference product.</td><td>Firm has submitted that as per the CTD guidance document, pharmaceutical equivalence can also be conducted against comparator product Page No. 21 “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”</td></tr>
<tr><td>Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis. Also specify if the applied product is with Eurocap or not.</td><td>We have BFS Machine Bottlepack (Rommelage), Bottle is being Blown, Filled and Sealed in a single cycle of 19 sec under Laminar Air Flow to ensure the Quality of our Product. Injectable grade LDPE is being used for the production of Packaging Material (Bottle). Which is manufactured by the well-known European company (Ineous). We have Eurocap machine (Rommelag Germany) for Eurocap Bottles. But in this particular case</td></tr>
</table>

	we have applied for Simple cap (With out Eurocap).
Provide details regarding the method of sterilization of the drug product, keeping in view the material of construction of LDPE bottle whether it is autoclavable or not.	Low Density Polyethylene LDPE) is being autoclaved worldwide which bears temperature up to 113°C. Principle for Sterilization is reduce the temperature and increase the time to achieve the required Sterility Assurance Level (SAL). Our Sterilizers/ autoclave is PLC controlled with Automatic additional time selection in Sterilization cycle.
Provide details including batch number, and COA of the reference standard / working standard used during the analysis and validation studies of the drug substance and drug product.	Copy of reference standard COA is provided by the firm.
Justify the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Stability study Performed at 30°C ± 2°C at 65% + 5%RH, and at 40°C + 2°C at 75% + 5%RH additional water loss study was performed as per ICH guidelines and the data for water loss was submitted.
Provide raw data sheet for calculation of results of stability studies at each month time point.	Firm has submitted raw data sheets for calculation of results of stability studies at each month time point.
Submit copy of commercial invoice along with evidence of import of the drug substance.	Firm has submitted copy of commercial invoice for both drug substance with following details **Glucose:** Firm has submitted copy of commercial invoice (No. F200907B) dated 15/01/2021. The invoice declare purchase of 75 Kg dextrose anhydrous (Batch No. F200303B manufactured by Xiwang Pharmaceutical Co. Ltd) from Qingdao Foture International Trade Co Ltd. Firm has also submitted copy of DHL invoice (Ref 12841) dated 15/01/2021. The invoice declare 3 containers each 25Kg of dextrose having a total weight 175 lbs. **Sodium Chloride:** Firm has submitted copy of commercial invoice (No. 1410008918) dated 07/01/2021. The invoice declare purchase of 300 Kg sodium chloride pharmaceutical quality (Batch No. 4102011902 manufactured by Dansk Salt A/S. Denmark) from Nouryon Middle East FZE. Firm has also submitted copy of DHL invoice (Ref 163842571) dated 07/01/2021. The invoice declare 12 containers each 25Kg of dextrose having a total weight 679 lbs.
Provide Batch Manufacturing Record (BMR) of three stability batches.	Firm has submitted copy of BMR of three stability batches.

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.

d. Routine cases of local manufacturing

25.	Name, address of Applicant / Marketing Authorization Holder	M/s Nicholas Pharmaceuticals, Plot # 34, National Industrial Zone, Rawat, Islamabad.
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (Pvt) Ltd., 581-Sundar Industrial Estate, Lahore.
	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 stallion Pharmaceuticals issued on the basis of inspection conducted dated 06-12-2019
	Evidence of approval of manufacturing facility	Firm has submitted copy of GMP certificate dated 10-12-2018 specifying Dry Powder Injection section (Penicillin) and dry powder 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. 27216: 18-12-2019
	Details of fee submitted	PKR 50,000/-: 16-12-2019
	Proposed proprietary name / brand name	**Tazonic Dry Powder Injection 2.25g**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Piperacillin (as Piperacillin Sodium)……..2g Tazobactam (as Tazobactam Sodium)....0.25g
	Pharmaceutical form of applied drug	Dry powder for injection
	Pharmacotherapeutic Group of (API)	Antibacterial for systemic use
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Zosyn Injection **USFDA** Approved.
	For generic drugs (me-too status)	Tacip Injection by Macter International (Reg#086976)
	Name and address of API manufacturer.	M/s Shandong (Previously Qilu) Anxin Pharmaceutical Co., Ltd. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China
	Module-II (Quality Overall Summary)	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 both drug substances. 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.
	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.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted accelerated and real time stability data of 3 batches of API as per Zone IVA.
	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 also submitted results of Pharmaceutical equivalence of their product with the Tanzo of M/s Bosch Pharma
	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	M/s Shandong (Previously Qilu) Anxin Pharmaceutical Co., Ltd. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China		
API Lot No.	TSP12001517N		
Description of Pack (Container closure system)	USP Type III Colorless 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	N5001	N5002	N5003
Batch Size	4250 Vials	4160 Vials	6380 Vials
Manufacturing Date	03-2015	03-2015	04-2015
Date of Initiation	25-05-2015	25-05-2015	12-06-2015
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.	M/s Shandong (Previously Qilu) Anxin Pharmaceutical Co., Ltd. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China has USFDA Drug establishment registration site and is valid upto 31/2021. The firm also has DML number 20160009 valid until 2025 issued by Shandong Provincial drug administration China.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (invoice # NLLA/16/1424) cleared by DRAP Lahore office dated 03-04-2017 specifying import 100 Kg Tazobactam Sodium (Batch # TSP12001517N)
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 has submitted data of product manufactured by M/s Stallion Pharmaceuticals on 18-12-2019, the firm was issued letter of shortcoming on 12-03-2020. Now the firm dated 22-10-2021 have submitted revised data of new batches of drug product manufactured by the same manufacturer i.e. Stallion Pharmaceuticals.
- The applied product to be manufactured by M/s Stallion Pharmaceuticals have already been approved by Registration Board in its 308th 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 308th meeting are as follows:

Applicant firm	M/s Healthtek (Pvt.) Limited. Plot No. 14, Sector 19, Korangi Industrial Area Karachi
Manufacturer firm	M/s. Stallion Pharmaceuticals (Pvt.) Ltd. 581-Sundar Industrial Estate, Lahore Pakistan
Brand Name	PITZO 2.25g Injection
Batch No. of drug product	N5001, N5002, N5003
Case No.	436

Decision: Approved.

- **Registration Board further decided that registration letter will be issued after submission of applicable fee for pre-registration variation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

26.	Name, address of Applicant / Marketing Authorization Holder	M/s Nicholas Pharmaceuticals, Plot # 34, National Industrial Zone, Rawat, Islamabad.
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (Pvt) Ltd., 581-Sundar Industrial Estate, Lahore.
	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 10-12-2018 specifying Dry Powder Injection section (Penicillin) and dry powder injection section (Carbapenem)
	Evidence of approval of manufacturing facility	Firm has submitted copy of GMP certificate dated 10-12-2018 specifying Dry Powder Injection section (Penicillin) and dry powder 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. 27217: 18-12-2019
	Details of fee submitted	PKR 50,000/-: 16-12-2019
	Proposed proprietary name / brand name	Tazonic Dry Powder Injection 4.5g
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Piperacillin (as Piperacillin Sodium) ……4g Tazobactam (as Tazobactam Sodium).....0.50g
	Pharmaceutical form of applied drug	Dry powder for injection
	Pharmacotherapeutic Group of (API)	Antibacterial for systemic use
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Zosyn Injection **USFDA** Approved.
	For generic drugs (me-too status)	Tacip Injection by Macter International (Reg#086976)
	Name and address of API manufacturer.	M/s Shandong (Previously Qilu) Anxin Pharmaceutical Co., Ltd. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China
	Module-II (Quality Overall Summary)	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 both drug substances. 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.
	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.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted accelerated and real time stability data of 3 batches of API as per Zone IVA.
	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	Firm has submitted results of Pharmaceutical equivalence of

	Comparative Dissolution Profile	their product with the Tanzo Injection of M/s Bosch Pharma
	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	M/s Shandong (Previously Qilu) Anxin Pharmaceutical Co., Ltd. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China		
API Lot No.	TSP12001517N		
Description of Pack (Container closure system)	USP Type III Colorless 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	P5001	P5002	P5003
Batch Size	8600 Vials	8600 Vials	10630 Vials
Manufacturing Date	03-2015	03-2015	04-2015
Date of Initiation	16-04-2015	16-04-2015	04-06-2015
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.	M/s Shandong (Previously Qilu) Anxin Pharmaceutical Co., Ltd. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China has USFDA Drug establishment registration site and is valid upto 31/2021. The firm also has DML number 20160009 valid until 2025 issued by Shandong Provincial drug administration China.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (invoice # NLLA/16/1424) cleared by DRAP Lahore office dated 03-04-2017 specifying import 100 Kg Tazobactam Sodium (Batch # TSP12001517N)
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 has submitted data of product manufactured by M/s Stallion Pharmaceuticals on 18-12-2019, the firm was issued letter of shortcoming on 12-03-2020. Now the firm dated 22-10-2021 have submitted revised data of new batches of drug product manufactured by the same manufacturer i.e. Stallion

Pharmaceuticals.

- The applied product to be manufactured by M/s Stallion Pharmaceuticals have already been approved by Registration Board in its 308th 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 308th meeting are as follows:

Applicant firm	M/s Healthtek (Pvt.) Limited. Plot No. 14, Sector 19, Korangi Industrial Area Karachi
Manufacturer firm	M/s. Stallion Pharmaceuticals (Pvt.) Ltd. 581-Sundar Industrial Estate, Lahore Pakistan
Brand Name	PITZO 4.5g Injection
Batch No. of drug product	P5001, P5002, P5003
Case No.	437

Decision: Approved.

- **Registration Board further decided that registration letter will be issued after submission of applicable fee for pre-registration variation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

27.	Name, address of Applicant / Marketing Authorization Holder	M/s Linz Pharmaceuticals (Pvt) Ltd. 31 G/H Sector 15, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Bosch Pharmaceuticals (Pvt) Ltd, Plot No. 221-223, sector-23, Korangi Industrial Area Karachi.
	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 11-05-2020 is submitted.
	GMP status of the firm	**Linz Pharmaceuticals:** Inspection dated 09/01/2020, GMP of the firm is rated as Good. **Bosch Pharmaceuticals:** GMP certificate issued on the basis of inspection dated 25-06-2019
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 0003500 of M/s Bosch Pharmaceuticals Karachi dated 03-02-2016 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. 5782: 22-02-2021
	Details of fee submitted	PKR 50,000/-: 16-09-2020
	Proposed proprietary name / brand name	MEROLINZ 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	Colourless to white or light yellow crystals or 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 ACS Dobfar SpA 2 Viale Addetta, 2a/12 – 3/5 20067 Tribiano Milano Italy.
	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 IV 500mg Manufactured by AstraZeneca UK Ltd. Marketing Authorization Holder (s) Pfizer Limited UK.
	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 ACS Dobfar SpA 2 Viale Addetta, 2a/12 – 3/5 20067 Tribiano Milano Italy.
API Lot No.	33080500616 33080500686 33080500220
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.	PO17032	PO18034	PO210010
Batch Size	24272 vials	16393 vials	8811 Vials
Manufacturing Date	04-2017	02-2018	10-2020
Date of Initiation	04-05-2017	26-02-2018	24-10-2020
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)	Firm has referred to onsite inspection report of their product "DOVIR Tablet 30mg and 60mg Tablets" which was presented in 288th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 25th January, 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.	Firm has submitted copy of GMP certificate (No. IT-API/125/H/2020) issued by Italian Medicine Agency dated 03-01-2019. The certificate is also verified from EudraGMP database.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**33080500616:** Firm has submitted copy of commercial invoice cleared dated 03-03-2017 specifying import of 84Kg Meropenem trihydrate. The commercial invoice is attested by AD (I&E) DRAP. **33080500686:** Firm has submitted copy of commercial invoice cleared dated 03-03-2017 specifying import of 84Kg Meropenem trihydrate. The commercial invoice is attested by AD (I&E) DRAP. **33080500220** Firm has submitted copy of commercial invoice cleared dated 06-03-2020 specifying import of 102Kg Meropenem trihydrate. 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 certificate of 21 CFR compliance of their HPLC system however the firm has not submitted audit trail reports of 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:

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	Firm has submitted copy of drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance &

routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."	Drug Product manufacturer.
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. Further justify how analysis of the drug substance was carried out without performing verification studies.	Firm has submitted verification study report for the drug substance.
Justify why the test for contents of sodium is not performed during the stability studies of the drug substance as recommended in USP monograph.	Firm has submitted test reports for the sodium contents of the drug product as per USP monograph at batch release stage.
Submit data in section 3.2.P.2.2.1 as per the guidance document approved by Registration Board which specifies 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 shall be submitted and discussed".	Firm has submitted pharmaceutical equivalence report against Meronem IV 500mg Manufactured by AstraZeneca UK Ltd. Marketing Authorization Holder (s) Pfizer Limited UK.
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".	Firm has submitted results of compatibility studies of the product with the recommended diluent.

Decision: Approved.

- **Firm shall submit applicable fee for revision of the specifications of the drug product before issuance of Registration letter.**

28.	Name, address of Applicant / Marketing Authorization Holder	M/s Linz Pharmaceuticals (Pvt) Ltd. 31 G/H Sector 15, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Bosch Pharmaceuticals (Pvt) Ltd, Plot No. 221-223, sector-23, Korangi Industrial Area Karachi.
	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 11-05-2020 is submitted.
	GMP status of the firm	**Linz Pharmaceuticals:** Inspection dated 09/01/2020, GMP of the firm is rated as Good. **Bosch Pharmaceuticals:** GMP certificate issued on the basis of inspection dated 25-06-2019
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of Grant of additional section / amendment under DML No 0003500 of M/s Bosch Pharmaceuticals Karachi dated 03-02-2016 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. 5783: 22-02-2021
	Details of fee submitted	PKR 50,000/-: 16-09-2020
	Proposed proprietary name / brand name	MEROLINZ 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	Colourless to white or light yellow crystals or 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 ACS Dobfar SpA 2 Viale Addetta, 2a/12 – 3/5 20067 Tribiano Milano Italy.
	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 IV 1g

		Manufactured by AstraZeneca UK Ltd. Marketing Authorization Holder (s) Pfizer Limited UK.
	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 ACS Dobfar SpA 2 Viale Addetta, 2a/12 – 3/5 20067 Tribiano Milano Italy.		
API Lot No.	33080500616 33080500686 33080500220		
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.	PO17034	PO18036	PO210009
Batch Size	20272 vials	8065 vials	17608 Vials
Manufacturing Date	05-2017	02-2018	10-2020
Date of Initiation	05-06-2017	09-03-2018	29-10-2020
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)	Firm has referred to onsite inspection report of their product "DOVIR Tablet 30mg and 60mg Tablets" which was presented in 288th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 25th January, 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.	Firm has submitted copy of GMP certificate (No. IT-API/125/H/2020) issued by Italian Medicine Agency dated 03-01-2019. The certificate is also verified from EudraGMP database.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**33080500616:** Firm has submitted copy of commercial invoice cleared dated 03-03-2017 specifying import of 84Kg Meropenem trihydrate. The commercial invoice is attested by AD (I&E) DRAP. **33080500686:** Firm has submitted copy of commercial invoice cleared dated 03-03-2017 specifying import of 84Kg Meropenem trihydrate. The commercial invoice is attested by AD (I&E) DRAP. **33080500220** Firm has submitted copy of commercial invoice cleared dated 06-03-2020 specifying import of 102Kg Meropenem trihydrate. 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 certificate of 21 CFR compliance of their HPLC system however the firm has not submitted audit trail reports of 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:

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 drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer.
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. Further justify how analysis of the drug substance was carried out without performing verification studies.	Firm has submitted verification study report for the drug substance.
Justify why the test for contents of sodium is not performed during the stability studies of the drug substance as recommended in USP monograph.	Firm has submitted test reports for the sodium contents of the drug product as per USP monograph at batch release stage.
Submit data in section 3.2.P.2.2.1 as per the guidance document approved by Registration Board which specifies 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 shall be submitted and discussed".	Firm has submitted pharmaceutical equivalence report against Meronem IV 500mg Manufactured by AstraZeneca UK Ltd. Marketing Authorization Holder (s) Pfizer Limited UK.
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".	Firm has submitted results of compatibility studies of the product with the recommended diluent.

Decision: Approved.

- **Firm shall submit applicable fee for revision of the specifications of the drug product before issuance of Registration letter.**

29.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road Lahore**
	Name, address of Manufacturing site.	M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road Lahore

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Last GMP inspection dated 11-01-2019 concluded as "Panel inspected the unit and evaluated documents are connection with production, quality control and quality assurance. After through inspection of the manufacturing facility and evaluation of documents panel concluded that on the day of inspection firm has satisfactory level of GMP compliance, hence panel recommended issuance of GMP certificate to the firm. Some advises were also given in the report to the firm for further up gradations.
	Evidence of approval of manufacturing facility	Firm has submitted copy of renewal of DML letter dated 24-02-2016 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. 26642: 10-12-2019
	Details of fee submitted	PKR 50,000/-: 10-12-2019
	Proposed proprietary name / brand name	DYFLOZIN Tablet 5/100mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ertugliflozin (as L-pyroglutamic acid)……5mg Sitagliptin (as phosphate monohydrate)…100mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	10's, 20's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Steglujan Tablet **(USFDA** Approved)
	For generic drugs (me-too status)	NA
	Name and address of API manufacturer.	**Ertugliflozin:** Shanghai Pharma group Changzhou Kony Pharmaceutical Co. Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105, China **Sitagliptin:** Saakh Pharma Pvt. Ltd. C-7/1, NWIZ, Port Qasim Karachi 75020, 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)	**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 for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 24 months. **Ertugliflozin:** 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 the innovator i.e. Steglujan 5mg/100mg tablet. Firm has also submitted results of comparative dissolution profile against the innovator i.e. Steglujan 5mg/100mg 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	**Ertugliflozin:** Shanghai Pharma group Changzhou Kony Pharmaceutical Co. Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105, China **Sitagliptin:** Saakh Pharma Pvt. Ltd. C-7/1, NWIZ, Port Qasim Karachi 75020, Pakistan		
API Lot No.	UIMRPS19021 18GN30002		
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, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T04	T05	T06
Batch Size	1000 Tablet	1000 Tablet	1000 Tablet
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	13-04-2020	13-04-2020	13-04-2020
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)	Firm has referred to onsite inspection report of their product "Sovir 400mg tablets", which was conducted on 06th February, 2018 and was presented in 279th meeting of Registration Board. Registration Board decided to approve registration of "Sovir tablet**"** by M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road 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. Firm has demonstrated audit trail reports (assay analysis on HPLC) for the submitted stability batches.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin:** Shanghai Pharma group Changzhou Kony Pharmaceutical Co. Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105, China **Sitagliptin:** Firm has submitted copy of GMP certificate issued on 23rd June 2020 by Additional Director DRAP Karachi. The certificate was issued based on inspection dated 18th June 2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Ertugliflozin:** Firm has submitted copy of commercial invoice dated 06-02-2019 specifying import of 80g ertugliflozin along with its working standard and impurity standard. **Sitagliptin:** Firm has submitted copy of invoice dated 24-12-2018 specifying purchase of 10kg sitagliptin from Saakh pharma.
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	Firm has submitted audit trail reports 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:

Shortcomings communicated	Response by the firm
Submit separate information for both drug substances in the submitted Quality Overall Summary (QOS)in section 2.3.S. Furthermore, the submitted QOS is not as per the WHO template or the template approved by Registration Board in its 296th meeting.	Firm has submitted revised QOS as per WHO template in which separate section of each drug substance has been added.
Submit data for sitagliptin 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 sitagliptin drug substance.
Submit data for Ertugliflozin drug substance in section	Firm has submitted report of verification studies of the

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".*	ertugliflozin drug substance.
Submit data of pharmaceutical equivalence and comparative dissolution profile against the innovator product	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the innovator i.e. Steglujan 5mg/100mg tablet. Firm has also submitted results of comparative dissolution profile against the innovator i.e. Steglujan 5mg/100mg tablet.
Submit batch analysis certificate for the stability batches in section 3.2.P.5.4.	Firm has submitted batch analysis certificates of all the stability batches
Submit COA of primary / secondary reference standard of both drug substances used in the testing of drug product including source and lot number shall be provided in section 3.2.P.6.	Firm has submitted COA of working standard for both drug substances.

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.**

30.	Name, address of Applicant / Marketing Authorization Holder	M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road Lahore
	Name, address of Manufacturing site.	M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Last GMP inspection dated 11-01-2019 concluded as "Panel inspected the unit and evaluated documents are connection with production, quality control and quality assurance. After through inspection of the manufacturing facility and evaluation of documents panel concluded that on the day of inspection firm has satisfactory level of GMP compliance, hence panel recommended issuance of GMP certificate to the firm. Some advises were also given in the report to the firm for further up gradations.
	Evidence of approval of manufacturing facility	Firm has submitted copy of renewal of DML letter dated 24-02-2016 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. 26643: 10-12-2019
	Details of fee submitted	PKR 50,000/-: 10-12-2019
	Proposed proprietary name / brand name	**DYFLOZIN Tablet 15/100mg**

	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ertugliflozin (as L-pyroglutamic acid)……15mg Sitagliptin (as phosphate monohydrate)…100mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	10's, 20's, 30's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Steglujan Tablet **(USFDA** Approved)
	For generic drugs (me-too status)	NA
	Name and address of API manufacturer.	**Ertugliflozin:** Shanghai Pharma group Changzhou Kony Pharmaceutical Co. Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105, China **Sitagliptin:** Saakh Pharma Pvt. Ltd. C-7/1, NWIZ, Port Qasim Karachi 75020, 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)	**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 for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 24 months. **Ertugliflozin:** 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 the innovator i.e. Steglujan 15mg/100mg tablet.

		Firm has also submitted results of comparative dissolution profile against the innovator i.e. Steglujan 15mg/100mg 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	**Ertugliflozin:** Shanghai Pharma group Changzhou Kony Pharmaceutical Co. Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105, China **Sitagliptin:** Saakh Pharma Pvt. Ltd. C-7/1, NWIZ, Port Qasim Karachi 75020, Pakistan		
API Lot No.	UIMRPS19021 18GN30002		
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, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T01	T02	T03
Batch Size	1000 Tablet	1000 Tablet	1000 Tablet
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	13-04-2020	13-04-2020	13-04-2020
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)	Firm has referred to onsite inspection report of their product "Sovir 400mg tablets", which was conducted on 06th February, 2018 and was presented in 279th meeting of Registration Board. Registration Board decided to approve registration of "Sovir tablet**"** by M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road 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. Firm has demonstrated audit trail reports (assay analysis on HPLC) for the submitted stability batches.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin:** Shanghai Pharma group Changzhou Kony Pharmaceutical Co. Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105, China **Sitagliptin:** Firm has submitted copy of GMP certificate issued on 23rd June 2020 by Additional Director DRAP Karachi. The certificate was issued based on inspection dated 18th June 2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Ertugliflozin:** Firm has submitted copy of commercial invoice dated 06-02-2019 specifying import of 80g ertugliflozin along with its working standard and impurity standard. **Sitagliptin:** Firm has submitted copy of invoice dated 24-12-2018 specifying purchase of 10kg sitagliptin from Saakh pharma.

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	Firm has submitted audit trail reports 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:

Shortcomings communicated	**Response by the firm**
Submit separate information for both drug substances in the submitted Quality Overall Summary (QOS)in section 2.3.S. Furthermore, the submitted QOS is not as per the WHO template or the template approved by Registration Board in its 296th meeting.	Firm has submitted revised QOS as per WHO template in which separate section of each drug substance has been added.
Submit data for sitagliptin 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 sitagliptin drug substance.
Submit data for Ertugliflozin 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 ertugliflozin drug substance.
Submit data of pharmaceutical equivalence and comparative dissolution profile against the innovator product	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the innovator i.e. Steglujan 5mg/100mg tablet. Firm has also submitted results of comparative dissolution profile against the innovator i.e. Steglujan 5mg/100mg tablet.
Submit batch analysis certificate for the stability batches in section 3.2.P.5.4.	Firm has submitted batch analysis certificates of all the stability batches
Submit COA of primary / secondary reference standard of both drug substances used in the testing of drug product including source and lot number shall be provided in section 3.2.P.6.	Firm has submitted COA of working standard for both drug substances.

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.**

31.	Name, address of Applicant / Marketing Authorization Holder	M/s Nawabsons Laboratories (Pvt) Ltd. Jia Bagga, Off Raiwind Road, Lahore.
	Name, address of Manufacturing site.	M/s Bloom Pharmaceuticals (Pvt) Ltd Plot No. 30, Phase-I and II, Industrial Estate Hattar.
	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 10-07-2020.
	GMP status of the firm	GMP inspection dated 07-04-2018, concluded that overall the firm was operating under good level of cGMP.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of DML dated 11-04-2016 which specifies 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. 10999: 09-04-2021
	Details of fee submitted	PKR 50,000/-: 15-03-2021
	Proposed proprietary name / brand name	CEZIM 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	Off white colored free flowing powder filled in labelled amber colored glass bottle.
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specification	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	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 quality tests for their product against Cefspan dry suspension.
	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.	00244/051/2020		
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.	SS-355	SS-361	SS-369
Batch Size	35000 packs	20000 packs	10000 packs
Manufacturing Date	06-2015	07-2015	08-2015
Date of Initiation	16-06-2015	16-07-2015	18-08-2015
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)	NA
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).	
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	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Evaluation by PEC:

- Submit GMP certificate / GMP inspection report of the contract manufacturer.
- Submit label claim in module 1 as per the reference product along with submission of requisite fee.
- Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.
- Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.
- 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.
- 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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.
- The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.
- The bottle fill weight mentioned in section 3.2.P.1 is 2939mg while the objective weight per capsule mentioned in process validation report is 17.64g. Justification is required in this regard.
- Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.
- The process validation studies have been conducted on three batches having 25000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 10000 and as high as 35000 capsules. Justification is required in this regard.
- USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.
- The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.
- Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.
- Submit data of in-use stability studies of the product after reconstitution with recommended solvent.
- 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, since the submitted GMP certificate is expired.
    - 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)

Decision: Deferred for following:

- **Submit GMP certificate / GMP inspection report of the contract manufacturer.**
- **Submit label claim in module 1 as per the reference product along with submission of requisite fee.**
- **Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.**
- **Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.**
- **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.

- **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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.**
- **The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.**
- **The bottle fill weight mentioned in section 3.2.P.1 is 2939mg while the objective weight per capsule mentioned in process validation report is 17.64g. Justification is required in this regard.**
- **Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.**
- **The process validation studies have been conducted on three batches having 25000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 10000 and as high as 35000 capsules. Justification is required in this regard.**
- **USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.**
- **The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.**
- **Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.**
- **Submit data of in-use stability studies of the product after reconstitution with recommended solvent.**
- **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, since the submitted GMP certificate is expired.**
    - **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)**

32.	Name, address of Applicant / Marketing Authorization Holder	M/s Nawabsons Laboratories (Pvt) Ltd. Jia Bagga, Off Raiwind Road, Lahore.
	Name, address of Manufacturing site.	M/s Bloom Pharmaceuticals (Pvt) Ltd Plot No. 30, Phase-I and II, Industrial Estate Hattar.
	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 10-07-2020.
	GMP status of the firm	GMP inspection dated 07-04-2018, concluded that overall the firm was operating under good level of cGMP.

	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of DML dated 11-04-2016 which specifies 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. 11000: 09-04-2021
	Details of fee submitted	PKR 50,000/-: 15-03-2021
	Proposed proprietary name / brand name	CEZIM 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	Off white colored free flowing powder filled in labelled amber colored glass bottle.
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	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 Cefspan dry suspension.
	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.	00244/051/2020		
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.	SS-356	SS-359	SS-363
Batch Size	31000 packs	26500 packs	10000 packs
Manufacturing Date	06-2015	06-2015	07-2015
Date of Initiation	18-06-2015	19-06-2015	20-07-2015
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)	NA
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).	
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	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Evaluation by PEC:

- Submit GMP certificate / GMP inspection report of the contract manufacturer.
- Submit label claim in module 1 as per the reference product along with submission of requisite fee.
- Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.
- Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.
- 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.

- 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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.
- The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.
- The bottle fill weight mentioned in section 3.2.P.1 is 3061mg while the objective weight per capsule mentioned in process validation report is 18.37g. Justification is required in this regard.
- Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.
- The process validation studies have been conducted on three batches having 15000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 26500 and as high as 31000 capsules. Justification is required in this regard.
- USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.
- The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.
- Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.
- Submit data of in-use stability studies of the product after reconstitution with recommended solvent.
- 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, since the submitted GMP certificate is expired.
    - 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)

Decision: Deferred for following:

- **Submit GMP certificate / GMP inspection report of the contract manufacturer.**
- **Submit label claim in module 1 as per the reference product along with submission of requisite fee.**
- **Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.**
- **Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.**
- **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.**
- **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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.**
- **The reference product recommends that the product should be reconstituted with 34 ml water,**

while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.

- **The bottle fill weight mentioned in section 3.2.P.1 is 3061mg while the objective weight per capsule mentioned in process validation report is 18.37g. Justification is required in this regard.**
- **Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.**
- **The process validation studies have been conducted on three batches having 15000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 26500 and as high as 31000 capsules. Justification is required in this regard.**
- **USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.**
- **The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.**
- **Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.**
- **Submit data of in-use stability studies of the product after reconstitution with recommended solvent.**
- **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, since the submitted GMP certificate is expired.**
    - **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)**

33.	Name, address of Applicant / Marketing Authorization Holder	M/s Dew-Max Pharmaceuticals (Pvt) Ltd Plot No. 6, Street SS-4 Main Industrial Area Rawat Islamabad.
	Name, address of Manufacturing site.	M/s Bloom Pharmaceuticals (Pvt) Ltd Plot No. 30, Phase-I and II, Industrial Estate Hattar.
	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 25-03-2020.
	GMP status of the firm	GMP inspection dated 07-04-2018, concluded that overall the firm was operating under good level of cGMP.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of DML dated 11-04-2016 which specifies 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. 7853: 10-03-2021

	Details of fee submitted	PKR 50,000/-: 11-11-2020
	Proposed proprietary name / brand name	AZDIME 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	Off white colored free flowing powder filled in labelled amber colored glass bottle.
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	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 Cefspan dry suspension.
	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.	00244/051/2020		
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.	SS-355	SS-361	SS-369
Batch Size	35000 packs	20000 packs	10000 packs
Manufacturing Date	06-2015	07-2015	08-2015
Date of Initiation	16-06-2015	16-07-2015	18-08-2015
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)	NA
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).	
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	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Evaluation by PEC:

- Submit GMP certificate / GMP inspection report of the contract manufacturer.
- Submit label claim in module 1 as per the reference product along with submission of requisite fee.
- Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.
- Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.
- 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.
- 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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.
- The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.
- The bottle fill weight mentioned in section 3.2.P.1 is 2939mg while the objective weight per capsule mentioned in process validation report is 17.64g. Justification is required in this regard.

- Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.
- The process validation studies have been conducted on three batches having 25000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 10000 and as high as 35000 capsules. Justification is required in this regard.
- USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.
- The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.
- Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.
- Submit data of in-use stability studies of the product after reconstitution with recommended solvent.
- 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, since the submitted GMP certificate is expired.
    - 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)

Decision: Deferred for following:

- **Submit GMP certificate / GMP inspection report of the contract manufacturer.**
- **Submit label claim in module 1 as per the reference product along with submission of requisite fee.**
- **Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.**
- **Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.**
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- **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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.**
- **The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.**
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- **Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.**
- **The process validation studies have been conducted on three batches having 25000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 10000 and as high as 35000 capsules. Justification is required in this regard.**
- **USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is**

8.775 minutes. Justification is required in this regard.

- **The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.**
- **Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.**
- **Submit data of in-use stability studies of the product after reconstitution with recommended solvent.**
- **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, since the submitted GMP certificate is expired.**
    - **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)**

34.	Name, address of Applicant / Marketing Authorization Holder	M/s Dew-Max Pharmaceuticals (Pvt) Ltd Plot No. 6, Street SS-4 Main Industrial Area Rawat Islamabad.
	Name, address of Manufacturing site.	M/s Bloom Pharmaceuticals (Pvt) Ltd Plot No. 30, Phase-I and II, Industrial Estate Hattar.
	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 25-03-2020.
	GMP status of the firm	GMP inspection dated 07-04-2018, concluded that overall the firm was operating under good level of cGMP.
	Evidence of approval of manufacturing facility	Firm has submitted copy of letter of renewal of DML dated 11-04-2016 which specifies 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. 7852: 10-03-2021
	Details of fee submitted	PKR 50,000/-: 11-11-2020
	Proposed proprietary name / brand name	AZDIME 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	Off white colored free flowing powder filled in labelled amber colored glass bottle.
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	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 Cefspan dry suspension.
	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.	00244/051/2020
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.	SS-356	SS-359	SS-363
Batch Size	31000 packs	26500 packs	10000 packs
Manufacturing Date	06-2015	06-2015	07-2015
Date of Initiation	18-06-2015	19-06-2015	20-07-2015
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)	NA
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).	
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	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Evaluation by PEC:

- Submit GMP certificate / GMP inspection report of the contract manufacturer.
- Submit label claim in module 1 as per the reference product along with submission of requisite fee.
- Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.
- Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.
- 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.
- 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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.
- The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.
- The bottle fill weight mentioned in section 3.2.P.1 is 3061mg while the objective weight per capsule mentioned in process validation report is 18.37g. Justification is required in this regard.
- Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.
- The process validation studies have been conducted on three batches having 15000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 26500 and as high as 31000 capsules. Justification is required in this regard.
- USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.
- The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.

- Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.
- Submit data of in-use stability studies of the product after reconstitution with recommended solvent.
- 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, since the submitted GMP certificate is expired.
    - 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)

Decision: Deferred for following:

- **Submit GMP certificate / GMP inspection report of the contract manufacturer.**
- **Submit label claim in module 1 as per the reference product along with submission of requisite fee.**
- **Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.**
- **Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.**
- **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.**
- **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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.**
- **The reference product recommends that the product should be reconstituted with 34 ml water, while you have specified that 20mL plastic ampoule of WFI will be accompanied with the product. Provide scientific rationale for the variation in the volume of accompanying solvent.**
- **The bottle fill weight mentioned in section 3.2.P.1 is 3061mg while the objective weight per capsule mentioned in process validation report is 18.37g. Justification is required in this regard.**
- **Submit data of compatibility of the drug product along with reconstitution solvent in section 3.2.P.2.6.**
- **The process validation studies have been conducted on three batches having 15000 packs batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 26500 and as high as 31000 capsules. Justification is required in this regard.**
- **USP monograph specifies that Adjust flow rate so that the retention time of cefexime is about 10 min, while the retention time in system suitability study in analytical method verification report is 8.775 minutes. Justification is required in this regard.**
- **The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 80mg, 100mg and 120mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.**
- **Submit stability data summary sheets for all the three batches as per the format approved by Registration Board in its 293rd and 296th meeting, since the submitted data sheets do not contain information like batch size, date of initiation of stability studies, and API lot number used in the manufacturing of the particular batch of drug product.**
- **Submit data of in-use stability studies of the product after reconstitution with recommended solvent.**

• **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:** o **Reference of previous approval of applications with stability study data of the firm (if any)** o **Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin, since the submitted GMP certificate is expired.** o **Documents for the procurement of API with approval from DRAP (in case of import).** o **Compliance Record of HPLC software 21CFR & audit trail reports on product testing** o **Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)**		
35.	Name, address of Applicant / Marketing Authorization Holder	M/s Dew-Max Pharmaceuticals (Pvt) Ltd Plot No. 6, Street SS-4 Main Industrial Area Rawat Islamabad.
	Name, address of Manufacturing site.	M/s Bloom Pharmaceuticals (Pvt) Ltd Plot No. 30, Phase-I and II, Industrial Estate Hattar.
	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 25-03-2020.
	GMP status of the firm	GMP inspection dated 07-04-2018, concluded that overall the firm was operating under good level of cGMP.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 11-04-2016 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. 13154: 06-05-2021
	Details of fee submitted	PKR 50,000/-: 11-11-2020
	Proposed proprietary name / brand name	AZDIME 400mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule Contains: Cefixime as trihydrate……400mg
	Pharmaceutical form of applied drug	Off white powder filled in Red/Red hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	JP
	Proposed Pack size	5's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Cefixime 400mg capsule **(MHRA** Approved)
	For generic drugs (me-too status)	Cefim Capsule 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 Cefspan 400mg Capsule. Firm has submitted results of CDP for their product against Cefspan 400mg 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.	00244/051/2020		
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.	427	455	565
Batch Size	35000 capsule	51745 capsule	50000 capsule
Manufacturing Date	06-2015	06-2015	11-2015
Date of Initiation	26-06-2015	27-06-2015	23-11-2015
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)	NA

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

Evaluation by PEC:

- Submit GMP certificate / GMP inspection report of the contract manufacturer.
- 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 / attachments.
- Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.
- Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.
- 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.
- 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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.
- Submit results of pharmaceutical equivalence of the developed formulation against the innovator / reference product in section 3.2.P.2.2.1, since the results of only comparative dissolution profile has been submitted against the said section.
- The capsule fill weight mentioned in section 3.2.P.1 is 482mg while the objective weight per capsule mentioned in process validation report is 585mg.
- The process validation studies have been conducted on three batches having 25000 capsule batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 35000 and as high as 50000 capsules. Justification is required in this regard.
- Justify the dissolution specifications of NLT 80% in 90 minutes, since the JP monograph specifies this limit only for 100mg potency capsule.
- The USFDA review of innovator product of cefixime 400mg capsule reveals that the acceptance criteria for dissolution test should be NLT (Q) in 45 minutes using 7.2pH phosphate buffer. Justify the results of comparative dissolution profile at 6.8 pH phosphate buffer in which the drug release of both test as well as comparator product was less than 70% in 45 minutes.
- The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 320mg, 400mg and 480mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.
- Precision studies are conducted on the target concentration of the sample solution or standard solution preparation as per the method specified in assay. As per your submitted method, the concentration of both standard as well as sample solution is 0.088mg/ml while as per the precision studies the analysis is carried out at 2mg/ml concentration which is many times higher than the concentration specified in the assay method. Justification is required in this regard.

- 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, since the submitted GMP certificate is expired.
    - 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
- You have submitted manual record of data logger for temperature and humidity monitoring. The submitted record shows that only 1 temperature and humidity reading was recorded on daily basis and there was no reading recorded on weekends and off days. Justify how it could be considered that no deviation in temperature and humidity occurred during off days and also throughout the day on working days.

Decision: Deferred for following:

- **Submit GMP certificate / GMP inspection report of the contract manufacturer.**
- **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 / attachments.**
- **Submit data in section 1.6.5 of Module 1, since information against this section is not submitted.**
- **Submit correct site address of the drug substance manufacturer in section 3.2.S.2 of module 3, since the submitted details are of office address.**
- **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.**
- **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 three batches of API are of 2013 while the drug product batches were manufactured in 2015.**
- **Submit results of pharmaceutical equivalence of the developed formulation against the innovator / reference product in section 3.2.P.2.2.1, since the results of only comparative dissolution profile has been submitted against the said section.**
- **The capsule fill weight mentioned in section 3.2.P.1 is 482mg while the objective weight per capsule mentioned in process validation report is 585mg.**
- **The process validation studies have been conducted on three batches having 25000 capsule batch size. While the batch size of the commercial batches for which stability study data is submitted, ranges from as low as 35000 and as high as 50000 capsules. Justification is required in this regard.**
- **Justify the dissolution specifications of NLT 80% in 90 minutes, since the JP monograph specifies this limit only for 100mg potency capsule.**
- **The USFDA review of innovator product of cefixime 400mg capsule reveals that the acceptance criteria for dissolution test should be NLT (Q) in 45 minutes using 7.2pH phosphate buffer. Justify the results of comparative dissolution profile at 6.8 pH phosphate buffer in which the drug release of both test as well as comparator product was less than 70% in 45 minutes.**
- **The accuracy and recovery studies in analytical assay method verification are conducted at three known concentrations i.e. 80%, 100% and 120% of the concentration of sample or standard solution. As per your submitted results you have added 320mg, 400mg and 480mg without specifying the exact concentration as specified in the initial background of the study on which the analysis was made.**
- **Precision studies are conducted on the target concentration of the sample solution or standard solution preparation as per the method specified in assay. As per your submitted method, the concentration of both standard as well as sample solution is 0.088mg/ml while as per the precision studies the analysis is carried out at 2mg/ml concentration which is many times higher than the concentration specified in the assay method. Justification is required in this regard.**

- **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, since the submitted GMP certificate is expired.**
  - **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**
- **You have submitted manual record of data logger for temperature and humidity monitoring. The submitted record shows that only 1 temperature and humidity reading was recorded on daily basis and there was no reading recorded on weekends and off days. Justify how it could be considered that no deviation in temperature and humidity occurred during off days and also throughout the day on working days.**

36.	Name, address of Applicant / Marketing Authorization Holder	M/s Bio-Next Pharmaceuticals Plot No. 50, St No. S-10, RCCI Industrial Estate 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)
	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. 7850: 10-03-2021
	Details of fee submitted	PKR 20,000/-: 05-01-2021
	Proposed proprietary name / brand name	NEXIDORE 500mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Doripenem Monohydrate Eq. to Doripenem…500mg
	Pharmaceutical form of applied drug	Glass vial filled with white to slightly yellowish, off white crystalline powder.
	Pharmacotherapeutic Group of (API)	Carbapenem
	Reference to Finished product specifications	~~In house~~
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Finibax Intravenous Infusion 0.5g (PMDA Japan Approved)
	For generic drugs (me-too status)	Dorinem Injection 500mg by ICI Pakistan Ltd.
	Name and address of API manufacturer.	KOPRAN RESEARCH LABORATORIES LIMITED K4/4, Additional MIDC, At & Post Birwadi, Taluka Mahad, District Raigad - 402 302 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, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, 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 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 for their product against the comparator i.e. Dorinem 500mg injection of ICI Pakistan Ltd Batch No. 0E458 Mfg date 05-2020.
	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	KOPRAN RESEARCH LABORATORIES LIMITED K4/4, Additional MIDC, At & Post Birwadi, Taluka Mahad, District Raigad - 402 302 Maharashtra, INDIA		
API Lot No.	DIPV/B2002002, DPIV/P2001003, DPIV/P2001004		
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.	DN-004	DN-005	DN-006
Batch Size	1200 vials	350 vials	350 vials
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	27-04-2020	27-04-2020	27-04-2020

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)	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. KD/89275/2020/11/33788) issued by FDA Mahrashtra dated 20-10-2020. The certificate is valid till 19-10-2023.
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 Doripenem 3Kg from M/s Kopran Research Laboratories Limited K4/4, Additional MIDC, At & Post Birwadi, Taluka Mahad, District Raigad - 402 302 Maharashtra, INDIA issued by AD (I&E) DRAP field office. The license was issued on 08-04-2020. • Firm has submitted copy of commercial invoice cleared dated 08-04-2020 specifying import of 3Kg doripenem Batch No. DIPV/B2002002, DPIV/P2001003, DPIV/P2001004.
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 partial 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:

Shortcomings communicated	**Response by the firm**
Submit evidence of approval of applied formulation in reference regulatory authorities in section 1.5.9, since the submitted reference is of Doribex Injection of Janssen cilag international N.V Belgium is currently withdrawn by EMA.	Firm has submitted evidence of approval in PMDA Japan Finibax Intravenous Infusion 0.5g **(PMDA Japan** Approved)
Justify the finished product specifications as "Inhouse specifications" since the drug product monograph is available in Japanese Pharmacopoeia. Revise your specifications along with submission of requisite fee.	Firm has revised the specification as per JP monograph and also submitted fee PKR 7500 for change in specifications. The revised method is still different from JP monograph in following terms • Test of purity as recommended by JP monograph is not added by the firm • Mobile phase A and B is used by the firm with run time upto 55 minutes while JP monograph recommends only one typ of mobile phase. • Flow rate set by the firm is 1ml/minute while JP monograph recommends "Adjust so that the retention time of doripenem is about 15 minutes" • System suitability requirements are not provided in the specifications of the firm while it is mentioned in JP monograph. During evaluation of already submitted data by the

	firm it was identified that firm has used 5 standard chromatograms while JP recommends 6 standards further the JP recommends that theoretical plates should be less than 5000 while the theoretical plates in the submitted data is way above 5000. Further JP monograph recommends a retention time of 15 minutes, while the retention time in firm's data was around 10 minutes.
Justify the use of drug substance having in house specifications while the drug substance specifications are present in JP monograph for "Doripenem hydrate"	Firm has revised the specification as per JP monograph The revised method is still different from JP monograph in following terms • Test of purity as recommended by JP monograph is not added by the firm • Mobile phase A and B is used by the firm with run time upto 55 minutes while JP monograph recommends only one typ of mobile phase. • Flow rate set by the firm is 1ml/minute while JP monograph recommends "Adjust so that the retention time of doripenem is about 15 minutes" • System suitability requirements are not provided in the specifications of the firm while it is mentioned in JP monograph. During evaluation of already submitted data by the firm it was identified that firm has used 5 standard chromatograms while JP recommends 6 standards further the JP recommends that theoretical plates should be less than 5000 while the theoretical plates in the submitted data is way above 5000. Further JP monograph recommends a retention time of 15 minutes, while the retention time in firm's data was around 10 minutes. Further. the analytical method of the drug substance manufacturer is different from JP monograph in terms of HPLC column specifications, column temperature, mobile phase, UV detector wavelength, flow rate, standard preparation method and final concentration of standard solution, sample preparation method and final concentration of sample solution, system suitability requirements and acceptance criteria and the formula for calculation of results of assay.
Justify the limit of water from 4.0 – 5.5% in drug substance specifications, while JP monograph specifies the limit from 4.0 – 5.0%.	Firm has submitted revised specifications in which limit of water has been changed as per JP monograph. The drug substance specifications still contain the limit of 4 – 5.5%.
Justify why the test for residue on ignition is not performed for the drug substance since it is recommended in JP monograph.	Firm has submitted revised specifications in which residue of ignition has been added as per JP monograph. The drug substance specifications still does not contain this test.
Justify the use of a different analytical method for assay testing of drug substance from that specified in JP monograph. The method of drug substance manufacturer is different in terms of HPLC column specifications, column temperature, mobile phase, UV detector wavelength, flow rate, standard preparation method and final concentration of standard solution, sample preparation method and	Firm has submitted that they have analysed the drug substance by using the method of analysis of drug substance manufacturer at the time of development that's why the testing conditions differ from JP monograph. Now, the firm has revised the drug substance specifications as per JP monograph but the revised specifications are not exactly as per JP monograph.

<table>
<tr><td>final concentration of sample solution, system suitability requirements and acceptance criteria and the formula for calculation of results of assay.</td><td></td></tr>
<tr><td>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 noncompendial 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.</td><td>Firm has submitted that the testing method of drug substance and drug product is same therefore we performed validation studies on drug product and considered it validated for drug substance as well.
However, the validation studies are performed on analytical method which is entirely different from that specified in JP monograph in terms of HPLC column specifications, column temperature, mobile phase, UV detector wavelength, flow rate, standard preparation method and final concentration of standard solution, sample preparation method and final concentration of sample solution, system suitability requirements and acceptance criteria and the formula for calculation of results of assay.</td></tr>
<tr><td>Justify how the applied drug is to be supplied with 10ml of sodium chloride 0.9% solution, since the innovator product recommends different volume for reconstitution.</td><td>Firm has submitted that 10ml of normal saline solution is for primary reconstitution which will be further diluted as per requirement.
The details of the innovator / reference product is as follows:
<table>
<tr><td>Particulars</td><td>PMDA</td><td>FDA</td></tr>
<tr><td>Date of initial approval</td><td>25-07-2005</td><td>12-10-2007</td></tr>
<tr><td>Brand name</td><td>Finibax</td><td>Doribax</td></tr>
<tr><td>Current status</td><td>Marketed</td><td>Discontinued</td></tr>
<tr><td>Reconstitution</td><td>contents of 1 bottle and 1 kit dissolved in 100 mL of physiological saline.</td><td>Constitute the 500 mg vial with 10 mL of sterile water for injection or 0.9% sodium chloride injection</td></tr>
</table>
DORIBAX® does not contain a bacteriostatic preservative. Aseptic technique must be followed in preparation of the infusion solution</td></tr>
<tr><td>The process validation protocols does not contain any steps to ensure the sterilization of vials and rubber stopper is adequately performed, further the time and temperature of sterilization cycle is also not validated. Justification is required in this regard.</td><td>Firm has now submitted revised process validation protocols in which vial washing and sterilization time as well as dry heat sterilization time and temperature is mentioned.
However, the firm has directly selected the sterilization temperature and time without providing any protocol how to reach to the final selection of sterilization time and temperature.</td></tr>
<tr><td>Justify the drug product specifications section (3.2.P.5.1) with water contents from 4.0% to 5.5% while the JP monograph for the drug product specifies water contents to be 4.0 to 5.0%.</td><td>Firm has submitted revised sections as per JP monograph</td></tr>
<tr><td>Justify the limit of assay from 90 – 120% since the JP monograph specifies the assay limit from 95 – 105%.</td><td>Firm has submitted revised sections as per JP monograph</td></tr>
<tr><td>Justify the use of a different analytical method for assay testing of drug product from that specified in JP monograph. The analytical method of drug product is different in terms of HPLC column specifications, column temperature, mobile phase,</td><td>Firm has submitted that they have analysed the drug substance by using the method of analysis of drug substance manufacturer at the time of development that’s why the testing conditions differ from JP monograph.</td></tr>
</table>

<table>
<tr><td>UV detector wavelength, flow rate, total run time and retention time, standard preparation method and final concentration of standard solution, sample preparation method and final concentration of sample solution, system suitability requirements and acceptance criteria and the formula for calculation of results of assay.</td><td>Now the firm has revised the drug substance specifications as per JP monograph but the revised specifications are not exactly as per JP monograph.</td></tr>
<tr><td>Justify why the test of specificity is not performed during the validation studies of the analytical method of drug product.</td><td>Nexidore injection is ready to fill product. It does not contain any inactive ingredient so there would not be any need of test of specificity during the validation studies.</td></tr>
<tr><td>Justify why the test of water contents and uniformity of dosage units is not performed in the batch analysis stage.</td><td>Firm has submitted that both tests have been performed now</td></tr>
<tr><td>Justify the release of drug product batches on 27-04-2020 after performing test of sterility, since the drug substance was released after testing on 24-04-2020. Justify how the three batches were manufactured and stability studies were being performed within 3 days only.</td><td>Firm has not submitted any justification.

Firm has only submitted sterility test reports but no justification is provided.</td></tr>
<tr><td>Justify the use of 25ml type-II glass vial for the applied drug product since as per your submission the drug product is to be reconstituted in 10ml normal saline.</td><td>It was a typo error the actual vials are 15 ml type I glass vial.</td></tr>
<tr><td>Justify the date of initiation of stability studies of 25-4-2020, since batches were released on 27-4-2020.</td><td>It was a typo error the actual date of placement in chamber was 27-04-2020.</td></tr>
<tr><td>You have submitted that all stability batches were manufactured using the drug substance batch No. DPIV/P2001003. For manufacturing of 3 batches each having batch size 1200 vials, approximately 1.87Kg drug substance is required, while as per the clearance documents and commercial invoice 1Kg drug substance of batch number DPIV/P2001003 was imported. Justify how three batches were manufactured using the drug substance having batch number DPIV/P2001003.</td><td>Firm has submitted that we used 3 different lots of API for manufacturing of 3 batches. It was typo error at time of dossier submission. Firm has submitted revised stability data sheets for all batches.
The newly submitted data sheets are different from previously submitted data sheets in following aspects.
<table>
<tr><th>Particulars</th><th>Previously submitted</th><th>Newly submitted</th></tr>
<tr><td colspan="3">Batch No DN-004</td></tr>
<tr><td>0 month date</td><td>25.04.2020</td><td>27.04.2020</td></tr>
<tr><td>3rd month date</td><td>25.07.2020</td><td>28.07.2020</td></tr>
<tr><td>6th month date</td><td>26.10.2020</td><td>27.10.2020</td></tr>
<tr><td>API lot #</td><td>DPIV/P2001003</td><td>DPIV/B2002002</td></tr>
<tr><td colspan="3">Batch No DN-005</td></tr>
<tr><td>0 month date</td><td>25.04.2020</td><td>27.04.2020</td></tr>
<tr><td>3rd month date</td><td>25.07.2020</td><td>28.07.2020</td></tr>
<tr><td>6th month date</td><td>26.10.2020</td><td>27.10.2020</td></tr>
<tr><td>API lot #</td><td>DPIV/P2001003</td><td>DPIV/P2001003</td></tr>
<tr><td colspan="3">Batch No DN-006</td></tr>
<tr><td>0 month date</td><td>25.04.2020</td><td>27.04.2020</td></tr>
<tr><td>3rd month date</td><td>25.07.2020</td><td>28.07.2020</td></tr>
<tr><td>6th month date</td><td>26.10.2020</td><td>27.10.2020</td></tr>
<tr><td>API lot #</td><td>DPIV/P2001003</td><td>DPIV/P2001004</td></tr>
</table>

Firm has also changed the date of testing of 3rd and 6 months as well.
The sterility test and particulate matter was not performed at 3rd or 6th month time point during initially submitted data, however in the newly submitted data sheets the results of both of these tests are also mentioned in the data sheets at 3rd as well as
</td></tr>
</table>

	6th month time point.
Justify why sterility testing was not performed for the drug product at the end of accelerated stability study.	Firm has submitted that we have already submitted complete accelerated stability data for 6 months however again we are attaching for your review. *The sterility test and particulate matter was not performed at 3rd or 6th month time point during initially submitted data, however in the newly submitted data sheets the results of both of these tests are also mentioned in the data sheets at 3rd as well as 6th month time point.*
Submit compliance record of HPLC software 21CFR & audit trail reports on product testing for each analysis performed during the study.	Firm has submitted that it was submitted along with the dossier. *However, complete audit trail report is not submitted, partial report of testing of only 24-4-2020 and 27-4-2020 is submitted.*
Justify how three batches were manufactured on 24-04-2020 in which the sterilization of vials for all the batches was performed collectively on 23-04-2020. Justify how having a single step of sterilization of vials for 3 batches can satisfy the definition of a batch.	Firm has submitted that three stability batches were manufactured on 24-04-2020 with sterilized vials. Vials are sterilized separately for each batch as these was loaded in sterilizer within a separate box, which are labelled for each batch. *Firm has not submitted any scientific justification for carrying out sterilization of vials collectively for all the three batches.*
The submitted BMR's does not contain any step after the filling of vials justify how the batches were released after the filling of vials including details of physical, analytical and microbiological tests.	After filling, reconciliation was done for batch consumption rejection and yields in BMRs while analytical and microbiological reports were separately prepared and incorporated in stability files.
As per the submitted BMR's 624g of drug substance was filled in each batch while the import documents specify that 3 containers each having 1Kg drug substance was imported. Justify how three batches were manufactured.	Stability batches were manufactured with 650gm of powder from each of 3 containers. The details of API use in each batch is as follows: **DN-004:** DPIV/B2002002 **DN-005:** DPIV/P2001003 **DN-006:** DPIV/P2001004

Decision: Deferred for following submissions:

- **Scientific justification for having drug product specification which is significantly different in terms of test of purity, mobile phase, flow rate / retention time, system suitability requirements, number of injections of the standard solution and theoretical plates from that specified in JP monograph.**
- **Scientific justification for the analysis of the drug product throughout the stability studies with theoretical plates above 5000, while JP monograph recommends that theoretical plates should be less than 5000.**
- **Scientific justification for using drug substance having in-house specifications (having completely different analytical method from that recommended in JP monograph) to develop a drug product complying JP pharmacopeia.**
- **Scientific justification for having limit of water contents from 4.0 – 5.0% while the water contents specified in the drug substance specifications is 4.0 – 5.5%.**
- **Scientific justification for using a drug substance without any test of residue on ignition, while the same test is recommended in the drug product.**
- **Justify the performance of verification studies of the drug substance using an analytical procedure which is entirely different from that specified in JP monograph.**
- **Justify the use of 10ml of 0.9% sodium chloride as diluent, since both USFDA as well as PMDA approved reference products recommends different diluent.**
- **Justify process validation protocls without defining procedure for validation of sterilization cycle.**

- **Justify analytical method verification studies of drug product without performing test of specificity.**
- **Justify the release of drug product batches on 27-04-2020 after performing test of sterility, since the drug substance was released after testing on 24-04-2020. Justify how the three batches were manufactured and stability studies were being performed within 3 days only.**
- **Justification for re-submission of stability data sheets having different dates for testing at 0, 3rd and 6th month time point and test of sterility and particulate matter for all the batches from that specified in initially submitted stability data sheet.**
- **Submission of complete audit trail report for all tests performed throughout the stability studies.**
- **Scientific justification for carrying out sterilization of vials collectively for all the three batches.**

g. Deferred cases

37.	Name, address of Applicant / Marketing Authorization Holder	Biogen Pharmaceuticals 8 km, Chakbeli road Rawat Rawalpindi
	Name, address of Manufacturing site.	Biogen Pharmaceuticals 8 km, Chakbeli road Rawat Rawalpindi
	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 19289 dated 09-07-2021
	Details of fee submitted	PKR 20,000/-: dated 13/01/2021
	Proposed proprietary name / brand name	BIOSUC Injection 100 mg/5ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 ml contain 100 mg iron sucrose
	Pharmaceutical form of applied drug	Dark brown color solution filled in amber glass ampoules
	Pharmacotherapeutic Group of (API)	Iron deficiency anemia
	Reference to Finished product specifications	B.P Specification
	Proposed Pack size	5×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Venofer 20 mg iron /mL Vifor France 100-101 Terrasse Boieldieu Tour Franklin La Défense 8 92042 Paris La Défense Cedex France
	For generic drugs (me-too status)	Global pharma G-FER injection 100 mg/5 ml
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	CHEMIWORLD (PVT) LTD. Address: PLOT # 97- J HAYATABAD INDUSTRIAL ESTATE PESHAWAR PAKISTAN
	Module-II (Quality Overall Summary)	Firm has submitted QOS. 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. However, required characterization is not submitted.
	Module III (Drug Substance)	Official monograph of Iron Sucrose is present in BP Specification. 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 However, firm has not submitted process validation from manufacturer of drug substance.
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 06 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (JISO1 MFD2011-009, JISO2 MFD2011-009. JISO3 MFD2011-009
	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. However, firm did not perform osmolarity test.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader G-FER INJECTION that is 100 MG/5ML by Global Pharma by performing quality tests (Identification, Assay, pH, Uniformity of dosage form). .
	Analytical method validation/verification of product	Validation is performed instead of verification of analytical procedures.

STABILITY STUDY DATA

Manufacturer of API	CHEMIWORLD (PVT) LTD. Address: PLOT # 97- J HAYATABAD INDUSTRIAL ESTATE PESHAWAR PAKISTAN		
API Lot No.	B20-ISC-008		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (5×5'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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-58	T-59	T-60
Batch Size	500 Amps	500 Amps	500 Amps
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	01--12-2020	01--12-2020	01--12-2020
No. of Batches	03		

Administrative Portion

Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	CHEMIWORLD (PVT) LTD. Address: PLOT # 97- J HAYATABAD INDUSTRIAL ESTATE PESHAWAR
Documents for the procurement of API with approval from DRAP (in case of import).	• NA
Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not provided.
Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not provided.

Remarks of Evaluator: Firm did not establish Iron core characterizations including but not limited to core size determination, iron oxide crystalline structure and iron environment, Composition of carbohydrate shell and surface properties, Particle morphology and Labile iron determination under physiologically relevant conditions. Furthermore, drug product specification did not include Osmolarity tests. Monograph is available in USP.
Absence of low molecular weight Fe (II) and Fe (III) complexes was not performed for Iron sucrose solution for injection.

Decision of 312nd meeting of Registration Board:
Deferred for following submissions:
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.
Documents for the procurement of API.
Characterization studies of the drug substance performed by drug substance manufacturer.
Drug substance specifications and analytical method from both drug substance and drug product manufacturer.
Drug product specifications and analytical method in the light on BP monograph.
Evidence of relevant analytical equipment required for carrying out all the tests as recommended in BP monograph.

Response by the firm:

Reason for deferment	**Response by the firm**
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of letter of secretary CLB to M/s Chemiworld Pvt Lt. dated 18-02-2020 for grant of additional API i.e. Iron Sucrose Complex.
Documents for the procurement of API.	Firm has submitted copy of invoice dated 03-03-2020 specifying purchase of 2Kg iron sucrose complex from Chemiworld Pvt Ltd. Peshawar.
Characterization studies of the drug substance performed by drug substance manufacturer.	Firm has submitted characterization and structure elucidation studies of the drug substance performed by drug substance manufacturer including studies of IR spectroscopy, UV and proton NMR
Drug substance specifications and analytical method from both drug substance and drug product manufacturer. Drug product specifications and analytical method in the light on BP monograph.	Firm has submitted copy of specifications and analytical method of drug substance and drug product specifications as per BP monograph.
Evidence of relevant analytical equipment required for carrying out all the tests as recommended in BP monograph.	Firm has submitted copy of invoice of Techno Lines Services Pvt Ltd dated 26-02-2020 specifying Schimadzu HPLC system along with SPD-10A Detector and RID-10A detector.

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 pharmaceutical equivalence of their product against the innovator before issuance of Registration letter.**	
38.	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.
	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. 7331: 05-03-2021
	Details of fee submitted	PKR 50,000/-: 03-03-2021
	Proposed proprietary name / brand name	INBRO DPI Capsule 27.5mcg+15.6mcg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Indacaterol (as maleate).……27.5mcg Glycopyrronium (as bromide)……15.6mcg Each delivered dose contains: Indacterol (as maleate).……20.8mcg Glycopyrronium (as bromide)……12.8mcg
	Pharmaceutical form of applied drug	Transparent cap and body, Hypromellose capsule size No. 3 containing white to off white powder
	Pharmacotherapeutic Group of (API)	LABAs and anticholinergic agent
	Reference to Finished product specifications	In house
	Proposed Pack size	30's
	Proposed unit price	As per DPC
	status in reference regulatory authorities	Could not be verified (Discontinued in FDA)
	For generic drugs (me-too status)	NA
	Name and address of API manufacturer.	Indacaterol: Harman Finochem Limited, Plot No A-100, A-100/1, A-100/2 & D-1, M.I.D.C Industrial Area, Shendra, Aurangabad Mahrashtra, India. Glycopyrronium: Harman Finochem Limited, Plot No E7, E8 & E9, M.I.D.C Industrial Area, Chikalthana, Aurangabad Mahrashtra, 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: 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. Glycopyrronium: 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.
	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 Utibron Neohaler 27.5mcg/15.6mcg DPI capsule (Batch No SPT48) Sunovion Pharmaceuticals Inc. Firm has also submitted results of invitro comparative delivered dose uniformity and aerodynamic particle size distribution for their product against the Utibron Neohaler 27.5mcg/15.6mcg DPI capsule Sunovion Pharmaceuticals Inc.
	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: Harman Finochem Limited, Plot No A-100, A-100/1, A-100/2 & D-1, M.I.D.C Industrial Area, Shendra, Aurangabad Mahrashtra, India. Glycopyrronium: Harman Finochem Limited, Plot No E7, E8 & E9, M.I.D.C Industrial Area, Chikalthana, Aurangabad Mahrashtra, India.
API Lot No.	Indacaterol: ICM/A-255/1920061 Glycopyrronium: QCP/013/2018-2019/A
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-921-L	NPD-C-922-P	NPD-C-923-P
Batch Size	6000 capsule	6000 capsule	6000 capsule
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	20-01-2020	20-01-2020	20-01-2020
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)	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: Firm has submitted copy of GMP certificate (No. 82221/2019/11/29136) dated 09-08-2019 issued by FDA Mahrashtra. The certificate is valid till 07-08-2022. Glycopyrronium: Firm has submitted copy of GMP certificate (No.AD/82606/2020/11/31613) of Harman Finochem Limited, Plot No E7, E8 & E9, M.I.D.C Industrial Area, Chikalthana, Aurangabad Mahrashtra, India issued by FDA Maharashtra. The certificate is valid till 13-04-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Indacaterol ICM/A-255/1920061: Firm has submitted copy of commercial invoice cleared dated 13-11-2019 specifying import of 20g Indacaterol maleate (Batch No. ICM/A-255/1920061, ICM/A-255/1920065). The commercial invoice is attested by AD (I&E) DRAP field office. Glycopyrronium: QCP/013/2018-2019/A: Firm has submitted copy of commercial invoice cleared dated 19-08-2019 specifying import of 0.015Kg Glycopyrronium. 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
Submit evidence of approval of applied formulation in reference regulatory authorities which were adapted by Registration Board in its 275th meeting in	Firm has again submitted the same reference of Utibron. However, the product is discontinued in FDA and the reason for discontinuation is not

section 1.5.9, since the submitted reference i.e. Ultibro breezhaler does not exist in USFDA, moreover the only available similar product in USFDA (Ultibron) is discontinued in USFDA.	mentioned on FDA website.
Justify the master formulation without using magnesium stearate as an excipient contrary to the reference product.	Indacaterol + Glycopyronium DPI Capsule was manufactured without the excipient Magnesium Stearate, a lubricant used to avoid sticking. As trials were performed with Lactose (DPI grade) without observing any such issue concerned with sticking and desired weight achieved satisfactorily and repeatedly along with all other quality parameters, thus manufacturer opted to exclude magnesium stearate from the formulation. Furthermore, Aerodynamic Particle Size Distribution (APSD) and Delivered Dose Uniformity (DDU) were performed which were also found within satisfactory limits, i.e., comparable to the innovator and thus pharmaceutical equivalence was established.
The target emitted dose of glycopyrronium mentioned in the raw data sheets for calculation of results of uniformity of delivered dose is 12.5mcg while the label claim for delivered dose specifies 12.8mcg. Clarification is required in this regard.	According to data of Innovator (Utibron 27.5/15.6 mcg capsule) and in Rx list, inhaler delivered a dose of 20.8mcg of indacaterol and 12.8 mcg glycopyrrolate for the 27.5/15.6 mcg strength. However, for Glycopyronium, it delivered 20.8mcg of indacaterol and 12.5mcg Glycopyronium for the strength of 27.5/15.6 mcg. As Martin Dow used Glycopyronium bromide, hence the delivered dose is 12.5mcg for Inbro DPI Capsules.
Specify the device along with its specifications which was used to test uniformity of delivered dose and aerodynamic particle size distribution.	Model No. BDD07 Capsule size # 3 Manufacturer: Shanghai Huarui Aerosol Co.,Ltd Shelf life: 3 years
Justify how the batches were released without testing uniformity of delivered dose and particle size distribution. Justify why the test of uniformity of delivered dose and particle size distribution is not performed at initial stability study time point.	For DPI FPP, Martin Dow prefers to conduct Delivered Dose Uniformity (DDU) and Aerodynamic Particle Size distribution (APSD) at release time point. However, in the case of Inbro Dry Powder for Inhalation capsules, the batches were released on the basis as all other physicochemical test attributes were found well within predefined limits and based on pharmaceutical development process including starting material selection, formulation, manufacturing process and container closer system. The DDU and APSD studies not performed. at release time point as the required DPI testing device (Copley Andresen Cascade Impactor with pre-separator) under shipment and after receiving and successful qualification had performed the finished product batches were tested at later and results comply with shelf-life specification.
Justify how the stability batches were manufactured even before the grant of additional section. Justify where the manufacturing of these batches was carried out.	We hereby inform the Authority that we have an approved Research & Development Laboratory (approval letter attached dated: 4th December 2018) which is non-specific for dosage forms. All the DPI Capsules applied for registration were developed in the abovementioned approved Research & Development laboratory with qualified equipment. Moreover, the Dry Powder Inhaler Capsule section was approved on the basis of a satisfactory panel

	inspection in which all of the requirements for manufacturing and testing of DPI capsules were identified and found complied.
Submit GMP certificate of Harman Finochem Limited, Plot No A-100, A-100/1, A-100/2 & D-1, M.I.D.C Industrial Area, Shendra, Aurangabad Mahrashtra, India which is the manufacturer of Indacaterol.	Firm has submitted copy of GMP certificate (No. 82221/2019/11/29136) dated 09-08-2019 issued by FDA Mahrashtra. Certificate is valid till 7-8-2022.
The stability study summary sheets specify that Batch number ICM/A-255/1920061 of indacaterol maleate was used for the manufacturing of all stability batches. The commercial invoice specifies that 20gm indacaterol Batch No. ICM/A-255/1920061 and ICM/A-255/1920065 is imported. Clarify the exact quantity of Batch number ICM/A-255/1920061 of indacaterol maleate which was imported.	Following two batches of Indacaterol Maleate were imported: Imported API batch No.: ICMA/A-255/1920061 = 15gm ICMA/A-255/1920065 = 5gm
The stability study summary sheets specify that Batch number QCP/013/20 of Glycopyronium bromide was used for the manufacturing of all stability batches. The commercial invoice specifies that 0.015Kg of Batch number GCP/013/2018-2019/A is imported. Clarify the exact batch which was imported and used in the manufacturing of stability batches.	The batch no. QCP/013/20 mentioned in the stability summary sheet is a typographical error. The actual batch of Glycopyronium imported is batch no. GCP/013/2018-2019/A which can be verified from the Commercial invoice and COA of the API

Decision of 307th meeting of Registration Board:
Deferred for evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.

Response by the firm:
We wish to bring into the knowledge of this authority that FDA defines those products as "Discontinued" that have been discontinued but approval of the NDA has not been withdrawn under § 314.150 or section 505(e) of the FD&C Act, and therefore new ANDAs must still refer the Discontinued reference product as the basis for their ANDA submission as per § 314.122(c). Moreover, FDA continues to list any discontinued drug product under "Discontinued" Drugs in FDA's "Approved Drug Products With Therapeutic Equivalence Evaluations" (the "Orange Book"), unless FDA determines that the drug product was withdrawn from sale for reasons of safety or effectiveness, in which case the drug product will be removed from the Orange Book. In addition to this, section 506C of the FD&C Act requires sole manufacturers to report to FDA discontinuances of drug products that are "life-supporting, life-sustaining, or intended for use in the prevention of a debilitating disease or condition."
In light of the above, we wish to inform the authority that the FDA approval for Utibron Neohaler (27.5mcg + 15.6mcg) manufactured by N-*ovartis is still valid and it has not been withdrawn due to any safety or efficacy reasons, however, it has only been discontinued as per the discretion of License holder and it is allowed by FDA to do so. No adverse events/complaints/user issues related to this product have been reported on the FDA website. Please find attached the screenshot from the Orange book on FDA website showing the Utibron Neohaler 27.5mcg and 15.6mcg is still present in the approved products list. Furthermore, the current status of this product strength can also be confirmed directly from FDA.
Moreover, Sunovian (the holder of US rights for Utibron Neohaler) in a statement to press/media has clarified that they have discontinued the product only due to the reason that they would like to focus their respiratory business on their core products. Therefore, kindly re-consider our drug registration application and approve our product in the upcoming DRB for approval.

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.

39.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Wilson's Pharmaceuticals. Plot No. 387-388, Sector I-9, Industrial Area, Islamabad.**
	Name, address of Manufacturing site.	M/s Wilson's Pharmaceuticals. Plot No. 387-388, Sector I-9, Industrial Area, Islamabad.

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Inspection report dated 24-01-2018 concludes very good level of cGMP compliance.
	Evidence of approval of manufacturing facility	Firm has submitted copy of Section approval letter dated 27-07-2015 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. 23542: 12-11-2019
	Details of fee submitted	PKR 50,000/-: 12-11-2019
	Proposed proprietary name / brand name	CONOFEN Tablet 10/200mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Phenylephrine HCl……10mg Ibuprofen……..200mg
	Pharmaceutical form of applied drug	Light brown colored film coated tablet, oval (Biconvex) with bisect line on one side and plain on other side
	Pharmacotherapeutic Group of (API)	NSAID in combination with sympathomimetic amine
	Reference to Finished product specifications	Manufacturer's specs
	Proposed Pack size	10's, 20's, 30's, 100's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Advil Congestion Relief Tablet 200mg/10mg (USFDA Approved)
	For generic drugs (me-too status)	NA
	Name and address of API manufacturer.	**Phenylephrine HCl:** Shenzhen oriental pharmaceutical Co. Ltd. #43, Dakeng Road, Tongle Village, Longgang District Shenzhen China. **Ibuprofen:** Zenith Chemical Industries (Pvt) Limited. MozaDhonday, JiaBaga Raiwind-Kahna Road, Raiwind 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.
	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.

		Firm has submitted DMF for both drug substances including their stability study data.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of both API at accelerated and real time conditions. The real time stability data is conducted as per zone IV-A 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 not submitted data of pharmaceutical equivalence as well as comparative dissolution profile
	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	**Phenylephrine HCl:** Shenzhen oriental pharmaceutical Co. Ltd. #43, Dakeng Road, Tongle Village, Longgang District Shenzhen China. **Ibuprofen:** Zenith Chemical Industries (Pvt) Limited. MozaDhonday, JiaBaga Raiwind-Kahna Road, Raiwind Pakistan.		
API Lot No.	**Phenylephrine HCl:** PEH-180101Y1 **Ibuprofen:** ZIBU18-009		
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, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial-01	Trial-02	Trial-03
Batch Size	1500 tablet	1500 tablet	1500 tablet
Manufacturing Date	01-2019	01-2019	01-2019
Date of Initiation	02-02-2019	02-02-2019	02-02-2019
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)	Firm has referred to their last inspection report for their product "saferon tablet " Registration Board in its 278th meeting decided to approve Registration of "Saferon (Sofosbuvir 400mg) tablets by M/s Wilson Pharmaceuticals, I-9 Industrial Area, Islamabad. Date of Inspection: 10-12-2015 , 19-04-2017 & 20-01-2018 • Software of HPLC present in the firm is 21CFR compliant and audit trail on the testing reports was available and confirmed.
2.	Approval of API/ DML/GMP certificate of	**Phenylephrine HCl:** Copy of GMP certificate (No.

	API manufacturer issued by concerned regulatory authority of country of origin.	GD20150448) issued by CFDA china is submitted by the firm. The certificate is valid till 07-12-2020. **Ibuprofen:** Copy of GMP certificate of M/s Zenith Chemical Industries (Pvt) Limited dated 22-05-2019 issued on the basis of inspection dated 06-12-2018 is submitted by the firm. The certificate is issued by Additional Director DRAP Lahore.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Phenylephrine HCl:** Firm has submitted copy of commercial invoice specifying import of 308.25g of phenylephrine dated 10-05-2018. The invoice is signed by AD (I&E) DRAP Islamabad. **Ibuprofen:** Firm has submitted copy of invoice specifying purchase of 250Kg Ibuprofen from Zenith Chemical Industries Lahore dated 26-06-2018.
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 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[3]:

Shortcomings communicated	**Response by the firm**
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 & the innovator / reference / comparator product should be submitted and discussed*."	Pharmaceutical equivalence dissolution study has not been performed due to non-availability of reference product in local market (Pakistan) and it is difficult to arrange. However, we are committed to conduct / perform pharmaceutical equivalence of reference product as available and will submit the requisite data.
Submit summary of the results of comparative dissolution profile in section 3.2.P.2.2.1. to comply the decision of 293rd meeting of Registration Board, which states that "*The results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 should be submitted and discussed. For comparative dissolution profile, the guidelines specified in WHO Technical Report Series No. 992, 2015, Annex 7, Appendix 1 Recommendations for conducting and assessing comparative dissolution profiles and USFDA Guidance for Industry Dissolution Testing of Immediate Release Solid Oral Dosage Forms - Dissolution Profile Comparisons may be followed".*	Comparative dissolution study has not been performed due to non-availability of reference product in local market (Pakistan) and it is difficult to arrange. However, we are committed to conduct / perform pharmaceutical equivalence of reference product as available and will submit the requisite data.
Scientific rationale for development of tablet having bisect line on one side of the tablet.	Our applied Drug products (Conofen Tablets 5/200mg and Conofen Tablets 10/200mg) compressed on oval (bi-convex) shaped having bisect line on one side and plain on other side which is our available punch design and the applied drug products are stable with

	afore mentioned punch design. Moreover, we had submitted the stability studies data of three batches (Trials) on accelerated and real-Time stability conditions (as per decision of 293rd meeting of Drug Registration Board.
Provide acceptance criteria in terms of the amount of dissolved active ingredient "Q" for dissolution test at 15 minutes.	Acceptance criteria in terms of the amount of dissolved active ingredient Q = NLT 80% for dissolution test of conofen tablets at 15minutes for both Phenylephrine HCL and Ibuprofen.

Decision of 296th meeting of Registration Board:

Deferred for following submissions:

- Pharmaceutical equivalence data of the applied product along with innovator / reference or comparator product.
- Comparative Dissolution Profile (CDP) data of the applied product along with innovator / reference or comparator product.

Response by the firm:

Reason for deferment	Response by the firm
Pharmaceutical equivalence data of the applied product along with innovator / reference or comparator product.	Firm has submitted results of pharmaceutical equivalence of their product against the reference product Advil Tablet. Manufacturer: Pfizer Madison NJ USA Batch No: R86956 Exp Date: 06/2023
Comparative Dissolution Profile (CDP) data of the applied product along with innovator / reference or comparator product.	Firm has submitted results of Comparative Dissolution Profile (CDP) of their product against the reference product Advil Tablet in three dissolution medium as recommended by WHO guidelines. Manufacturer: Pfizer Madison NJ USA Batch No: R86956 Exp Date: 06/2023

Decision: Deferred for following:

- **Updated GMP status of the firm from QA&LT Division DRAP.**
- **Submission of fee for revision of specifications of the drug product.**

40.	Name, address of Applicant / Marketing Authorization Holder	M/s Rogen Pharmaceuticals (Pvt) Ltd. Plot #30, S-4, 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 18-12-2019 is submitted.
	GMP status of the firm	Rogen Pharmaceuticals: Inspection date 25/01/2019, The firm is operating in compliance with GMP. 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	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 in 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. 1848: 14-01-2021
	Details of fee submitted	PKR 50,000/-: 07-05-2020
	Proposed proprietary name / brand name	IMIPENEM 500mg Injection IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Imipenem (as monohydrate).……500mg Cilastatin (as sodium)……500mg
	Pharmaceutical form of applied drug	White to pale yellow powder filled in clear glass vials with grey rubber stopper and blue color 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
	Status in reference regulatory authorities	Primaxin Injection (USFDA Approved)
	For generic drugs (me-too status)	Onem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	Zhuhai United Laboratories Co., Ltd. No. 2428, Anji Road, Sanzao Town, Jinwan District, Zhuhai City Guangdong 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 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 25°C ± 2°C / 60% ± 5% RH for 6 months. The real time stability data is conducted at 5°C ± 3°C 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 Primaxin Injection IV of Merck & Co.
	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	Zhuhai United Laboratories Co., Ltd. No. 2428, Anji Road, Sanzao Town, Jinwan District, Zhuhai City Guangdong Province China		
API Lot No.	3951902009 3951903005		
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.	19G096	19G097	19G098
Batch Size	9041 vials	9041 vials	9041 vials
Manufacturing Date	07-2019	07-2019	07-2019
Date of Initiation	07-08-2019	07-08-2019	23-08-2019
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)	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. GD20180909) issued by China Food and Drugs Administration. The certificate is valid till 12-05-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**3951902009:** Firm has submitted copy of commercial invoice cleared dated 27-06-2019 specifying import of 50Kg imipenem and cilastatin for injection. The commercial invoice is attested by AD (I&E) DRAP field office.
		3951903005: No evidence of import is submitted for this 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 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 & 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 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 not as per reference product.	Firm has revised the label claim as per the reference product without submission of fee.
Justify your drug substance without sodium bicarbonate since USP as well as reference product specifies that sodium bicarbonate is present in the finished drug product.	Firm has submitted that the drug substance contains sodium bicarbonate. Firm has also submitted COA of drug substance which specify sodium bicarbonate.
Provide 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". Further justify how the analysis of drug substance was carried out without performing verification studies.	Firm has submitted that we have performed method verification for drug product and we are using the same testing method for the drug substance therefore we did not perform verification studies of the drug substance.
Submit CoA of reference standard used in the testing of drug substance in section 3.2.S.5.	Firm has submitted USP certificate of reference standard for imipenem as well as cilastatin. However the method of analysis submitted by the firm specify that they are not using this reference standard.
Justify how 1106mg drug substance is equivalent to 500mg of imipenem and 500mg cilastatin along with sodium bicarbonate.	Firm has not submitted any justification against this observation
Justify the use of 10ml WFI as a diluent along with applied product. Since this diluent is not used by the innovator / reference product.	Firm has submitted that WFI is used for reconstitution of those injectables vials which is injected through IV. Innovator mentioned on label of the vials that after suspension, vial contents transferred to 100ml of infusion solution and does not describe the procedure for preparation of the suspension of the vial contents. So based on this fact use of WFI is suitable and justified. Innovator product does not recommend reconstitution with WFI
Justify why the pharmaceutical equivalence study does not include all critical steps as mentioned in USP monograph.	As per WHO guidelines pharmaceutical equivalence for parenteral drugs is not required but we applied two test for quality and safety of our product that are pH and assay. Firm has not submitted any evidence of such guidelines. Nor they have submitted any scientific justification for skipping important tests.
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."	Firm has submitted that Innovator mentioned on label of the vials that after suspension, vial contents transferred to 100ml of infusion solution and does not describe the procedure for preparation of the suspension of the vial contents and particular diluent. WFI is used for reconstitution of those injectables vials which is injected through IV so based on this fact we used WFI as diluent. Firm has not submitted compatibility studies as per the requirement of CTD.
Justify why the test of "constituted solution" and "particulate matter in injection" is not included in your product specification since these tests are recommended by USP.	Firm has submitted that testing method has been revised as per USP. Firm has not submitted any fee for revision of specification and testing method. Moreover the submitted testing method is different from USP monograph in terms of standard preparation, and assay calculation method and formula.

Justify the test of pH in section 3.2.P.5.2 which specifies that reconstitute the sample in 10ml WFI, however USP specifies that reconstitute as directed in the labelling. The labelling of the innovator / reference product does not recommend reconstitution in WFI.	Firm has submitted that Innovator mentioned on label of the vials that after suspension, vial contents transferred to 100ml of infusion solution and does not describe the procedure for preparation of the suspension of the vial contents and particular diluent. WFI is used for reconstitution of those injectables vials which is injected through IV so based on this fact we used WFI as diluent. Firm has not submitted any justification for the observation.
Justify the use of imipenem + cilastatin working standard for the assay since USP has recommended separate standard preparation for imipenem as well as cilastatin for the assay test.	Firm has again submitted separate USP certificate of reference standard for imipenem as well as cilastatin. However, the method of analysis submitted by the firm specify that they are not using seprate reference standard.
Justify why the calculation formula used for the assay test is different from that specified in USP monograph.	Firm has submitted that testing method is revised and all required formulas incorporated. However as per the revised testing method the formula is different from that specified in USP monograph.
Clarify the batch size of stability batches, since batch size of 9041 vials is mentioned in stability data sheets, while 4520 vials is mentioned in product batch analysis certificate.	Typographic error. The batch size is 9041 vials.
USP recommends separate injections of imipenem and cilastatin standard preparation, while you have used same standard preparation containing both drug substances. Justification is required in this regard.	Firm has submitted that seprate imipenem and cilastatin sodium commercial material is not available with us. We standardized our combined available material with USP reference standard of imipenem and cilatstatin and using it as secondary working standard for routine testing of drug substance and product. Firm has not submitted any scientific justification.
Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
Documents for the procurement of API (Batch number 3951903005) with approval from DRAP.	Not submitted
Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted

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.

- Scientific justification for not performing verification studies for analytical method of drug substance.
- Certificate of analysis of reference standard which is actually used in the analysis of drug substance and drug product.
- Scientific justification for using pre-mixed drug substance having both imipenem as well as cilatatin as working standard for analysis of commercial bathes of drug product.
- Scientific justification for having a master formulation containing 1106mg of drug substance in pre-mixed form containing imipenem monohydrate, cilastatin sodium as well as sodium bicarbonate which is equivalent to 500mg imipenem and 500mg cilastatin.
- Scientific justification for using water for injection as a diluent for your commercial batches contrary to the diluent recommended by the innovator / reference product.
- Scientific justification for not performing complete pharmaceutical equivalence studies as per the USP specifications against the innovator product.
- Scientific justification for not performing compatability studies of your product with the recommended diluent.
- Scientific justification for not performing test of "constituted solution" and "particulate matter in injection" in your commercial batches since these tests have been recommended in USP monograph.
- Scientific justification for your test of pH which specifies that "reconstitute the sample in 10ml WFI", however USP specifies that reconstitute as directed in the labelling and the labelling of the innovator /

reference product does not recommend reconstitution in WFI.

- 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 using an entirely different formula for calculation of assay resultsof commercial batches from that specified in USP monograph.
- Scientific justification for using standard preparation containing both drug substances i.e. imipenem and cilastatin in a single injection for testing your commercial batches while USP recommends separate injections of imipenem and cilastatin standard preparation.
- Documents confirming import of drug substance having drug substance batch number 3951903005.
- 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:

Shortcoming	**Reply**
Scientific justification for not performing verification studies for analytical method of drug substance.	Method verification for the drug product (Imipenem and Cilastatin for Injection) is performed and same testing method is being used for the drug substance (because it is ready to fill powder). As method is same therefore this method verification is applicable for both. Method verification of Imipenem and Cilastatin for Injection is also provided. The verification studies were performed on the analytical method in which standard preparation and sample preparation is not exactly as per USP monograph.
Certificate of analysis of reference standard which is actually used in the analysis of drug substance and drug product.	In house working standard analytical report as Standardization report of API with reference standard is provided by the firm. Firm has used the premixed drug substance as working standard which is not recommended by USP.
Scientific justification for using pre-mixed drug substance having both Imipenem as well as Cilastatin as working standard for analysis of commercial batches of drug product.	We used premix of drug substance (Imipenem & Cilastatin for Injection) as working standard (batch no. 2009R0099) after standardizing it against Imipenem USP reference standard (lot no. R038R0) & Cilastatin USP reference standard (lot no. R012Y0). Firm has used the premixed drug substance as working standard which is not recommended by USP.
Scientific justification for having a master formulation containing 1106mg of drug substance in pre-mixed form containing Imipenem monohydrate, Cilastatin sodium as well as sodium bicarbonate which is equivalent to 500 mg Imipenem and 500mg Cilastatin.	Below is the calculation of fill weight if Imipenem & Cilastatin for Injection: For assay of API, attached certificate of analysis specifies NLT 400µg/mg of Imipenem and 400µg/mg of Cilastatin, while ratio of Imipenem to Cilastatin is 0.95 ~ 1.05 : 1. Therefore, in order to adjust claim of drug substance we have to choose component with lower potency. In this case Imipenem has low potency i.e. 452 µg/mg. Now, $\frac{452\mu g/mg}{1000} \times 100 = 45.2\%$ After considering both Imipenem & Cilastatin at 45.2 For Onem 500mg = $\frac{100 \times 500}{45.2\%} = 1106.19$mg/vial
Scientific justification for using water for injection as a diluent for your commercial batches contrary to the diluent recommended by the innovator /	Water for Injection will not be part of Cilsnim Injection; we have revised our artwork in order to eliminate the water for injection.

reference product.	The revised artwork specifies that after reconstitution administer the solution within 12 hours while the innovator product recommends that the product should be administered within 4 hours after reconstitution.
Scientific justification for not performing complete pharmaceutical equivalence studies as per the USP specification against the innovator product.	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 your product with the recommended diluent.	Compatibility studies were performed but were not made of CTD application. Copy of compatibility studies is provided by the firm.
Scientific justification for not performing test of "constituted solution" and "particulate matter in injection" in your commercial batches since these test have been recommended in USP monograph.	As for as test of particulate matter is concerned, we have purchase Liquid particle counter in March 2020, that why this test was not performed during manufacturing of stability batches. Currently we use Liquid particle counter to perform this test. Firm has submitted following documents • Service report of IQ, OQ and PQ of Liquid Particle counter is enclosed for your review. • Report including test of particulate matter is attached. • Revised test method is also attached.
Scientific justification for your test for pH which specifies that "reconstitutes the sample in 10ml WFI", however USP specifies that reconstitute as directed in the labeling and the labeling of the innovator / reference product does not recommend reconstitution in WFI.	As per USP monograph pH of Imipenem and Cilastatin for Injection should be "between 6.5 and 8.5, when constituted as directed in the labeling". Based upon above statement, we reconstitute content of vial using sterile water for injection, then make the volume up to 100ml using normal saline (saline TS) and then check pH of solution using calibrated pH meter.
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 mentioned in our testing method is same as in USP. Copy of revised test method and USP monograph is also provided. The testing method which was submitted along with the original application was not as per USP monograph.
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. Documents provided are; • Copy of revised test method and USP monograph is attached.
Scientific justification for using standard preparation containing both drug substance i.e. Imipenem and Cilastatin in a single injection for testing your commercial batches while USP recommends separate injection of Imipenem and Cilastatin standard preparation	We used premix of drug substance (Imipenem & Cilastatin for Injection) as working standard while testing of our standard solution as working standard was made after standardizing it against separate Imipenem USP reference standard & Cilastatin USP reference standard. Moreover, for future we have planned to import/purchase separate Imipenem and Cilastatin and standardize against USP reference standards. Firm has used the premixed drug substance as working standard which is not recommended by USP.
Documents confirming import of drug substance having drug substance batches number 3951903005.	Firm has submitted copy of commercial invoice but for batch number 3951805003.

Submission of fee for pre-registration changes in the drug product specifcations.	Firm has not submitted any fee 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: 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.

41.	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:** 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	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 in 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. 1847: 14-01-2021
	Details of fee submitted	PKR 50,000/-: 07-01-2021
	Proposed proprietary name / brand name	CILSNIM 500mg Injection IV
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Imipenem (as monohydrate).……500mg Cilastatin (as sodium)……500mg
	Pharmaceutical form of applied drug	White to pale yellow powder filled in clear glass vials with grey rubber stopper and blue color 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
	Status in reference regulatory authorities	Primaxin Injection (USFDA Approved)
	For generic drugs (me-too status)	Onem Injection of Global Pharmaceuticals
	Name and address of API manufacturer.	Zhuhai United Laboratories Co., Ltd. No. 2428, Anji Road, Sanzao Town, Jinwan District, Zhuhai City Guangdong 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 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 25°C ± 2°C / 60% ± 5% RH for 6 months. The real time stability data is conducted at 5°C ± 3°C 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 Primaxin Injection IV of Merck & Co.
	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	Zhuhai United Laboratories Co., Ltd. No. 2428, Anji Road, Sanzao Town, Jinwan District, Zhuhai City Guangdong Province China
API Lot No.	3951902009 3951903005
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.	19G096	19G097	19G098
Batch Size	9041 vials	9041 vials	9041 vials
Manufacturing Date	07-2019	07-2019	07-2019
Date of Initiation	07-08-2019	07-08-2019	23-08-2019
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)	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. GD20180909) issued by China Food and Drugs Administration. The certificate is valid till 12-05-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**3951902009:** Firm has submitted copy of commercial invoice cleared dated 27-06-2019 specifying import of 50Kg imipenem and cilastatin for injection. The commercial invoice is attested by AD (I&E) DRAP field office.
		3951903005: No evidence of import is submitted for this 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 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:

Shortcomings communicated	Response by the firm
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 not as per reference product.	Firm has revised the label claim as per the reference product without submission of fee.
Justify your drug substance without sodium bicarbonate since USP as well as reference product specifies that sodium bicarbonate is present in the finished drug product.	Firm has submitted that the drug substance contains sodium bicarbonate. Firm has also submitted COA of drug substance which specify sodium bicarbonate.
Provide 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)	Firm has submitted that we have performed method verification for drug product and we are using the same testing method for the drug substance therefore we did not perform verification studies of the drug substance.

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 carried out without performing verification studies.	
Submit CoA of reference standard used in the testing of drug substance in section 3.2.S.5.	Firm has submitted USP certificate of reference standard for imipenem as well as cilastatin.However the method of analysis submitted by the firm specify that they are not using this reference standard.
Justify how 1106mg drug substance is equivalent to 500mg of imipenem and 500mg cilastatin along with sodium bicarbonate.	Firm has not submitted any justification against this observation
Justify the use of 10ml WFI as a diluent along with applied product. Since this diluent is not used by the innovator / reference product.	Firm has submitted that WFI is used for reconstitution of those injectables vials which is injected through IV. Innovator mentioned on label of the vials that after suspension, vial contents transferred to 100ml of infusion solution and does not describe the procedure for preparation of the suspension of the vial contents. So based on this fact use of WFI is suitable and justified. Innovator product does not recommend reconstitution with WFI
Justify why the pharmaceutical equivalence study does not include all critical steps as mentioned in USP monograph.	As per WHO guidelines pharmaceutical equivalence for parenteral drugs is not required but we applied two test for quality and safety of our product that are pH and assay. Firm has not submitted any evidence of such guidelines. Nor they have submitted any scientific justification for skipping important tests.
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."	Firm has submitted that Innovator mentioned on label of the vials that after suspension, vial contents transferred to 100ml of infusion solution and does not describe the procedure for preparation of the suspension of the vial contents and particular diluent. WFI is used for reconstitution of those injectables vials which is injected through IV so based on this fact we used WFI as diluent. Firm has not submitted compatibility studies as per the requirement of CTD.
Justify why the test of "constituted solution" and "particulate matter in injection" is not included in your product specification since these tests are recommended by USP.	Firm has submitted that testing method has been revised as per USP. Firm has not submitted any fee for revision of specification and testing method. Moreover the submitted testing method is different from USP monograph in terms of standard preparation, and assay calculation method and formula.
Justify the test of pH in section 3.2.P.5.2 which specifies that reconstitute the sample in 10ml WFI, however USP specifies that reconstitute as directed in the labelling. The labelling of the innovator / reference product does not recommend reconstitution in WFI.	Firm has submitted that Innovator mentioned on label of the vials that after suspension, vial contents transferred to 100ml of infusion solution and does not describe the procedure for preparation of the suspension of the vial contents and particular diluent. WFI is used for reconstitution of those injectables vials which is injected through IV so based on this fact we used WFI as diluent. Firm has not submitted any justification for the observation.

Justify the use of imipenem + cilastatin working standard for the assay since USP has recommended separate standard preparation for imipenem as well as cilastatin for the assay test.	Firm has again submitted separate USP certificate of reference standard for imipenem as well as cilastatin. However the method of analysis submitted by the firm specify that they are not using seprate reference standard.
Justify why the calculation formula used for the assay test is different from that specified in USP monograph.	Firm has submitted that testing method is revised and all required formulas incorporated. However as per the revised testing method the formula is different from that specified in USP monograph.
Clarify the batch size of stability batches, since batch size of 9041 vials is mentioned in stability data sheets, while 4520 vials is mentioned in product batch analysis certificate.	Typographic error. The batch size is 9041 vials.
USP recommends separate injections of imipenem and cilastatin standard preparation, while you have used same standard preparation containing both drug substances. Justification is required in this regard.	Firm has submitted that seprate imipenem and cilastatin sodium commercial material is not available with us. We standardized our combined available material with USP reference standard of imipenem and cilatstatin and using it as secondary working standard for routine testing of drug substance and product. Firm has not submitted any scientific justification.
Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
Documents for the procurement of API (Batch number 3951903005) with approval from DRAP.	Not submitted
Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted

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.

- Scientific justification for not performing verification studies for analytical method of drug substance.
- Certificate of analysis of reference standard which is actually used in the analysis of drug substance and drug product.
- Scientific justification for using pre-mixed drug substance having both imipenem as well as cilatatin as working standard for analysis of commercial bathes of drug product.
- Scientific justification for having a master formulation containing 1106mg of drug substance in pre-mixed form containing imipenem monohydrate, cilastatin sodium as well as sodium bicarbonate which is equivalent to 500mg imipenem and 500mg cilastatin.
- Scientific justification for using water for injection as a diluent for your commercial batches contrary to the diluent recommended by the innovator / reference product.
- Scientific justification for not performing complete pharmaceutical equivalence studies as per the USP specifications against the innovator product.
- Scientific justification for not performing compatability studies of your product with the recommended diluent.
- Scientific justification for not performing test of “constituted solution” and “particulate matter in injection” in your commercial batches since these tests have been recommended in USP monograph.
- Scientific justification for your test of pH which specifies that “reconstitute the sample in 10ml WFI”, however USP specifies that reconstitute as directed in the labelling and the labelling of the innovator / reference product does not recommend reconstitution in WFI.
- 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 using an entirely different formula for calculation of assay resultsof commercial batches from that specified in USP monograph.
- Scientific justification for using standard preparation containing both drug substances i.e. imipenem and cilastatin in a single injection for testing your commercial batches while USP recommends separate injections of imipenem and cilastatin standard preparation.

- Documents confirming import of drug substance having drug substance batch number 3951903005.
- 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:

Shortcoming	**Reply**
Scientific justification for not performing verification studies for analytical method of drug substance.	Method verification for the drug product (Imipenem and Cilastatin for Injection) is performed and same testing method is being used for the drug substance (because it is ready to fill powder). As method is same therefore this method verification is applicable for both. Method verification of Imipenem and Cilastatin for Injection is also provided. The verification studies were performed on the analytical method in which standard preparation and sample preparation is not exactly as per USP monograph.
Certificate of analysis of reference standard which is actually used in the analysis of drug substance and drug product.	In house working standard analytical report as Standardization report of API with reference standard is provided by the firm. Firm has used the premixed drug substance as working standard which is not recommended by USP.
Scientific justification for using pre-mixed drug substance having both Imipenem as well as Cilastatin as working standard for analysis of commercial batches of drug product.	We used premix of drug substance (Imipenem & Cilastatin for Injection) as working standard (batch no. 2009R0099) after standardizing it against Imipenem USP reference standard (lot no. R038R0) & Cilastatin USP reference standard (lot no. R012Y0). Firm has used the premixed drug substance as working standard which is not recommended by USP.
Scientific justification for having a master formulation containing 1106mg of drug substance in pre-mixed form containing Imipenem monohydrate, Cilastatin sodium as well as sodium bicarbonate which is equivalent to 500 mg Imipenem and 500mg Cilastatin.	Below is the calculation of fill weight if Imipenem & Cilastatin for Injection: For assay of API, attached certificate of analysis specifies NLT 400µg/mg of Imipenem and 400µg/mg of Cilastatin, while ratio of Imipenem to Cilastatin is 0.95 ~ 1.05 : 1. Therefore, in order to adjust claim of drug substance we have to choose component with lower potency. In this case Imipenem has low potency i.e. 452 µg/mg. Now, $\frac{452\mu g/mg}{1000} \times 100 = 45.2\%$ After considering both Imipenem & Cilastatin at 45.2 For Onem 500mg = $\frac{100 \times 500}{45.2\%} = 1106.19$mg/vial
Scientific justification for using water for injection as a diluent for your commercial batches contrary to the diluent recommended by the innovator / reference product.	Water for Injection will not be part of Cilsnim Injection; we have revised our artwork in order to eliminate the water for injection. The revised artwork specifies that after reconstitution administer the solution within 12 hours while the innovator product recommends that the product should be administered within 4 hours after reconstitution.
Scientific justification for not performing complete pharmaceutical equivalence studies as per the USP specification against the innovator product.	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 your product with the recommended diluent.	Compatibility studies were performed but were not made of CTD application. Copy of compatibility studies is provided by the firm.
Scientific justification for not performing test of "constituted solution" and "particulate matter in injection" in your commercial batches since these test have been recommended in USP monograph.	As for as test of particulate matter is concerned, we have purchase Liquid particle counter in March 2020, that why this test was not performed during manufacturing of stability batches. Currently we use Liquid particle counter to perform this test. Firm has submitted following documents • Service report of IQ, OQ and PQ of Liquid Particle counter is enclosed for your review. • Report including test of particulate matter is attached. • Revised test method is also attached.
Scientific justification for your test for pH which specifies that "reconstitutes the sample in 10ml WFI", however USP specifies that reconstitute as directed in the labeling and the labeling of the innovator / reference product does not recommend reconstitution in WFI.	As per USP monograph pH of Imipenem and Cilastatin for Injection should be "between 6.5 and 8.5, when constituted as directed in the labeling". Based upon above statement, we reconstitute content of vial using sterile water for injection, then make the volume up to 100ml using normal saline (saline TS) and then check pH of solution using calibrated pH meter.
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 mentioned in our testing method is same as in USP. Copy of revised test method and USP monograph is also provided. The testing method which was submitted along with the original application was not as per USP monograph.
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. Documents provided are; • Copy of revised test method and USP monograph is attached.
Scientific justification for using standard preparation containing both drug substance i.e. Imipenem and Cilastatin in a single injection for testing your commercial batches while USP recommends separate injection of Imipenem and Cilastatin standard preparation	We used premix of drug substance (Imipenem & Cilastatin for Injection) as working standard while testing of our standard solution as working standard was made after standardizing it against separate Imipenem USP reference standard & Cilastatin USP reference standard. Moreover, for future we have planned to import/purchase separate Imipenem and Cilastatin and standardize against USP reference standards. Firm has used the premixed drug substance as working standard which is not recommended by USP.
Documents confirming import of drug substance having drug substance batches number 3951903005.	Firm has submitted copy of commercial invoice but for batch number 3951805003.
Submission of fee for pre-registration changes in the drug product specifcations.	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	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.

	USP Specifications for already registered drug products.	
Decision: 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.		
42.	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:** 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	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	Firm has submitted copies of IR spectra of drug substance from the API manufacturer.

generally sufficient to provide copies of the IR spectrum.	
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	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.

performed without complying the system suitability requirements as per USP monograph.	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 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	Firm has only provided a statement of shelf life after reconstitution. No data has been submitted. The reference product specify the shelf life after

are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided".	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± 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 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: 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.

43.	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:** 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	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	Firm has submitted revised specification and testing method. As per revised testing method the sample

the initial quantity of material taken and the dilution steps is not permitted by any guidelines.	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	The calculation provided by the firm does not incorporate the sodium carbonate contents.

meropenem.	
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: 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.

Agenda of Evaluator PEC-I:
Agenda Item of AD PEC-I:
Case No. 01: Registration applications for local manufacturing submitted on Form 5F
A: Deferred Applications:

44.	Name, address of Applicant / Marketing Authorization Holder	M/s Healthtek (pvt) Ltd., Plot no. 14, Sector 19, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Stallion Pharmaceuticals (pvt) Ltd., 581 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. 24043: 16-09-2020
	Details of fee submitted	PKR 50,000/-: 20-04-2020
	Proposed proprietary name / brand name	Cilomen 500mg injection
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Imipenem as monohydrate……500mg Cilastatin as sodium...500mg
	Pharmaceutical form of applied drug	Powder for solution for injection
	Pharmacotherapeutic Group of (API)	Anti bacterial / dehydropeptidase inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Primaxin injection (500mg/500mg) by M/s Merck, USFDA Approved.
	For generic drugs (me-too status)	Cilapen 500mg injection by M/s Bosch, Reg. No. 048491
	GMP status of the Finished product manufacturer	GMP certificate issued on 06/12/2019 on the basis of inspection conducted on 16/09/2019. Dry powder injectable (Penicillin, Carbapenem) section is approved.
	Name and address of API manufacturer.	M/s Aurobindo Pharma limited, Unit-V, Plot no. 68-70, 73-91, 95, 96, 260, 261 IDA., Chemical zone, Pashmylaram, Patancheru Mandal, Saga 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 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 drug substance is sterile bulk mixture of Imipenem abd cilastin in a ratio of 1:1.The firm as 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 of Drug Substance conditions, duration	• 60 months real time stability data at 30˚C ± 2˚C / 65% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches Batches: EEC0821002, EEC0821003, EEC0821004
	Module-III (Drug Product):	Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Analytical method validation/verification	Th firm has submitted analytical method verification studies. Official monograph for the product is available in USP.
	Comparative dissolution profile/Pharmaceutical Equivalence	

STABILITY STUDY DATA			
Manufacturer of API	M/s Aurobindo Pharma limited, Unit-V, Plot no. 68-70, 73-91, 95, 96, 260, 261 IDA., Chemical zone, Pashmylaram, Patancheru Mandal, Saga Reddy district, Telangana, India. Copy of GMP certificate of API manufacturer is submitted.		
API Lot No.	1605204528		
Description of Pack (Container closure system)	USP type I colorless 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, 1, 2, 3, 4, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	V6001	V7001	V8001
Batch Size	17600 vials	8700 vials	4400 vials
Manufacturing Date	10/2016	08/2017	02/2018
Date of Initiation	25/10/2016	23/08/2017	09/03/2018
No. of Batches	03		

Administrative Portion	
Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted.
Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Certificate No.
Documents for the procurement of API with approval from DRAP (in case of import).	ADC attested Invoice No. U05/17-18/73 dated 20th, July, 2017

Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted supported documents including chromatograms, raw data sheets, COAs summary 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)	Not submitted

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

S.#	Query	Response by the firm
1	The documents from the API manufacturer in the submitted dossier show that Imipenem as monohydrate 500mg has been used in the manufacturing of blend of Imipenem and Cilastatin as well as the reference product contains Imipenem as monohydrate 500mg while documents from finished product manufacturer show that Imipenem anhydrous 500mg is used, clarify.	According to the firm's response, "It was a typographical error which is corrected from onward as we are procuring the material as monohydrate and our calculations are entirely as per monohydrate material". However, earlier the firm has submitted that the material is received in either form Monohydrate or Anhydrous.
2	Blend of 02 APIs is used for the manufacturing of finished product, for such products potency adjustment becomes very critical because by adjusting the potency of one API would cause the actual potency of the other API to be changed. Therefore, provide procedure for potency adjustment for the applied product.	According to firm "As the material is received in the blend form with ratio of 1:1 so the 100% material contains 50% of Imipenem and 50% of Cilastatin. Considering standard potency of both APIs equal to 50% (500mg) each, theoretical calculations are given in the following. Imipenem: Theoretical quantity= 500mg+2% = 510mg Cilastatin: Theoretical quantity= 500mg+2% = 510mg Total quantity of blend= 510+510 = 1020mg per vial
3	Section 3.2.P.2.2.1 shall include detail of all the quality tests along with the results performed on the developed product against innovator/reference/comparator product foe establishing the pharmaceutical equivalence.	The firm has submitted the required data of pharmaceutical equivalence in relevant section by performing the quality tests against the comparator product Cilapen 500mg by M/s Bosch Pharmaceuticals. The firm has stated that the innovator's product is not available in Pakistan.
4	Valid GMP certificate of API manufacturer is required.	Copy of renewal letter of drug manufacturing license of API manufacturer is submitted. License No.:48/MD/AP/98/B/R Valid till: 31/12/2021
5	Significant change has been observed in real time stability testing of batch number V8001 in assay value of both Imipenem as well as Cilastatin, justify.	According to the reply of the firm has placed 3 more batches in the year 2018 wherein no significant change has been observed, detail of which is given as under. Real time: 30°C ± 2°C / 65% ± 5%RH of 03 batches till 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH of 03 batches till 06 months

Batch No.	V8003	V8004	V8005
Batch Size	8900 vials	17540 vials	8900 vials
Manufacturing Date	04/2018	04/2018	08/02018
Date of Initiation	27/04/2018	10/05/2018	29/08/2018

- The diluent mentioned in section 3.2.P.2.6 is Water for Injection while as per the available information regarding innovator/reference product the contents of the vials must be reconstituted by adding approximately 10 mL of the appropriate diluent to the vial.
- List of appropriate diluents are as follows:

0.9% Sodium Chloride Injection
5% Dextrose Injection
5% Dextrose and 0.9% Sodium Chloride
5% Dextrose Injection with 0.225% or 0.45% saline solution

- The submitted testing method for analysis of drug product is different from the method described in USP monograph in terms of standard preparation, assay calculation and formula.
- The test of pH in which the firm specifies that 1gram of sample should be dissolved 100ml of distilled water, however USP specifies that reconstitute as directed in the labelling. The labelling of the innovator / reference product does not recommend reconstitution in WFI.

Decision of 312th meeting:

Registration Board deliberated 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. Accordingly, the Board deferred for the case for following submissions:

 Scientific justification for your test of pH which specifies that "reconstitute the sample in 10ml WFI", however USP specifies that reconstitute as directed in the labelling and the labelling of the innovator / reference product does not recommend reconstitution in WFI.

 Scientific justification for having the method of sample solution preparation for the commercial batches which is different from that specified in USP monograph.

 Scientific justification for using an entirely different formula for calculation of assay results of commercial batches from that specified in USP monograph.

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.

Submission by the firm:

- The firm has submitted, "Imipenem & Cilastatin material is available and used in blend powder form for injection. For potency adjustment, the lower potency API will be adjusted so the quantity of other API might be slightly adjusted over the target value due to slight difference of potency of both API's.
  Calculations for potency adjustment:
  Batch of blend: AB88390
  Potency of Imipenem: 44.67%
  Potency of Cilastatin: 47.25%
  After considering both Imipenem & Cilastatin at 44.67%
  For the applied product: Cilomen 500mg = $\frac{100 \times 500}{44.67\%}$ = 1119.319 mg/vial
- "We would like to inform you that, we had tested the product according to USP but unfortunately due to some misunderstanding the different formula and concentration were used against USP. We have placed three new batches for stability studies and test it according to USP in all aspects. Revised method and raw data sheets with correct calculation has been attached for your reference".
- The firm has stated, "for the applied product, we have used 10ml of 0.9% Sodium chloride for testing purpose only'.
- The standard solutions have been run for Cilastatin and Imipenem separately for analysis of the sample.
- The chromatographic conditions include 50°C column temperature, 300mm×4.6mm with packing L1, flow rate 2mL/min, wavelength 254nm, Injection volume 10uL. Detail of the tailing factor and theoretical plates not provided by the firm.
- The firm has submitted the data of 03 batches detail of which is given as under;

Batch No.	V1002	V1001	V0003
Batch Size	16000	18340	9000 vials
Manufacturing Date	07/2021	03/2021	11/2020

Date of Initiation	19/07/2021	19/07/2021	19/07/2021
API Lot No.	9900680007E1	DBIMCNF002	AB88390
Attested Invoice no.	Not provided	7000057843 dated 31/12/2020	7000053843 dated 30/09/2020
Source of drug substance	ACS Doofar, Italy	Sun Pharmaceutical industries Ltd., India	Sun Pharmaceutical industries Ltd., India
Frequency	0, 3 (months)	0, 3 (months)	0, 3 (months)

- The formula used for calculation by the firm is given in the following along with complete calculation of a sample.

$$\frac{\text{Area of sp. x wt. of std. x 100 x 100 x Potency}}{\text{Area of std. x 25 x 1 x 10 x 100}} = \_\_\_\_\_ \text{mg of Imipenem / Vial}$$

Decision: Registration Board deliberated that the commercial batches manufactured by the manufacturer i.e. Stallion 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.

B: New Cases:

45.	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. 7322 dated 05/03/2021
	Details of fee submitted	PKR 50,000/-: dated 30/12/2020
	Proposed proprietary name / brand name	Ertuvia-M 7.5mg/500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ertugliflozin L-pyroglutamic acid eq to Ertugliflozin…….7.5mg Metformin hydrochloride…….500mg
	Pharmaceutical form of applied drug	Brown color, oblong biconvex film coated tablets having "f" on one side and scored on other side.
	Pharmacotherapeutic Group of (API)	Ertugliflozin…..Anti diabetic (SGLT2 inhibitor) Metformin…..Anti diabetic (biguanides)
	Reference to Finished product specifications	In-house
	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	Segluromet Tablets (2.5/500, 2.5/1000, 7.5/500, 7.5/1000) by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	NA
	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.	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad (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)	**Ertugliflozin L-pyroglutamic acid:** Ertugliflozin L-pyroglutamic acid is a co-crystal with ratio of 1:1 and falls in BCS class I. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, B & unknown individual impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted **Metformin HCl:** The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, F & and any specified impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Stability study conditions: **Ertugliflozin L-pyroglutamic acid:** 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: (ETG20161201, ETG20161202, ETG20170101) **Metformin HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (9002ML2RMI, 9003ML2RMI, 9004ML2RMI)
	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 Segluromet 7.5mg/500mg tablet by Merck sharp & Dohme USA by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Segluromet 7.5mg/500mg tablet by Merck sharp & Dohme USA. Dissolution profile of Ertuvia-M 7.5mg/500mg Tablets and Segluromet 7.5mg/500mg Tablets 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 15 minutes. And no calculation is required for Similarity factor f2
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad 431136 (Maharashtra) India
API Lot No.	**Ertugliflozin L-pyroglutamic acid:** ETG20190101 **Metformin HCl:** 18119ML2ARMI
Description of Pack (Container closure system)	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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ERTab-019	ERTab-020	ERTab-021
Batch Size	650 Tablets	650 Tablets	650 Tablets
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	13-07-2020	13-07-2020	13-07-2020
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 previous approval.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin L-pyroglutamic acid:** Copy of valid GMP certificate No.JS20180935 issued by China Food and Drug Administration dated: 27/11/2018 valid till 26/11/2023 is submitted. **Metformin HCl:** Copy of GMP certificate No. NEW-WHO-GMP/CERT/AD/67318/2018/11/24741 valid until 27-08-2021 is submitted. Copy of DML certificate No 25-AD/070, validity period 01-04-2019 to31-03-2024 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Ertugliflozin L-pyroglutamic acid:** Copy of Form-6 No.00197/2019-DRAP (P)/811 Dated: 26-02-2019, DRAP Acknowledgment for receiving of Ertugliflozin L-pyroglutamic acid, commercial invoice, packing list, Form-3, Form-7 is submitted. **Metformin HCl:** Copy of attested invoice No: MEG1819/1631905 dated: 12-10-2018 from DRAP Peshawar, packing list, Form-3, Form-7 and GD are 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 From 16/06/2020 to 21/01/2021
Remarks by PEC-I:		
Observations		**Response**
The title of the firm is not similar to the title mentioned		**Title as per Online Link:**

in submitted copy of GMP certificate when the certificate is verified from the available data base of CFDA's official website, please clarify.	Shagnghai Pharmaceuticals Kangli (Changzhou) Pharmaceutical Co., Ltd. **Title as per submitted copy of GMP:** Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd **Address: (**Address is same in both cases) Daixi Street, Luoyang Town, Wujin District, Changzhou. Response: The firm is unable to provide justification of difference in title and has provided the weblink for online verification of GMP certificate.
As per submitted drug substance specifications, the assay test is performed for estimation of content of "Ertugliflozin-LPGA", while the assay test for the content of "Ertugliflozin" should have been included in the specifications as per the available literature of the innovator product, moreover, the COA of working standard describes the assay content of "Ertugliflozin", please clarify.	• The firm has submitted assay detail of Ertugliflozin L-pyroglutamic acid. The summary of which is given below. • "The analysis of Ertugliflozin-LPGA shows that the content of Ertugliflozin-LPGA (anhydrous basis) equal to 99.65%. Assay for L-pyroglutamic acid was estimated to be 22.26% so the content of Ertugliflozin (on anhydrous basis) is 77.39%. The water content determined in 0.20%. • The firm has not used the formula for conversion of potency of Ertugliflozin (anhydrous) to Ertugliflozin (as is basis) in order to adjust the final potency instead of; the firm had just subtracted the value of water content from the potency of Ertugliflozin (anhydrous basis) to get the potency of 77.19% (ertugliflozin as is basis). • Upon communication, the firm has revised the calculation sheet and used the formula given in pharmacopoeia for calculation of potency on As Is basis which is 77.23%.
Decision: Approved with innovator's specifications. 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 • **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.**	

46.	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	Dy. No. 7324 dated 05/03/2021

	submission	
	Details of fee submitted	PKR 50,000/-: dated 30/12/2020
	Proposed proprietary name / brand name	Ertuvia-M 7.5mg/1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ertugliflozin L-pyroglutamic acid eq to Ertugliflozin…….7.5mg Metformin hydrochloride…….1000mg
	Pharmaceutical form of applied drug	Brown color, oblong biconvex coated tablets having "f" on one side and plain on other side.
	Pharmacotherapeutic Group of (API)	Ertugliflozin…..Anti diabetic (SGLT2 inhibitor) Metformin…..Anti diabetic (biguanides)
	Reference to Finished product specifications	In-House
	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	Segluromet Tablets (2.5/500, 2.5/1000, 7.5/500, 7.5/1000) by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	NA
	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.	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad (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)	**Ertugliflozin L-pyroglutamic acid:** Ertugliflozin L-pyroglutamic acid is a co-crystal with ratio of 1:1 and falls in BCS class I. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, B & unknown individual

		impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted **Metformin HCl:** Metformin Hydrochloride is present in B.P. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, F & and any specified impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Stability study conditions: **Ertugliflozin L-pyroglutamic acid:** 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: (ETG20161201, ETG20161202, ETG20170101) **Metformin HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (9002ML2RMI, 9003ML2RMI, 9004ML2RMI)
	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 Segluromet 7.5mg/1000mg tablet by Merck sharp & Dohme,USA by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Segluromet 7.5mg/1000mg tablet by Merck sharp & Dohme USA. Dissolution profile of Ertuvia-M 7.5mg/1000mg Tablets and Segluromet 7.5mg/1000mg Tablets 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 15 minutes. And no calculation is required for Similarity factor f2.
	Analytical method validation/verification of	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

	product		
STABILITY STUDY DATA			
Manufacturer of API	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) India		
API Lot No.	**Ertugliflozin L-pyroglutamic acid:** ETG20190101 **Metformin HCl:** 18119ML2ARMI		
Description of Pack (Container closure system)	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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ERTab-022	ERTab-023	ERTab-024
Batch Size	650 Tablets	650 Tablets	650 Tablets
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	02-07-2020	02-07-2020	02-07-2020
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 submitted reference of previous approval.	
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin L-pyroglutamic acid:** Copy of valid GMP certificate No.JS20180935 issued by China Food and Drug Administration dated: 27/11/2018 valid till 26/11/2023 is submitted. **Metformin HCl:** Copy of GMP certificate No. NEW-WHO-GMP/CERT/AD/67318/2018/11/24741 valid until 27-08-2021 is submitted. Copy of DML certificate No 25-AD/070, validity period 01-04-2019 to31-03-2024 is submitted.	
9.	Documents for the procurement of API with approval from DRAP (in case of import).	**Ertugliflozin L-pyroglutamic acid:** Copy of Form-6 No.00197/2019-DRAP (P)/811 Dated: 26-02-2019, DRAP Acknowledgment for receiving of Ertugliflozin L-pyroglutamic acid, commercial invoice, packing list, Form-3, Form-7 is submitted **Metformin HCl:** Copy attested invoice No: MEG1819/1631905 dated: 12-10-2018, packing list, Form-3, Form-7 and good declaration is submitted	

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 From 16/06/2020 to 21/01/2021

Remarks OF Evaluator:

Observations	**Response**
The title of the firm is not similar to the title mentioned in submitted copy of GMP certificate when the certificate is verified from the available data base of CFDA's official website, please clarify.	**Title as per Online Link:** Shagnghai Pharmaceuticals Kangli (Changzhou) Pharmaceutical Co., Ltd. **Title as per submitted copy of GMP:** Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd **Address: (**Address is same in both cases) Daixi Street, Luoyang Town, Wujin District, Changzhou. Response: The firm is unable to provide justification of difference in title and has provided the weblink for online verification of GMP certificate.
As per submitted drug substance specifications, the assay test is performed for estimation of content of "Ertugliflozin-LPGA", while the assay test for the content of "Ertugliflozin" should have been included in the specifications as per the available literature of the innovator product, moreover, the COA of working standard describes the assay content of "Ertugliflozin", please clarify.	• The firm has submitted assay detail of Ertugliflozin L-pyroglutamic acid. The summary of which is given below. • "The analysis of Ertugliflozin-LPGA shows that the content of Ertugliflozin-LPGA (anhydrous basis) equal to 99.65%. Assay for L-pyroglutamic acid was estimated to be 22.26% so the content of Ertugliflozin (on anhydrous basis) is 77.39%. The water content determined in 0.20%. • The firm has not used the formula for conversion of potency of Ertugliflozin (anhydrous) to Ertugliflozin (as is basis) in order to adjust the final potency instead of; the firm had just subtracted the value of water content from the potency of Ertugliflozin (anhydrous basis) to get the potency of 77.19% (ertugliflozin as is basis). • Upon communication, the firm has revised the calculation sheet and used the formula given in pharmacopoeia for calculation of potency on As Is basis which is 77.23%.

Decision: Approved with innovator's specifications. 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

- **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.**		
47.	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. 7323 dated 05/03/2021
	Details of fee submitted	PKR 50,000/-: dated 30/12/2020
	The proposed proprietary name / brand name	Ertuvia-M 2.5mg/500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ertugliflozin L-pyroglutamic acid eq to Ertugliflozin…….2.5mg Metformin hydrochloride…….500mg
	Pharmaceutical form of applied drug	Light pink color, oblong biconvex coated tablets scored on one side and "FEROZSONS" on other side.
	Pharmacotherapeutic Group of (API)	Ertugliflozin…..Anti diabetic (SGLT2 inhibitor) Metformin…..Anti diabetic (biguanides)
	Reference to Finished product specifications	In-House
	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	Segluromet Tablets (2.5/500, 2.5/1000, 7.5/500, 7.5/1000) by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	NA
	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.	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India

		Address: H-4, M.I.D.C., Waluj Aurangabad (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)	**Ertugliflozin L-pyroglutamic acid:** Ertugliflozin L-pyroglutamic acid is a co-crystal with ratio of 1:1 and falls in BCS class I. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, B & unknown individual impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted **Metformin HCl:** Metformin Hydrochloride is present in B.P. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, F & and any specified impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Stability study conditions: **Ertugliflozin L-pyroglutamic acid:** 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: (ETG20161201, ETG20161202, ETG20170101) **Metformin HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (9002ML2RMI, 9003ML2RMI, 9004ML2RMI)
	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 Segluromet 2.5mg/500mg tablet by Merck sharp & Dohme,USA by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Segluromet 2.5mg/500mg tablet by Merck sharp & Dohme, USA. Dissolution profile of Ertuvia-M 2.5mg/500mg Tablets and Segluromet 2.5mg/500mg Tablets 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 15 minutes. And no calculation is required for Similarity factor f2	
	Analytical method validation/verification of product	Method verification studies have been submitted including linearity, range, accuracy, precision, specificity.	
STABILITY STUDY DATA			
Manufacturer of API	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) India		
API Lot No.	**Ertugliflozin L-pyroglutamic acid:** ETG20190101 **Metformin HCl:** 18119ML2ARMI		
Description of Pack (Container closure system)	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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ERTab-013	ERTab-014	ERTab-015
Batch Size	650 Tablets	650 Tablets	650 Tablets
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	22-06-2020	22-06-2020	22-06-2020
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 previous approval.	

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin L-pyroglutamic acid:** Copy of valid GMP certificate No.JS20180935 issued by China Food and Drug Administration dated: 27/11/2018 valid till 26/11/2023 is submitted. **Metformin HCl:** Copy of GMP certificate No. NEW-WHO-GMP/CERT/AD/67318/2018/11/24741 valid until 27-08-2021 is submitted. Copy of DML certificate No 25-AD/070, validity period 01-04-2019 to31-03-2024 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Ertugliflozin L-pyroglutamic acid:** Copy of Form-6 No.00197/2019-DRAP (P)/811 Dated: 26-02-2019, DRAP Acknowledgment for receiving of Ertugliflozin L-pyroglutamic acid, commercial invoice, packing list, Form-3, Form-7 is submitted **Metformin HCl:** Copy attested invoice No: MEG1819/1631905 dated: 12-10-2018, packing list, Form-3, Form-7 and GD 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 From 16/06/2020 to 21/01/2021
Remarks OF Evaluator:		
Observations		**Response**
The title of the firm is not similar to the title mentioned in submitted copy of GMP certificate when the certificate is verified from the available data base of CFDA's official website, please clarify.		**Title as per Online Link:** Shagnghai Pharmaceuticals Kangli (Changzhou) Pharmaceutical Co., Ltd. **Title as per submitted copy of GMP:** Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd **Address: (**Address is same in both cases) Daixi Street, Luoyang Town, Wujin District, Changzhou. Response: The firm is unable to provide justification of difference in title and has provided the weblink for online verification of GMP certificate.
As per submitted drug substance specifications, the assay test is performed for estimation of content of "Ertugliflozin-LPGA", while the assay test for the content of "Ertugliflozin" should have been included in the specifications as per the available literature of the innovator product, moreover, the COA of working		• The firm has submitted assay detail of Ertugliflozin L-pyroglutamic acid. The summary of which is given below. • "The analysis of Ertugliflozin-LPGA shows that the content of Ertugliflozin-LPGA (anhydrous basis) equal to 99.65%. Assay for L-pyroglutamic

standard describes the assay content of "Ertugliflozin", please clarify.	acid was estimated to be 22.26% so the content of Ertugliflozin (on anhydrous basis) is 77.39%. The water content determined in 0.20%. • The firm has not used the formula for conversion of potency of Ertugliflozin (anhydrous) to Ertugliflozin (as is basis) in order to adjust the final potency instead of; the firm had just subtracted the value of water content from the potency of Ertugliflozin (anhydrous basis) to get the potency of 77.19% (ertugliflozin as is basis). • Upon communication, the firm has revised the calculation sheet and used the formula given in pharmacopoeia for calculation of potency on As Is basis which is 77.23%.

Decision: Approved with innovator's specifications. 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

- **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.**

48.	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. 7321 dated 05/03/2021
	Details of fee submitted	PKR 50,000/-: dated 30/12/2020
	Proposed proprietary name / brand name	Ertuvia-M 2.5mg/1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ertugliflozin L-pyroglutamic acid eq to Ertugliflozin…….2.5mg Metformin hydrochloride…….1000mg
	Pharmaceutical form of applied drug	Light pink color, oblong biconvex coated tablets having "f" on side and plain on other side
	Pharmacotherapeutic Group of (API)	Ertugliflozin…..Anti diabetic (SGLT2 inhibitor) Metformin…..Anti diabetic (biguanides)
	Reference to Finished product specifications	Innovator 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	Segluromet Tablets (2.5/500, 2.5/1000, 7.5/500, 7.5/1000) by M/s Merck Sharp & Dohme, USFDA Approved.
	For generic drugs (me-too status)	NA
	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.	**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad (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)	**Ertugliflozin L-pyroglutamic acid:** Ertugliflozin L-pyroglutamic acid is a co-crystal with ratio of 1:1 and falls in BCS class I. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, B & unknown individual impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted **Metformin HCl:** Metformin Hydrochloride is present in B.P. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, F & and any specified impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance is submitted
	Stability studies	Stability study conditions: **Ertugliflozin L-pyroglutamic acid:**

		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: (ETG20161201, ETG20161202, ETG20170101) **Metformin HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months of 3 batches Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months of 3 batches Batches: (9002ML2RMI, 9003ML2RMI, 9004ML2RMI)
	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 Segluromet 2.5mg/1000mg tablet by Merck sharp & Dohme, USA by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Segluromet 2.5mg/1000mg tablet by Merck sharp & Dohme, USA. Dissolution profile of Ertuvia-M 2.5mg/1000mg Tablets and Segluromet 2.5mg/1000mg Tablets 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 15 minutes. And no calculation is required for Similarity factor f2
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API		**Ertugliflozin L-pyroglutamic acid:** Name: M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd – China Address: Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu 213105-China **Metformin HCl:** Name : IPCA Laboratories Limited – India Address: H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) India
API Lot No.		**Ertugliflozin L-pyroglutamic acid:** ETG20190101 **Metformin HCl:** 18119ML2ARMI
Description of Pack (Container closure system)		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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ERTab-016	ERTab-017	ERTab-018
Batch Size	650 Tablets	650 Tablets	650 Tablets
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	04-07-2020	04-07-2020	04-07-2020
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 previous approval.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ertugliflozin L-pyroglutamic acid:** Copy of valid GMP certificate No.JS20180935 issued by China Food and Drug Administration dated: 27/11/2018 valid till 26/11/2023 is submitted. **Metformin HCl:** Copy of GMP certificate No. NEW-WHO-GMP/CERT/AD/67318/2018/11/24741 valid until 27-08-2021 is submitted. Copy of DML certificate No 25-AD/070, validity period 01-04-2019 to31-03-2024 is submitted.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Ertugliflozin L-pyroglutamic acid:** Copy of Form-6 No.00197/2019-DRAP (P)/811 Dated: 26-02-2019, DRAP Acknowledgment for receiving of Ertugliflozin L-pyroglutamic acid, commercial invoice, packing list, Form-3 ,Form-7 is submitted **Metformin HCl:** Copy attested invoice No: MEG1819/1631905 dated: 12-10-2018, packing list, Form-3, Form-7 and GD 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 & accelerated)	Submitted From 16/06/2020 to 21/01/2021	
Remarks OF Evaluator:			
Observations		**Response**	

The title of the firm is not similar to the title mentioned in submitted copy of GMP certificate when the certificate is verified from the available data base of CFDA's official website, please clarify.	**Title as per Online Link:** Shagnghai Pharmaceuticals Kangli (Changzhou) Pharmaceutical Co., Ltd. **Title as per submitted copy of GMP:** Shanghai Pharma Group Changzhou Kony Pharmaceutical Co, Ltd **Address: (**Address is same in both cases) Daixi Street, Luoyang Town, Wujin District, Changzhou. Response: The firm is unable to provide justification of difference in title and has provided the weblink for online verification of GMP certificate.
As per submitted drug substance specifications, the assay test is performed for estimation of content of "Ertugliflozin-LPGA", while the assay test for the content of "Ertugliflozin" should have been included in the specifications as per the available literature of the innovator product, moreover, the COA of working standard describes the assay content of "Ertugliflozin", please clarify.	• The firm has submitted assay detail of Ertugliflozin L-pyroglutamic acid. The summary of which is given below. • "The analysis of Ertugliflozin-LPGA shows that the content of Ertugliflozin-LPGA (anhydrous basis) equal to 99.65%. Assay for L-pyroglutamic acid was estimated to be 22.26% so the content of Ertugliflozin (on anhydrous basis) is 77.39%. The water content determined in 0.20%. • The firm has not used the formula for conversion of potency of Ertugliflozin (anhydrous) to Ertugliflozin (as is basis) in order to adjust the final potency instead of; the firm had just subtracted the value of water content from the potency of Ertugliflozin (anhydrous basis) to get the potency of 77.19% (ertugliflozin as is basis). • Upon communication, the firm has revised the calculation sheet and used the formula given in pharmacopoeia for calculation of potency on As Is basis which is 77.23%.
Decision: Approved with innovator's specifications. 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 • **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.**	

49.	Name, address of Applicant / Marketing Authorization Holder	M/S Ferozsons Laboratories Limited, PO Ferozsons Amangarh Nowshera Khyber Pakhtunkhwa - Pakistan.
	Name, address of Manufacturing site.	M/s Ferozsons Laboratories Limited, PO 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. 11785 dated 20/04/2021
	Details of fee submitted	PKR 50,000/-: dated 08/01/2021
	The proposed proprietary name / brand name	Empagen-L 5mg/25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Linagliptin……...5mg Empagliflozin…..25mg
	Pharmaceutical form of applied drug	Pale pink color, Round biconvex film coated tablets having "f "on one side and plain on other side.
	Pharmacotherapeutic Group of (API)	**Linagliptin** Anti-daibetic(Antihyperglycemic drug)Inhibitor of dipeptidyl peptidase-4 (DPP-4) enzyme. **Empagliflozin** Anti-daibetic (Antihyperglycemic drug) Inhibitor of sodium glucose co-transporter (SGLT2).
	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	Glyxambi (5mg/25mg. 10mg/25mg) film coated tablet by M/s Boehringer Ingelheim Pharmaceutical, Inc, USFDA Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate No. F. 11-6/2019-DRAP-06 granted on 29/01/2019 Valid up to 25-01-2022. Tablet (General) section approved vide letter No. F.3-14/2004-Lic, dated: 08-04-2015 is submitted.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Fuxin Long Rui Pharmaceutical Co, Ltd, Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China. **Linagliptin:** M/s Glenmark Life Sciences Limited, Plot No 3109, GIDC Industrial Estate, Ankleshwar District Bharuch, Gujarat - 393 002, 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)	**Empagliflozin:** Empagliflozin is inhouse, the firm submitted detail of

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, 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. **Linagliptin:** Linagliptin is inhouse, the firm submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, B, any other individual impurity 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 : **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: (20160606, 20161017, 20161219) **Linagliptin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (061307463, 061307486, 061307518)
	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 Glyxambi 5mg/25mg tablet by M/s Boehringer Ingelheim Pharmaceutical, Inc, USA by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Glyxambi 5mg/25mg tablet by M/s Boehringer Ingelheim Pharmaceutical, Inc, USA The dissolution profile of Empagen-L 5mg/25mg mg Tablets and Glyxambi 5mg/25mg mg Tablets 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 15 minutes.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.
STABILITY STUDY DATA		
Manufacturer of API	**Empagliflozin** M/s Fuxin Long Rui Pharmaceutical Co, Ltd,	

	Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China. **Linagliptin** M/s Glenmark Life Sciences Limited, Address: Plot No 3109, GIDC Industrial Estate, Ankleshwar District Bharuch, Gujarat - 393 002, India		
API Lot No.	**Empagliflozin :** L-E-20200409-D01-E06-01 **Linagliptin:** 801900693		
Description of Pack (Container closure system)	Alu-Alu blister packed in cardboard box.		
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.	EGTab-034	EGTab-035	EGTab-036
Batch Size	1000 Tablets	1000 Tablets	1000 Tablets
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	04-08-2020	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)	The firm has submitted reference of previous approval.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	• **Empagliflozin:** Copy of GMP certificate issued on dated: 24/08/2020, valid till 20/12/2022 by Liaoning Fuxin Management Committee – China is submitted. Copy of DML certificate No. Liao20150233, dated: 21/12/2017 valid till 20/12/2022, issued by Food & Drug Administration of Liaoning Province- China is submitted. • **Linagliptin:** Copy of GMP certificate No. 19061427, dated: 18/06/2019, valid till 17/06/2022 issued by Food & Drugs Control Administration Gujrat State – India is submitted. Copy of DML certificate No. G/25/1629, dated: 01/01/2019 valid till 31/12/2023, issued by Food & Drugs Control Administration Gujrat State – India is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• **Empagliflozin** Copy of attested invoice, No. HN20060501-H dated 05/06/2020, packing list, Form-3, Form-7 & GD is submitted wherein the permission to import Empagliflozin for the purpose of test/analysis and stability studies is granted. • **Linagliptin** Copy of Form-6, No. 00374/2019-DRAP)P)/1539 dated 22/04/2019, DRAP acknowledgment for receiving of Linagliptin, unattested Commercial

		invoice Nio. F30018000476 dated 29/05/2019, packing list, Form-3, Form-7 & airway bill is submitted wherein the permission to import Linagliptin 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.	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:		
Observations		**Response by the firm**
The test for uniformity of dosage form is include in the specifications of the innovator's product while the stability studies are conducted without performing the test for uniformity of dosage form, please clarify.		"Although uniformity of dosage form is included in the specifications of the innovator's product but during stability of the product, samples were tested according to the specifications, except for the test of identity and uniformity of dosage units, as per available EMA assessment report for GLYXAMBI".
Please explain and refer the guideline as well, according to which the acceptance criteria of analytical validation parameter (specificity) is defined in the submitted dossier in terms of %RSD.		The firm has stated that the acceptance criteria for specificity parameter in analytical method validation is "the absence of interference with elution of analyte".
Decision: Approved with innovator's specifications. 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 • **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.**		
50.	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	☒ Domestic sale

	product	☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8324 dated 15-3-2021
	Details of fee submitted	PKR 20,000/-: dated 10/02/2021
	Proposed proprietary name / brand name	Empator-M Tablet 5mg + 850mg
	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)	Drugs used in diabetics (Combination of oral blood glucose lowering drugs)
	Reference to Finished product specifications	Manufacturer specifications
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	EMA Approved.
	For generic drugs (me-too status)	Xenglu-Met Tablet 5mg + 850mg by M/s Hilton Pharma, Reg. No. 093104
	GMP status of the Finished product manufacturer	The firm has been inspected on 08/07/2021 for renewal of DML. The panel recommended renewal of DML.
	Name and address of API manufacturer.	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS details 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)	The firm has 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 both drug substances
	Stability studies	Stability study conditions: Empagliflozin: Real time: 25˚C ± 2˚C / 60% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503 Metformin 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: MH/00107/07, MH/00207/07, MH/00307/07
	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 Synjardy tablet 5mg + 850mg by Boehringer Ingelheim, USA by performing quality tests (Identification, Disintegration, Assay, Dissolution, Uniformity of dosage form including the tests for impurities). CDP has been performed against the same brand that is Synjardy tablet 5mg + 850mg by Boehringer Ingelheim, USA 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	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India
API Lot No.	Empagliflozin: 190700224, 202004002 Metformin HCl: 1802000053
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2x7'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.	NPD-T-1018-L	NPD-T-1082-P	NPD-T-1083-P
Batch Size	6000 tablets	6000 tablets	6000 tablets
Manufacturing Date	08-05-2020	21-7-2020	21-7-2020
Date of Initiation	12-8-2020	12-8-2020	12-8-2020
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 Empator 10mg Tablets which was conducted on 6th August 2019 and was presented in 291st meeting of Registration Board held on 02nd - 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.	**Empagliflozin:** Copy of GMP Certificate for RUYUAN HEC Pharm Co., Ltd. (Certificate: 2018024) issued by Shaoguan Food and Drug Administration & valid upto 04-12-2021 is submitted. **Metformin HCl:** Copy of GMP certificate for Sohan Healthcare PVT LTD (Certificate: NEW-WHO-GMP/CERT/PD/72513/2018/11/25589) issued by Food & Drug Administration, M.S. & Valid upto 5-Nov-2021 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Firm has submitted copy of invoice (invoice# SHPL/17-18/ECP/39) Dated: 17-1-2018 from Sohan Healthcare PVT LTD, attested by DRAP Karachi office dated 25-01-2018 specifying import of 1000Kg Metformin HCl (Batch# MS 0181 12 17). Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.
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)	Record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted.

Remarks OF Evaluator:

Observations	**Response**
Drug substance specifications along with the analytical procedures used for routine testing of the Drug substance (Empagliflozin & Metformin HCl) by Drug Product manufacturer is required along with the clarification of analytical method used for assay of Metformin HCl as well as the analytical method verification studies performed by drug product manufacturer for both drug substances should be submitted.	• The firm has submitted drug substances specifications along with the detail of analytical procedures used for routine testing from drug product manufacturer. • "Previously, USP-42 described the potentiometric titration method for Metformin and the same method was used for analysis but in USP-43, HPLC method is given and accordingly, potentiometric method is switched to HPLC method". Verification studies for HPLC method are submitted. • Method verification studies for Empgliflozin including accuracy, precision and specificity submitted performed by drug product manufacturer.
The submitted real time stability date for Empagliflozin is not according to Zone IV-A, therefore, as per the decision of Registration Board taken in 297th meeting, you are required to submit degradation studies of the finished product for 6 months or otherwise submit real time stability data according to the conditions of Zone IV-A.	The firm has submitted stability studies for Empgliflozin with the following details; Empagliflozin: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503
Please submit documents confirming the procurement of drug substances (Empagliflozin & Metformin HCl).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Firm has submitted copy of invoice (invoice# SHPL/17-18/ECP/39) Dated: 17-1-2018 from Sohan Healthcare PVT LTD, attested by DRAP Karachi office dated 25-01-2018 specifying import of 1000Kg Metformin HCl (Batch# MS 0181 12 17). Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.
Clarification is required regarding the source of Metformin HCl since 02 different sources are mentioned in in the submitted application dossiers of different strengths of Empator-M tablets. 1. Ipca Laboratories Limited H-4, M.I.D.C., Waluj Aurangabad Maharashtra) Pin : 431136, India. 2. SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-	"Metformin HCl is already registered in our other products and hence both the sources mentioned below are our approved sources. The range of Empator-M tablets was developed using both these sources in order to develop confidence on both the sources for this particular combination of EMpator-M tablets as they will be utilized for

Daund Pune 413B02 Maharashtra State, India.	commercial products. Following is the table specifying the source of used drug Substance for manufacturing of the product;

Strength	Source (Metformin)	Product Status
12.5mg/500mg	IPCA Laboratories Limited, India	Registration letter issued on 30-7-2021
5mg/500mg	IPCA Laboratories Limited, India	Approved in 312th DRB meeting
12.5mg/850mg	IPCA Laboratories Limited, India	Being presented in 313th meeting
12.5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/850mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting

Decision: Approved with innovator's specifications. 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

- **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.**

51.	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. 8001 dated 11-3-2021
	Details of fee submitted	PKR 20,000/-: dated 7/01/2021
	Proposed proprietary name / brand name	Empator-M Tablet 5mg + 1000mg
	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)	Drugs used in diabetics (Combination of oral blood glucose lowering drugs)
	Reference to Finished product specifications	Manufacturer specifications
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference	SYNJARDY 5mg/1000mg by Boehringer

	regulatory authorities	Ingelheim, USFDA Approved.
	For generic drugs (me-too status)	Adrance-M tablet 5mg + 1000mg by M/s Atco Laboratories, Reg. No. 095151
	GMP status of the Finished product manufacturer	The firm has been inspected on 08/07/2021 for renewal of DML. The panel recommended renewal of DML.
	Name and address of API manufacturer.	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS details 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)	The firm has 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 in APIMFs of both drug substances
	Stability studies	Stability study conditions: Empagliflozin: Real time: 25˚C ± 2˚C / 60% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503 Metformin 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: MH/00107/07, MH/00207/07, MH/00307/07
	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 Synjardy tablet 5mg + 1000mg by Boehringer Ingelheim, USA by performing quality tests (Identification, Disintegration, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Synjardy tablet 5mg + 1000mg by Boehringer Ingelheim, USA 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	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India		
API Lot No.	Empagliflozin: 200300114, 202004002 Metformin HCl: 1802000053		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2x7'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.	NPD-T-1041-L	NPD-T-1050-P	NPD-T-1051-P
Batch Size	6000 tablets	6000 tablets	6000 tablets
Manufacturing Date	12-06-2020	25-6-2020	25-6-2020
Date of Initiation	10-7-2020	10-7-2020	10-7-2020
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 Empator 10mg Tablets which was conducted on 6th August 2019 and was presented in 291st meeting of Registration Board held on 02nd - 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.	**Empagliflozin:** Copy of GMP Certificate for RUYUAN HEC Pharm Co., Ltd. (Certificate: 2018024) issued by Shaoguan Food and Drug Administration & valid upto 04-12-2021 is submitted. **Metformin HCl:** Copy of GMP certificate for Sohan Healthcare PVT LTD (Certificate: NEW-WHO-GMP/CERT/PD/72513/2018/11/25589) issued by Food & Drug Administration, M.S. & Valid upto 5-Nov-2021 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Firm has submitted copy of invoice (invoice# SHPL/17-18/ECP/39) Dated: 17-1-2018 from Sohan Healthcare PVT LTD, attested by DRAP Karachi office dated 25-01-2018 specifying import of 1000Kg Metformin HCl (Batch# MS 0181 12 17). Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.
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)	Record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted.
Remarks OF Evaluator:		
Observations		**Response**
Drug substance specifications along with the analytical procedures used for routine testing of the Drug substance (Empagliflozin & Metformin HCl) by Drug Product manufacturer is required along with the clarification of analytical method used for assay of Metformin HCl as well as the analytical method verification studies performed by drug product manufacturer for both drug substances should be submitted.		• The firm has submitted drug substances specifications along with the detail of analytical procedures used for routine testing from drug product manufacturer. • "Previously, USP-42 described the potentiometric titration method for Metformin and the same method was used for analysis but in USP-43, HPLC method is given and accordingly, potentiometric method is switched to HPLC method". Verification studies for

	HPLC method are submitted. • Method verification studies for Empgliflozin including accuracy, precision and specificity submitted performed by drug product manufacturer.
The submitted real time stability date for Empagliflozin is not according to Zone IV-A, therefore, as per the decision of Registration Board taken in 297th meeting, you are required to submit degradation studies of the finished product for 6 months or otherwise submit real time stability data according to the conditions of Zone IV-A.	The fir has submitted stability studies for Empgliflozin with the following details; Empagliflozin: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503
Please submit documents confirming the procurement of drug substances (Empagliflozin & Metformin HCl).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Firm has submitted copy of invoice (invoice# SHPL/17-18/ECP/39) Dated: 17-1-2018 from Sohan Healthcare PVT LTD, attested by DRAP Karachi office dated 25-01-2018 specifying import of 1000Kg Metformin HCl (Batch# MS 0181 12 17). Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.
Clarification is required regarding the source of Metformin HCl since 02 different sources are mentioned in in the submitted application dossiers of different strengths of Empator-M tablets. 1. Ipca Laboratories Limited H-4, M.I.D.C., Waluj Aurangabad Maharashtra) Pin : 431136, India. 2. SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India.	"Metformin HCl is already registered in our other products and hence both the sources mentioned below are our approved sources. The range of Empator-M tablets was developed using both these sources in order to develop confidence on both the sources for this particular combination of EMpator-M tablets as they will be utilized for commercial products. Following is the table specifying the source of used drug Substance for manufacturing of the product;

Strength	Source (Metformin)	Product Status
12.5mg/500mg	IPCA Laboratories Limited, India	Registration letter issued on 30-7-2021
5mg/500mg	IPCA Laboratories Limited, India	Approved in 312th DRB meeting
12.5mg/850mg	IPCA Laboratories Limited, India	Being presented in 313th meeting
12.5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/850mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting

Decision: Approved with innovator's specifications. 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

- **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.**

52.	Name, address of Applicant / Marketing Authorization	M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi

	Holder	
	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. 8002 dated 11-3-2021
	Details of fee submitted	PKR 20,000/-: dated 10/02/2021
	The proposed proprietary name / brand name	Empator-M Tablet 12.5mg + 850mg
	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	Manufacturer specifications
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	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	The firm has been inspected on 08/07/2021 for renewal of DML. The panel recommended renewal of DML.
	Name and address of API manufacturer.	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** Ipca Laboratories Limited H-4, M.I.D.C., Waluj Aurangabad Maharashtra) Pin : 431136, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS details 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)	The firm has 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 both drug substances
	Stability studies	Stability study conditions: Empagliflozin: Real time: 25˚C ± 2˚C / 60% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503 Metformin 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: MH/00107/07, MH/00207/07, MH/00307/07
	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 Synjardy tablet 12.5mg + 850mg by Boehringer Ingelheim, USA by performing quality tests (Identification, Disintegration, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Synjardy tablet 12.5mg + 850mg by Boehringer Ingelheim, USA 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	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County,	

	Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** Ipca Laboratories Limited H-4, M.I.D.C., Waluj Aurangabad Maharashtra) Pin : 431136, India		
API Lot No.	Empagliflozin: 2020004002 Metformin HCl: 1908000095		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2x7'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.	NPD-T-990-L	NPD-T-1084-P	NPD-T-1085-P
Batch Size	6000 tablets	6000 tablets	6000 tablets
Manufacturing Date	03-04-2020	22-7-2020	22-7-2020
Date of Initiation	12-8-2020	12-8-2020	12-8-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.

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 Empator 10mg Tablets which was conducted on 6th August 2019 and was presented in 291st meeting of Registration Board held on 02nd - 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.	**Empagliflozin:** Copy of GMP Certificate for RUYUAN HEC Pharm Co., Ltd. (Certificate: 2018024) issued by Shaoguan Food and Drug Administration & valid upto 04-12-2021 is submitted. **Metformin HCl:** Copy of GMP Certificate for Ipca Laboratories limited (Certificate: New-WHO-GMP/CERT/AD/6731/2018/ 11/24741) issued by Food and Drug Administration, M..S. Bandra-kurla Complex, Bandra (E), Mumbai-400051 Maharashtra, India valid upto 27-08-2021 is submitted

3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.
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:

Observations	Response
Drug substance specifications along with the analytical procedures used for routine testing of the Drug substance (Empagliflozin & Metformin HCl) by Drug Product manufacturer is required along with the clarification of analytical method used for assay of Metformin HCl as well as the analytical method verification studies performed by drug product manufacturer for both drug substances should be submitted.	• The firm has submitted drug substances specifications along with the detail of analytical procedures used for routine testing from drug product manufacturer. • "Previously, USP-42 described the potentiometric titration method for Metformin and the same method was used for analysis but in USP-43, HPLC method is given and accordingly, potentiometric method is switched to HPLC method". Verification studies for HPLC method are submitted. • Method verification studies for Empgliflozin including accuracy, precision and specificity submitted performed by drug product manufacturer.
The submitted real time stability date for Empagliflozin is not according to Zone IV-A, therefore, as per the decision of Registration Board taken in 297th meeting, you are required to submit degradation studies of the finished product for 6 months or otherwise submit real time stability data according to the conditions of Zone IV-A.	The firm has submitted stability studies for Empgliflozin with the following details; Empagliflozin: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503
Please submit documents confirming the procurement of drug substances (Empagliflozin & Metformin HCl).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from

	IPCA Laboratories limited attested by DRAP Karachi.
Clarification is required regarding the source of Metformin HCl since 02 different sources are mentioned in in the submitted application dossiers of different strengths of Empator-M tablets. 1. Ipca Laboratories Limited H-4, M.I.D.C., Waluj Aurangabad Maharashtra) Pin : 431136, India. 2. SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India.	"Metformin HCl is already registered in our other products and hence both the sources mentioned below are our approved sources. The range of Empator-M tablets was developed using both these sources in order to develop confidence on both the sources for this particular combination of EMpator-M tablets as they will be utilized for commercial products. Following is the table specifying the source of used drug Substance for manufacturing of the product;

Strength	Source (Metformin)	Product Status
12.5mg/500mg	IPCA Laboratories Limited, India	Registration letter issued on 30-7-2021
5mg/500mg	IPCA Laboratories Limited, India	Approved in 312th DRB meeting
12.5mg/850mg	IPCA Laboratories Limited, India	Being presented in 313th meeting
12.5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/850mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting

Decision: Approved with innovator's specifications. 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

- **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.**

53.	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. 8324 dated 15-3-2021
	Details of fee submitted	PKR 20,000/-: dated 7/01/2021
	The proposed proprietary name / brand name	Empator-M Tablet 12.5mg + 1000mg
	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)	Drugs used in diabetics (Combination of oral blood glucose lowering drugs)
	Reference to Finished product specifications	Manufacturer specifications
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SYNJARDY 12.5mg/1000mg by Boehringer Ingelheim, USFDA Approved.
	For generic drugs (me-too status)	Adrance-M tablet 12.5mg + 1000mg by M/s Atco Laboratories, Reg. No. 095150
	GMP status of the Finished product manufacturer	The firm has been inspected on 08/07/2021 for renewal of DML. The panel recommended renewal of DML.
	Name and address of API manufacturer.	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS details 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)	The firm has 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 both drug substances
	Stability studies	Stability study conditions: Empagliflozin: Real time: 25˚C ± 2˚C / 60% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503 Metformin 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: MH/00107/07, MH/00207/07, MH/00307/07
	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 Synjardy tablet 12.5mg + 1000mg by Boehringer Ingelheim, USA by performing quality tests (Identification, Disintegration, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Synjardy tablet 12.5mg + 1000mg by Boehringer Ingelheim, USA 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	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India		
API Lot No.	Empagliflozin: 190700224, 202004002 Metformin HCl: 1802000053		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2x7'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.	NPD-T-1022-L	NPD-T-1052-P	NPD-T-1053-P
Batch Size	6000 tablets	6000 tablets	6000 tablets
Manufacturing Date	15-05-2020	26-6-2020	26-6-2020
Date of Initiation	10-7-2020	10-7-2020	10-7-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.		
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 Empator 10mg Tablets which was conducted on 6th August 2019 and was presented in 291st meeting of Registration Board held on 02nd - 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.	**Empagliflozin:** Copy of GMP Certificate for RUYUAN HEC Pharm Co., Ltd. (Certificate: 2018024) issued by Shaoguan Food and Drug Administration & valid upto 04-12-2021 is submitted. **Metformin HCl:** Copy of GMP certificate for Sohan Healthcare PVT LTD (Certificate: NEW-WHO-GMP/CERT/PD/72513/2018/11/25589) issued by Food & Drug Administration, M.S. & Valid upto 5-Nov-2021 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively. **Metformin HCl:** Firm has submitted copy of invoice (invoice# SHPL/17-18/ECP/39) Dated: 17-1-2018 from Sohan Healthcare PVT LTD, attested by DRAP Karachi office dated 25-01-2018 specifying import of 1000Kg Metformin HCl (Batch# MS 0181 12 17). Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.
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)	Record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted.
Remarks OF Evaluator:		

<table>
<tr><td>Observations</td><td>Response</td></tr>
<tr><td>Drug substance specifications along with the analytical procedures used for routine testing of the Drug substance (Empagliflozin & Metformin HCl) by Drug Product manufacturer is required along with the clarification of analytical method used for assay of Metformin HCl as well as the analytical method verification studies performed by drug product manufacturer for both drug substances should be submitted.</td><td>• The firm has submitted drug substances specifications along with the detail of analytical procedures used for routine testing from drug product manufacturer.
• “Previously, USP-42 described the potentiometric titration method for Metformin and the same method was used for analysis but in USP-43, HPLC method is given and accordingly, potentiometric method is switched to HPLC method”. Verification studies for HPLC method are submitted.
• Method verification studies for Empgliflozin including accuracy, precision and specificity submitted performed by drug product manufacturer.</td></tr>
<tr><td>The submitted real time stability date for Empagliflozin is not according to Zone IV-A, therefore, as per the decision of Registration Board taken in 297th meeting, you are required to submit degradation studies of the finished product for 6 months or otherwise submit real time stability data according to the conditions of Zone IV-A.</td><td>The firm has submitted stability studies for Empgliflozin with the following details;
Empagliflozin:
Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24 months
Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503</td></tr>
<tr><td>Please submit documents confirming the procurement of drug substances (Empagliflozin & Metformin HCl).</td><td>Empagliflozin: Firm has submitted copy of invoice (invoice# WIS190056) Dated: 02-07-2019 & Invice # WIS200011 dated 27/02/2020 attested by DRAP Karachi office dated 23-7-2019 specifying import 10kg + 10Kg respectively.
Metformin HCl: Firm has submitted copy of invoice (invoice# SHPL/17-18/ECP/39) Dated: 17-1-2018 from Sohan Healthcare PVT LTD, attested by DRAP Karachi office dated 25-01-2018 specifying import of 1000Kg Metformin HCl (Batch# MS 0181 12 17).
Invoice No. MEG1020/1630406 dated 06/05/2019 (diary No. 6106 dated 16/05/2019) imported from IPCA Laboratories limited attested by DRAP Karachi.</td></tr>
<tr><td>Clarification is required regarding the source of Metformin HCl since 02 different sources are mentioned in in the submitted application dossiers of different strengths of Empator-M tablets.
1. Ipca Laboratories Limited H-4, M.I.D.C., Waluj Aurangabad Maharashtra) Pin : 431136, India.
2. SOHAN HEALTHCARE, D-30 MIDC, Kurkumbh, Tal-Daund Pune 413B02 Maharashtra State, India.</td><td>“Metformin HCl is already registered in our other products and hence both the sources mentioned below are our approved sources. The range of Empator-M tablets was developed using both these sources in order to develop confidence on both the sources for this particular combination of EMpator-M tablets as they will be utilized for commercial products.
Following is the table specifying the source of used drug Substance for manufacturing of the product;</td></tr>
</table>

Strength	**Source (Metformin)**	**Product Status**
12.5mg/500mg	IPCA Laboratories Limited, India	Registration letter issued on 30-7-2021
5mg/500mg	IPCA Laboratories Limited, India	Approved in 312th DRB meeting
12.5mg/850mg	IPCA Laboratories Limited, India	Being presented in 313th meeting
12.5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting
5mg/1000mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting

5mg/850mg	Sohan Healthcare Pvt.Ltd, India	Being presented in 313th meeting

Decision: Approved with innovator's specifications. 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

- **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.**

54.	Name, address of Applicant / Marketing Authorization Holder	M/s Dynatis Pakistan (Pvt.) Ltd. Plot No. 710, Sunder Industrial Estate, Lahore
	Name, address of Manufacturing site.	M/s Dynatis Pakistan (Pvt.) Ltd. Plot No. 710, 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. 7452 dated 08/03/2021
	Details of fee submitted	PKR 20,000/-: dated 29/01/2021
	The proposed proprietary name / brand name	Glifo Tablet 10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….10mg
	Pharmaceutical form of applied drug	White to off-white round, biconvex, film coated immediate release tablet
	Pharmacotherapeutic Group of (API)	Sodium-glucose co-transporter 2 (SGLT2) inhibitors
	Reference to Finished product specifications	In-House
	Proposed Pack size	7's, 10's, 14's, 28's and 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Jardiance Tablet 10mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, CT 06877 USA.
	For generic drugs (me-too status)	Empozin Tablet 10mg by M/s Macter International Limited Reg. No. 093078
	GMP status of the Finished product manufacturer	The firm has been inspected on 08/07/2021 for renewal of DML. The panel recommended renewal of DML.
	Name and address of API manufacturer.	M/s Anhui Haikang Pharmaceutical Co., Ltd., No. 21 Huancheng west road, Anqing city, Anhui Province, 246000 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 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 complete validation studies, batch analysis and justification of specification, details of reference standards (Empagliflozin RS and impurities), 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: (20160301, 20160302, 20160303)
	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 Jardiance Tablet 10mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, USA. by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that Jardiance Tablet 10mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, USA. in HCl buffer pH 1.2, Acetate Buffer pH 4.5 and Phosphate buffer pH 6.8. Calculation for f2 value is not required since the release is more than 85% in 15 minutes for innovator's as well as the applied product.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, LOD/LOQ, Robustness, Solution stability, system suitability
STABILITY STUDY DATA		
Manufacturer of API	M/s Anhui Haikang Pharmaceutical Co., Ltd., No. 21 Huancheng west road, Anqing city, Anhui Province, 246000 China	

API Lot No.	20190703		
Description of Pack (Container closure system)	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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TCX-004	TCX-006	TCX-007
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	06-2020	06-2020	07-2020
Date of Initiation	11-07-2020	11-07-2020	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)	No inspection has been done yet.
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 09-09-2019 issued by Anqing Biomedical Industry Association. The certificate is valid till 09-09-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice attested by AD DRAP I&E LAHORE, dated 11-11-2019, in the name of M/s Dynatis Pakistan (Pvt.) Ltd. specifying the quantity of 800 gm of Empagliflozin (Batch# 20190703) and copy of form 6.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted supporting document including chromatograms, raw data sheets, COAs, and summary data sheets etc.
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:

Observations	**Response**
Submit certificate of analysis from the drug product manufacturer of same batches used for development of the applied product.	The COA from drug product manufacturer is submitted for lot number 20190703, analysis date 20/02/2020.
As per the submitted dossier, the critical quality attributes include that 80% of the drug should be released in 30 minutes, moreover the acceptance criteria mentioned in 3.2.P.2.2.1 under formulation development and in section 3.2.P.5 under Control of finished product for dissolution testing is NLT 80% in 30 minutes while as per available information of	"As per FDA dissolution data base, Empagliflozin dissolution criteria has been refer to FDA's dissolution Guidance, 2018 which is (Dissolution Testing and Acceptance criteria for immediate release solid oral dosage form drug products containing high solubility drug substances) updated on 07/02/2020. According to FDA's dissolution guidance, 2018 (Dissolution Testing and Acceptance criteria for

innovator's product the drug should be released in 15 minutes.	immediate release solid oral dosage form drug products containing high solubility drug substances); for immediate release solid oral dosage form the dissolution criterion is Q=80% in 30 minutes.

Remarks:

According to available literature of innovator's product on the official website of USFDA the drug should be released in 15 minutes.

Response by the firm:

- The firm has revised the dissolution specifications as per the innovator's product i.e NLT 80% of labelled amount in 15 minutes.
- The firm has submitted stability data of 03 more batches. The detail of which is given in the following table.

Batch No.	TCX008	TCX009
Batch Size	5000 tablets	5000 tablets
Manufacturing Date	09/2021	09/2021
Date of Initiation	21/09/2021	21/09/2021
API Lot No.	20060201	20060201
Frequency	0, 1 (months)	0, 1 (months)

- The firm has submitted Audit trail report for Batch No. TCX008 & TCX009 for stability testing.
- The firm has submitted record of digital data logger for humidity and temperature for accelerated as well as for real time stability.
- The relevant chromatograms and raw data sheets are submitted.
- Copy of attested Invoice No. WD202003005 dated 28/07/2020 from DRAP Lahore is submitted. For API lot No. 20060201 along with the certificate of analysis.

A brief description of process validation including the proposed protocol shall be described and submitted.	The firm has submitted manufacturing process validation protocol for the applied product including description regarding purpose, scope, contents of validation, analytical procedure along with product development details, manufacturing process flow chart and other relevant details.
Approval of GMP/drug manufacturing license from the concerned authority of country of origin should be submitted.	The firm has submitted copy of drug manufacturing license No. Anhui 20190399 valid till 31/12/2025.

Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of ~~ful~~ applicable fee 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.**
- **The Board directed the firm to submit the data of dissolution testing as per revised dissolution specifications as set by the innovator (i.e. in 15minutes 80% release) at batch release for the first 02 commercial batches and submit data to PE&R division.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

55.	Name, address of Applicant / Marketing Authorization Holder	M/s Dynatis Pakistan (Pvt.) Ltd. Plot No. 710, Sunder Industrial Estate, Lahore
	Name, address of Manufacturing site.	M/s Dynatis Pakistan (Pvt.) Ltd. Plot No. 710, 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. 7453 dated 08/03/2021
	Details of fee submitted	PKR 20,000/-: dated 29/01/2021
	The proposed proprietary name / brand name	Glifo Tablet 25mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….25mg
	Pharmaceutical form of applied drug	Orange colored oblong biconvex, film coated immediate release tablets with bisecting line on one side and plain on other side
	Pharmacotherapeutic Group of (API)	Sodium-glucose co-transporter 2 (SGLT2) inhibitors
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	7's, 10's, 14's, 28's and 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Jardiance Tablet 25mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, CT 06877 USA.
	For generic drugs (me-too status)	Empozin Tablet 25mg by M/s Macter International Limited Reg. No. 093077
	GMP status of the Finished product manufacturer	GMP certificate based on evaluation conducted on 26-03-2021.
	Name and address of API manufacturer.	M/s Anhui Haikang Pharmaceutical Co., Ltd., No. 21 Huancheng west road, Anqing city, Anhui Province, 246000 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 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 complete validation studies, batch analysis and justification of specification, details of reference standards (Empagliflozin RS and impurities), 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: (20160301, 20160302, 20160303)
	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 Jardiance Tablet 25mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, USA. by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that Jardiance Tablet 25mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, USA. in HCl buffer pH 1.2, Acetate Buffer pH 4.5 and Phosphate buffer pH 6.8. The values for f1 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, LOD/LOQ, Robustness, Solution stability, system suitability

STABILITY STUDY DATA			
Manufacturer of API	M/s Anhui Haikang Pharmaceutical Co., Ltd., No. 21 Huancheng west road, Anqing city, Anhui Province, 246000 China		
API Lot No.	20190703		
Description of Pack (Container closure system)	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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TCY-003	TCY-004	TCY-005
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	08-07-2020	08-07-2020	08-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No inspection has been done yet.

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 09-09-2019 issued by Anqing Biomedical Industry Association. The certificate is valid till 09-09-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice attested by AD DRAP I&E LAHORE, dated 11-11-2019, in the name of M/s Dynatis Pakistan (Pvt.) Ltd. specifying the quantity of 800 gm of Empagliflozin (Batch# 20190703) and copy of form 6.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted supporting document including chromatograms, raw data sheets, COAs, and summary data sheets etc.
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:

Observations	**Response**
Submit certificate of analysis from the drug product manufacturer of same batches used for development of the applied product.	The COA from drug product manufacturer is submitted for lot number 20190703, analysis date 20/02/2020.
As per the submitted dossier, the critical quality attributes include that 80% of the drug should be released in 30 minutes, moreover the acceptance criteria mentioned in 3.2.P.2.2.1 under formulation development and in section 3.2.P.5 under Control of finished product for dissolution testing is NLT 80% in 30 minutes while as per available information of innovator's product the drug should be released in 15 minutes.	"As per FDA dissolution data base, Empagliflozin dissolution criteria has been refer to FDA's dissolution Guidance, 2018 which is (Dissolution Testing and Acceptance criteria for immediate release solid oral dosage form drug products containing high solubility drug substances) updated on 07/02/2020. According to FDA's dissolution guidance, 2018 (Dissolution Testing and Acceptance criteria for immediate release solid oral dosage form drug products containing high solubility drug substances); for immediate release solid oral dosage form the dissolution criterion is Q=80% in 30 minutes.

Remarks:

According to available literature of innovator's product on the official website of USFDA the drug should be released in 15 minutes.

Response by the firm:

- The firm has revised the dissolution specifications as per the innovator's product i.e NLT 80% of labelled amount in 15 minutes.
- The firm has submitted stability data of 03 more batches. The detail of which is given in the following table.

Batch No.	TCY005	TCY006
Batch Size	5000 tablets	5000 tablets
Manufacturing Date	09/2021	09/2021
Date of Initiation	22/09/2021	22/09/2021
API Lot No.	20060201	20060201
Frequency	0, 1 (months)	0, 1 (months)

• The firm has submitted Audit trail report for Batch No. TCX008 & TCX009 for stability testing. • The firm has submitted record of digital data logger for humidity and temperature for accelerated as well as for real time stability. • The relevant chromatograms and raw data sheets are submitted. • Copy of attested Invoice No. WD202003005 dated 28/07/2020 from DRAP Lahore is submitted. For API lot No. 20060201 along with the certificate of analysis.	
A brief description of process validation including the proposed protocol shall be described and submitted.	The firm has submitted manufacturing process validation protocol for the applied product including description regarding purpose, scope, contents of validation, analytical procedure along with product development details, manufacturing process flow chart and other relevant details.
Approval of GMP/drug manufacturing license from the concerned authority of country of origin should be submitted.	The firm has submitted copy of drug manufacturing license No. Anhui 20190399 valid till 31/12/2025.

Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of ~~ful~~ applicable fee 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.**

The Board directed the firm to submit the data of dissolution testing as per revised dissolution specifications as set by the innovator (i.e. in 15minutes 80% release) at batch release for the first 02 commercial batches and submit data to PE&R division.

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

56.	Name, Address of Applicant / Marketing Authorization Holder	M/s Bio-Labs (Pvt).Ltd Plot No. 145 industrial 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. 7210 dated 04-03-2021
	Details of fee submitted	PKR 20,000/-: dated 23-10-2020
	The proposed proprietary name / brand name	Empamet 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 tablets
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product	In-House

	specifications	
	Proposed Pack size	2 x 7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	EMA approved.
	For generic drugs (me-too status)	Xenglu-Met 12.5/850mg by Hilton Pharma.
	GMP status of the Finished product manufacturer	GMP certificate issued based on inspection conduct 23-4-2019, valid upto 22-4-2022.
	Name and address of API manufacturer.	Empagliflozin: Shanghai Pharma Group Changzhou Kony pharmaceutical Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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. 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 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 for drug substance as well as for the impurities, batch analysis and justification of specification, detail of reference standard, container closure system and stability studies of drug substance.
	Stability studies	Empagliflozin: • 48 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: EGF20151201, EGF20151202 & EGF20151203 Metformin HCl: • 48 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):	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 by performing all the quality test against the reference product Synjardy 12.5/850mg. Comparative dissolution for all the quality tests for their product against the reference product. Synjardy 12.5/850mg. The results are within the acceptable limits.
	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	Empagliflozin: Shanghai Pharma Group Changzhou Kony pharmaceutical Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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.	EGF20180801, MEF/18122462		
Description of Pack (Container closure system)	Alu-Alu blister pack of 2 x 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	EMT-016	EMT-017	EMT-017
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	05-2019	05-2019	05-2019
Date of Initiation	18-5-19	18-5-19	18-5-19
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empaglif 10mg & 25mg tablet in 296th meeting
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 No. JS20170734 valid till 25/12/2022. Metformin HCl:

		Copy of GMP certificate No. 1801541 valid till 09-01-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/09/2018 for Empagliflozin, Empagliflozin W/S, Empagliflozin Impurity A, Empagliflozin Impurity B along with the attested invoice No. PSPW-180904 dated 27/09/2018. Metformin HCl: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/03/2019 for Metformin HCl along with the attested invoice No. EXP/2411/18-19 dated 27/03/2019.
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 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 and HPLC CFR Compliance record.
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:

Observations	**Response by the firm**
Analytical Method Verification/Validation studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for Empagliflozin as well as for Metformin Hydrochloride should be submitted in section 3.2.S.4.3 under Validation of Analytical Procedures.	• Analytical method verification studies performed by drug product manufacturer including specificity, accuracy and precision are submitted along with the relevant chromatograms and data sheets. • The specificity parameter of validation/verification studies is performed by taking a blank solution instead of spiking/force degradation against the test solution containing the sample. The firm has responded that the test is performed by taking blank solution because the impurities were analysed individually and there is no peak for any impurity interacting with peak of drug substance that is empagliflozin. • The firm has not clarified the specificity test procedure selected for Metformin HCl (analysis is done by using titration method) wherein performance of blank determination is carried out. Moreover, USP-43 describes the HPLC method for analysis for content estimation of Metformin but the firm has performed the assay by using titration method. • The firm has not submitted revised method for analysis of Metformin HCl as described by USP-43 nor the verifications studies are submitted.

Decision: The Board deferred the case for submission of analytical method verification studies (including specificity, accuracy and method precision) for drug substance performed by drug product manufacturer according to the official monograph present tin USP-43.

57.	Name, Address Of Applicant / Marketing Authorization Holder	M/s Bio-Labs (Pvt).Ltd Plot No. 145industrial Triangle Kahuta road Islamabad.
	Name, address of	M/s Bio-Labs (Pvt).Ltd

	Manufacturing site.	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. 7857 dated 10-03-2021
	Details of fee submitted	PKR 20,000/-: dated 23-10-2020
	The proposed proprietary name / brand name	Empamet 5/500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin ……..5mg Metformin HCl……..500mg
	Pharmaceutical form of applied drug	Film coated tablets
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Xenglu-Met 5/500mg by Hilton Pharma.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 23-4-2019, valid upto 22-4-2022.
	Name and address of API manufacturer.	Empagliflozin: Shanghai Pharma Group Changzhou Kony pharmaceutical Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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. 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 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 for drug substance as well as for the impurities, batch analysis and justification of specification, detail of reference standard, container closure system and stability studies of drug substance.
	Stability studies	Empagliflozin: • 48 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: EGF20151201, EGF20151202 & EGF20151203 Metformin HCl: • 48 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):	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 by performing all the quality test against the reference product Synjardy 5/500mg. Comparative dissolution for all the quality tests for their product against the reference product. Synjardy 5/500mg. The results are within the acceptable limits.
	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	Empagliflozin: Shanghai Pansopharm Technology Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, China Metformin HCl: Aarti Drugs Limited Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat, INDIA.
API Lot No.	EGF20180801, MEF/18122462
Description of Pack (Container closure system)	Alu-Alu blister pack of 2 x 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: 24 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	EMT-007	EMT-008	EMT-009
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	04-2019	04-2019	04-2019
Date of Initiation	1-5-19	1-5-19	1-5-19
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empaglif 10mg & 25mg tablet in 296th meeting
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 No. JS20170734 valid till 25/12/2022. Metformin HCl: Copy of GMP certificate No. 1801541 valid till 09-01-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/09/2018 for Empagliflozin, Empagliflozin W/S, Empagliflozin Impurity A, Empagliflozin Impurity B along with the attested invoice No. PSPW-180904 dated 27/09/2018. Metformin HCl: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/03/2019 for Metformin HCl along with the attested invoice No. EXP/2411/18-19 dated 27/03/2019.
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 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 and HPLC CFR Compliance record.
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:

Observations	**Response by the firm**
Analytical Method Verification/Validation studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for Empagliflozin as well as for Metformin Hydrochloride should be submitted in section 3.2.S.4.3 under Validation of	• Analytical method verification studies performed by drug product manufacturer including specificity, accuracy and precision are submitted along with the relevant chromatograms and data sheets. • The specificity parameter of validation/verification studies is performed by taking a blank solution instead of spiking/force degradation against the test solution containing the sample. The firm has responded that the test is performed by taking blank solution because the impurities were analysed individually and there is no peak for any impurity interacting with peak of drug substance that is empagliflozin. • The firm has not clarified the specificity test procedure selected for

Analytical Procedures.		Metformin HCl (analysis is done by using titration method) wherein performance of blank determination is carried out. Moreover, USP-43 describes the HPLC method for analysis for content estimation of Metformin but the firm has performed the assay by using titration method. • The firm has not submitted revised method for analysis of Metformin HCl as described by USP-43 nor the verifications studies are submitted.
Decision: The Board deferred the case for submission of analytical method verification studies (including specificity, accuracy and method precision) for drug substance performed by drug product manufacturer according to the official monograph present tin USP-43.		
58.	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. 7858 dated 10-03-2021
	Details of fee submitted	PKR 20,000/-: dated 23-10-2020
	The proposed proprietary name / brand name	Empamet 5/1000mg 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 tablets
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 7’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Xenglu-Met 5/1000mg by Hilton Pharma.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 23-4-2019, valid upto 22-4-2022.
	Name and address of API manufacturer.	Empagliflozin: Shanghai Pharma Group Changzhou Kony pharmaceutical Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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. 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 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 for drug substance as well as for the impurities, batch analysis and justification of specification, detail of reference standard, container closure system and stability studies of drug substance.
	Stability studies	Empagliflozin: • 48 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: EGF20151201, EGF20151202 & EGF20151203 Metformin HCl: • 48 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):	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 by performing all the quality test against the reference product Synjardy 5/1000mg. Comparative dissolution for all the quality tests for their product against the reference product. Synjardy 5/1000mg. The results are within the acceptable limits.

	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	Empagliflozin: Shanghai Pansopharm Technology Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, China Metformin HCl: Aarti Drugs Limited Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat, INDIA.		
API Lot No.	EGF20180801, MEF/18122462		
Description of Pack (Container closure system)	Alu-Alu blister pack of 2 x 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	EMT-010	EMT-011	EMT-012
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	04-2019	04-2019	04-2019
Date of Initiation	6-5-19	6-5-19	6-5-19
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empaglif 10mg & 25mg tablet in 296th meeting
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 No. JS20170734 valid till 25/12/2022. Metformin HCl: Copy of GMP certificate No. 1801541 valid till 09-01-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/09/2018 for Empagliflozin, Empagliflozin W/S, Empagliflozin Impurity A, Empagliflozin Impurity B along with the attested invoice No. PSPW-180904 dated 27/09/2018. Metformin HCl: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/03/2019 for Metformin HCl along with the attested invoice No. EXP/2411/18-19 dated 27/03/2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.

	data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail and HPLC CFR Compliance record.
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:

Observations	**Response by the firm**
Analytical Method Verification/Validation studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for Empagliflozin as well as for Metformin Hydrochloride should be submitted in section 3.2.S.4.3 under Validation of Analytical Procedures.	• Analytical method verification studies performed by drug product manufacturer including specificity, accuracy and precision are submitted along with the relevant chromatograms and data sheets. • The specificity parameter of validation/verification studies is performed by taking a blank solution instead of spiking/force degradation against the test solution containing the sample. The firm has responded that the test is performed by taking blank solution because the impurities were analysed individually and there is no peak for any impurity interacting with peak of drug substance that is empagliflozin. • The firm has not clarified the specificity test procedure selected for Metformin HCl (analysis is done by using titration method) wherein performance of blank determination is carried out. Moreover, USP-43 describes the HPLC method for analysis for content estimation of Metformin but the firm has performed the assay by using titration method. • The firm has not submitted revised method for analysis of Metformin HCl as described by USP-43 nor the verifications studies are submitted.

Decision: The Board deferred the case for submission of analytical method verification studies (including specificity, accuracy and method precision) for drug substance performed by drug product manufacturer according to the official monograph present tin USP-43.

59.	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. dated 10-03-2021
	Details of fee submitted	PKR 20,000/-: dated 23-10-2020
	The proposed proprietary name / brand name	Empamet 5/850mg 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 tablets
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	EMA Approved.
	For generic drugs (me-too status)	Xenglu-Met 5/850mg by Hilton Pharma.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 23-4-2019, valid upto 22-4-2022.
	Name and address of API manufacturer.	Empagliflozin: Shanghai Pharma Group Changzhou Kony pharmaceutical Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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. 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 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 for drug substance as well as for the impurities, batch analysis and justification of specification, detail of reference standard, container closure system and stability studies of drug substance.
	Stability studies	Empagliflozin: • 48 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: EGF20151201, EGF20151202 & EGF20151203 Metformin HCl: • 48 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):	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 by performing all the quality test against the reference product Synjardy 5/850mg. Comparative dissolution for all the quality tests for their product against the reference product. Synjardy 5/850mg. The results are within the acceptable limits.
	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	Empagliflozin: Shanghai Pansopharm Technology Co., Ltd. Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, China Metformin HCl: Aarti Drugs Limited Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat, INDIA.		
API Lot No.	EGF20180801, MEF/18122462		
Description of Pack (Container closure system)	Alu-Alu blister pack of 2 x 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	EMT-013	EMT-014	EMT-018
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	05-2019	05-2019	05-2019
Date of Initiation	13-5-19	13-5-19	13-5-19
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empaglif 10mg & 25mg tablet in 296th meeting

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 No. JS20170734 valid till 25/12/2022. Metformin HCl: Copy of GMP certificate No. 1801541 valid till 09-1-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/09/2018 for Empagliflozin, Empagliflozin W/S, Empagliflozin Impurity A, Empagliflozin Impurity B along with the attested invoice No. PSPW-180904 dated 27/09/2018. Metformin HCl: Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis" dated 27/03/2019 for Metformin HCl along with the attested invoice No.EXP/2411/18-19 dated 27/03/2019.
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 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 and HPLC CFR Compliance record.
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.

Remarks OF Evaluator:

Observations	**Response by the firm**
Analytical Method Verification/Validation studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for Empagliflozin as well as for Metformin Hydrochloride should be submitted in section 3.2.S.4.3 under Validation of Analytical Procedures.	• Analytical method verification studies performed by drug product manufacturer including specificity, accuracy and precision are submitted along with the relevant chromatograms and data sheets. • The specificity parameter of validation/verification studies is performed by taking a blank solution instead of spiking/force degradation against the test solution containing the sample. The firm has responded that the test is performed by taking blank solution because the impurities were analysed individually and there is no peak for any impurity interacting with peak of drug substance that is empagliflozin. • The firm has not clarified the specificity test procedure selected for Metformin HCl (analysis is done by using titration method) wherein performance of blank determination is carried out. Moreover, USP-43 describes the HPLC method for analysis for content estimation of Metformin but the firm has performed the assay by using titration method. • The firm has not submitted revised method for analysis of Metformin HCl as described by USP-43 nor the verifications studies are submitted.

Decision: The Board deferred the case for submission of analytical method verification studies (including specificity, accuracy and method precision) for drug substance performed by drug product manufacturer according to the official monograph present tin USP-43.

Case No. 02: Registration applications of Imported Products submitted on Form-5.F.
New Cases:

60.	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 SABA İlaç Sanayii ve Ticaret A.Ş. Halkali Merkez Mah. Basın Ekspres Cad. No: 1 34303 Küçükçekmece - 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) • Firm has submitted original, legalized COPP certificate (No. 2020/1456) dated 03-06-2020 issued by Republic of TURKEY MEDICINE AND MEDICAL DIVICES AGENCY For EPIRUBICIN HYDROCHLORIDE 10MG 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 SABA ILAC SAN. VE TIC.A.S Turkey authorized M/s AMgomed to apply for registration, for marketing, distribution and sale of below mentioned product; Pirucin 10mg /5ml LYO.I.V/INTRAVESICAL.ING 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.7449 : 08-003-2021
	Details of fee submitted	PKR 100,000/-: 30-09-2020
	The proposed proprietary name / brand name	PIRUCIN 10 mg Lyophilized Powder for Solution for IV/Intravesical Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Epirubicin hydrochloride……..10mg

Pharmaceutical form of applied drug	Lyophilised powder for solution for I.V/ Intravesical Injection
Pharmacotherapeutic Group of (API)	Cytotoxic antibiotics and related substances (Anthracyclines and related substances)
Reference to Finished product specifications	In-House
Proposed Pack size	1's
Proposed unit price	As per SRO
The status in reference regulatory authorities	Epirubicin Actavis 10mg Powder for Injection (type I glass vial) by M/s Medis Pharma, TGA Australia Approved.
For generic drugs (me-too status)	Ciazil Injection 10mg vial (5ml) by M/s Rotexmedica (R#063978)
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	Zhejiang Hisun Pharmaceutical Co., Ltd. 56 Binhai Road, Jiaojiang District Taizhou City, Zhejiang Province 318000 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, solubilities, physical form, manufacturers, description of manufacturing process and controls, 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 5oC±3 for 36 months of 3 batches • Accelerated stability study is conducted at 25oC±2 and 60%RH±5% for 6 months of 3 batches Batches: B140101, B140102, B140103
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 the reference product Farmorubicin RD trockensub 10mg C solve Amp by M/s Pfizer AG, Zurich Switzerland by performing quality tests including appearance, appearance of solution, pH, water content, asaay of API and preservative against the applied product (B:2FN0045).
Analytical method validation/verification of product	The firm has submitted relevant data including analytical method validation for the drug product for assay method of drug substance, preservative including the impurities

		and related substances.
	Container closure system of the drug product	Pirucin Lyophilised Powder for I.V./Intravesical Injection is packed in colourless Type III glass vial, butyl rubber lyophilisation stopper, aluminium cap with flip-off component.
	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: A035348, A035349, A035350

Evaluation by PEC:

- In-use stability after reconstitution with WFI is submitted. At 25ºC the assay is well in the limits till 24 hours and at 2-8ºC till 28 hours.

Observations	**Response**
The primary container used for reference product is Type I glass vial while for the applied product type III glass vial is used, please provide scientific justification considering USP chapter <660>.	The firm has stated that as per USP chapter <660>, "Type I glass containers are suitable for most products for parenteral and non-parenteral uses. Type II glass containers are suitable for most acidic and neutral aqueous products. Type II containers are also used for alkaline parenteral products where stability data demonstrate their suitability. *Type III glass containers are not used for parenteral products or for powders for parenteral used, except where suitable stability test data indicate that type III glass is satisfactory*". Based on this explanation and because of we have 24 months stability data, it is a suitable to use type III glass vial material for this product.
Provide scientific justification of the specifications for the finished product in detail in section 3.2.P.5.6 under Justification of Specifications.	The firm has submitted justification of specifications for the drug product and stated, "Control of the quality of the finished product is achieved by the use of a combination of in-process and appropriate release and shelf life specifications by taking into account EMA guidelines, pharmacopoeial general chapters and ICH guidelines".

Decision: Since the primary container closure is Type III glass vial for the applied product while USP does not recommend Type III glass vials for parenteral product as well as the container closure for the reference product is Type I glass vial. Therefore, the Board decided to deferred the case and directed the firm to switch to Type I glass vial accordingly.

61.	Name, address of Applicant / Importer	M/s Mediair Pharma, 178-A Firdousi Lane, Tariqabad Rawalpindi Cantt.
	Details of Drug Sale License of importer	DSL No: 01-374-0176-026469D Address: Mediair Pharma, 178-A Firdousi Lane Tariqabad Rawalpindi Cantt. Address of Godown: 178-A Firdousi Lane Tariqabad Rawalpindi Cantt. Validity: 03/04/2022 Status: Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Xian Libang Pharmaceutical Co., Ltd., No. 22 Keji Yi road, Xi'an Hi-tech Industrial Development Zone, Xi'an City, Shaanxi, China.
	Name, address of manufacturer(s)	M/s Xian Libang Pharmaceutical Co., Ltd., No. 22 Keji Yi road, Xi'an Hi-tech Industrial Development Zone, Xi'an City, Shaanxi, China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	

• Original legalized CoPP (certificate No. 20190009) issued by Shaanxi Medical Products Administration valid till 26/06/2021. The product is available in free sale in exporting country. The facilities and operations conform to Chinese-GMP. • Original legalized GMP certificate No. SN20180317 valid till 13/12/2023 issued by China Food and Drug Administration.	
Details of letter of authorization / sole agency agreement: • Authorization letter dated 21/09/2020 (3 years validity from date obtaining registration certificate) from M/s Xi'an Libang Pharmaceutical Co., Ltd., is submitted whereby M/s Mediair Pharma is declared as the sole agent 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.630 : 13-04-2021
Details of fee submitted	PKR 100,000/-: 09-10-2020
proposed proprietary name / brand name	Propofol injectable Emulsion 200mg/20ml
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Propofol……10mg
Pharmaceutical form of applied drug	White colored, sterile, nonpyrogenic emulsion (oil in water) for IV infusion
Pharmacotherapeutic Group of (API)	Anesthetic
Reference to Finished product specifications	In-House
Proposed Pack size	5 ampoules in one box
Proposed unit price	As per SRO
The status in reference regulatory authorities	Diprivan Injectable emulsion 10mg/ml (200mg/20ml), USFDA Approved.
For generic drugs (me-too status)	Fresofol Injection 1% 10mg/ml (20ml), reg. No. 27384
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 Xi'an Libang Pharmaceutical Co., Ltd., West-Door outside, Guo town, Chencang District, Baoji City, China. GMP certificate No. SN20180273 valid till 22/04/2023
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 including I, II and unspecified impurity (with the details of reference standards), specifications, analytical procedures and its validation, batch analysis, 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 and60%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: 060101, 060102, 060103
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, compatibility of all the excipients with the API, validation of analytical procedures, batch analysis, impurity testing, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is established against the reference product Diprivan Injectable emulsion 10mg/ml, USFDA Approved by performing al the quality tests including pH, identification, globule size, free fatty acid content, peroxide valueimputiety testing, assay etc.
Analytical method validation/verification of product	Firm has submitted relevant data including analytical method validation for the drug product including the impurities
Container closure system of drug product	Type I glass ampoule (20ml), 5amp in one box.
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 12 months of 3 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches

Evaluation by PEC:

- CoPP is expired. However, it was valid at the time submission of Dossier.

Observations	**Response by the firm**
Since the monograph of the applied product is present in USP while the method and specifications are adopted from Chinese Pharmacopoeia (C.P.) which are different from specifications and method described in USP, therefore you are required to submit analytical method validation studies along with the comparison of specifications of Chinese Pharmacopoeia and USP to establish that the Chinese Pharmacopoeial specifications are more stringent than USP. It should be noted that USP describes Impurity A (2,6-Diisopropylphenyl isopropyl ether) which has not been described by Chinese Pharmacopoeia (C.P.), instead of; C.P. describes unspecified impurity with specification limit of ≥0.2%.	The firm has stated that the Chinese pharmacopoeial specifications are stricter and tighter than USP and submitted validation of analytical methods along with a comparison of specifications described in USP and of Chinese Pharmacopoeia.

Test	**USP limits**	**Chinese Pharmacopoeial limits**
Identification (HPLC)	The retention time of the major peak of the sample solution corresponds to that of standard solution	The retention time of the major peak of the sample solution corresponds to that of the standard solution
pH	4.5-8.5	6.0-8.5
Globule size distribution	PFAT5 should be less than 0.05%	PFAT5 should be less than 0.05%
	Mean droplet diameter should be less than 0.5um	Mean droplet diameter should be less than 0.5um

Free fatty acid	NMT 5mmol/L	The volume of sodium hydroxide VS (0.001mol/L) consumed by test solution should not be more than that by reference solution.
Peroxide value	Not included in USP	The consumed sodium thiosulfate VS (0.01mol/L)
Impuity A	NMT 0.5%	NMT 0.1%
Impurity B	NMT 0.5%	NMT 0.1%
Unspecified	Not included in USP	NMT 0.2%
Anisidine	Not included in USP	NMT 5.0
LPC**	Not included in USP	NMT 2mg/ml
LPE***	Not included in USP	NMT 06mg/ml
Glycerol	Not included in USP	20.2-24.8mg/ml
Phosphorus	Not included in USP	0.40-0.50mg/ml
Bacterial endotoxine	Less than 0.33EU/mg	Less than 0.33EU/mg
Sterility test	No evidence of microbial growth	No evidence of microbial growth
Assay	90-110%	95-105%
Osmolality	Not included in USP	280-330mOsmol/kg

* Percentage of fat residing in globules larger than 5um.
**Lyosophosphatidylcholine
***Lysophosphatidylethanolamine

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 for revision of specifications from In-house to USP as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021

62.	Name, address of Applicant / Importer	M/s Al-Habib Pharmaceuticals, 81 B Block, S.M.C.H.S Karachi.
	Details of Drug Sale License of importer	DSL No: Address: Address of Godown: Validity: Status: Drug License by way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Jodas Expoim Pvt. Ltd. Plot No. 55, Phase-3, Biotech Park, Karkapatla (V), Markook (M), Siddipet, Telangana State Pin-502 279 India.
	Name, address of manufacturer(s)	M/s Jodas Expoim Pvt. Ltd. Plot No. 55, Phase-3, Biotech Park, Karkapatla (V), Markook (M), Siddipet, Telangana State Pin-502 279 India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. L.Dis.No.3349/E1/2020) valid till 08/08/2021 issued by Drugs control Administration Telangana, India. The product is available in free sale in exporting country. The facilities and operations conform to Chinese-GMP.	
	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.7094 : 03-03-2021
	Details of fee submitted	PKR 100,000/-: 12-02-2021
	The proposed proprietary name / brand name	AHP-Cita 500mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Capecitabine……500mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specification	In-house
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xeloda film coated tablet 500mg by M/ s Hoffmann LA Roche, USFDA Approved.
	For generic drugs (me-too status)	CAPEGARD-500MG FILM COATED TABLETS by M/s AJ Mirza Pharma, Reg. No. 72593
	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 Acebright (India) Pharma Private Limited (formerly Cdymax (India) Pharma Privtae Limited), No. 77D & 116/117, KIADB Industrial Area, Jigani Bangalore-560 105, Kamataka, 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 including I, II and unspecified impurity (with the details of reference standards), specifications, analytical procedures, batch analysis, 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 and60%RH±5% for 24 months of 3 batches • Real time stability studies have been conducted at

		30oC±2 and65%RH±5% for 12 months of 3 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batch size: CD100139, CD100142, CD120006
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, compatibility of excipients with the drug substance since the excipients used in manufacturing of applied product are different from the excipients used in the manufacturing of the reference product, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, compatibility of all the excipients with the API, validation of analytical procedures, batch analysis, impurity testing, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Comparative dissolution profile of the applied product against the reference product Xeloda approved by USFDA (B:U9146B01) is submitted in pH 1.2, 4.5 and 6.8.
	Analytical method validation/verification of product	Not submitted
	Container closure system of the drug product	10 tablets are packed in Alu/Alu blister, aluminium cold forming foil. 12 blisters packed in printed carton.
	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 Batch size: NV10015CB50, NV10215CB50, NV10115CB50
Observations		**Response by the firm**
Analytical method for assay/quantitative estimation of Capecitabine is present in USP, therefore, method verification studies including specificity, accuracy and method-precision should be performed and subsequently be presented in section 3.2.S.4.3 under Validation of Analytical Procedures.		The firm has submitted complete analytical method validation report for residual solvents including specificity, accuracy, linearity, LOQ, LoD, robustness and precision but has not submitted the analytical method verification studies for analysis of drug substance.
The official monograph for Capecitabine tablets is present in USP while the testing of the applied product is done according to In-House standard, please justify scientifically by comparing the specifications & methods described in USP with methods & specifications of In-House standard.		Justification is not submitted.
The comparison of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted for establishing pharmaceutical equivalence. Moreover, data of Comparative dissolution profile is submitted against the reference product Xeloda without the submission of calculations of f2 and f1 values, please submit complete data.		Comparative dissolution profile of the applied product against the reference product Xeloda approved by USFDA (B:U9146B01) is submitted in pH 1.2, 4.5 and 6.8. The values for F1 and F2 are in the acceptable limits.
Product specific sole agency agreement is required.		Copy of distribution agreement is submitted and M/s Al-Habib Pharmaceuticals is designated as Distributor by M/s

	Jodas Expoim Pvt Ltd for different product s including the applied product.
Submit valid copy of drug sale license.	DSL No: 1245 Address: Al Habib Pharmaceuticals, 81-B Block B, SMCHS Karachi. Address of Godown: 1. Plot No. 10 Sector 25 KIA Karachi. 2. HT-8, Landhi Industrial Area, Karachi. Validity: 18/05/2022 Status: Drug License by way of Wholesale

Decision: The Board deferred the case for the following;

- **Submission of analytical method verification studies (including specificity, accuracy and method precision) for analysis of drug substance performed by drug product manufacturer.**
- **Clarification / Scientific justification since the monograph of the applied product is present in USP and the applied product is developed according to In-House specifications.**

63.	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 25ºC±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 (30ºC±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 Calcium folinate (Leucovorin Calcium) is present in USP while the testing of the applied product is done according to In-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.	The firm has submitted a comparison of specifications of Chinese Pharmacopoeia and 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	"The difference of excipient and brand of reagents

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.	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: 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.**

64.	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: 1162 Address: Ghazali Borthers19-SR-7, Campbel Street, Azzainab Court, 1st Floor, Karachi- Pakistan Validity: 28th Oct 2021 Status: Drug License by the way of Wholesale
	Name and address of marketing authorization holder (abroad)	**MAH Holder:** M/s Jiangsu Huayang Pharmacuticals CO., LTD., NO.21, ChangJiang Road, Si Yang County, P.R.China **EXPORTER:** M/s Shanghai Pharmaceutical CO., LTD., No.450 FENGLIN ROAD, shanghai 200032, China
	Name, address of manufacturer(s)	M/s Jiangsu Huayang Pharmacuticals CO., LTD., NO.21, ChangJiang Road, Si Yang County, P.R.China
	Name of exporting country	China

Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)

- Copy of GMP certificate No. JS20191088 valid till 27/06/2024 is submitted.
- Original legalized CoPP issued by Jiangsu province Drug Administration Suqian Inspection Branch, China on 12/03/2020.
  The applied product is available in market of exporting country for free sale.
  The facilities sand operations conform to WHO-GMP.

Details of letter of authorization / sole agency agreement

- Copy of agency agreement is submitted which is signed by the exporter, manufacturer and the importer (M/s Ghazali Brothers) whereby M/s Ghazali Brothers is declared as a solo agent for the exporter for registration, tender and marketing for Gentamycin injection 80mg/2ml.

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. 7317 : 05-03-2021
	Details of fee submitted	PKR 100,000/- : 10-02-2021
	The proposed proprietary name / brand name	GENTA-S Injection 80mg/2ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml ampoule contains: Gentamycin Sulphate …….80mg
	Pharmaceutical form of applied drug	Solution for injection in ampoule (intramuscular injection) I.M
	Pharmacotherapeutic Group of (API)	Antibiotic of aminoglycosides class
	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)	Gentamed Injection 80mg/2ml ampoule by M/s Mediate Pharmaceuticals, Reg. No. 53243
	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 Fuan Pharmaceutical Group, Yantai Justaware Pharmaceutical Co., Ltd., No.1,Yanfu Road, Zhifu District, Yantai 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 analytical procedures and validation for impurities, 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 48 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: 16021001, 16021002, 16021003
	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 the reference product Gentamycin sulfate BP solution for injection 2ml by M/s Hameln Pharma ltd, UK by performing all the quality tests.
	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 low borosilicate glass ampoule (2ml)
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30ºC±2 and 65%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: 6514092031, 14092231, 14092331

Evaluation by PEC:

Please provide complete method of analysis for Gentamicin Sulfate drug substance along with the complete method validation / verification studies.	The firm has submitted specifications and complete method of analysis for drug substance in section 3.2.S.4 under Control of Drug Substance along with the verification studies including specificity, accuracy and precision for related substances and drug substance.
Pharmaceutical equivalence studies are not provided with the relevant details. Provide the required data of pharmaceutical equivalence against the reference product.	Pharmaceutical equivalence is established against the reference product Gentamycin sulfate BP solution for injection 2ml by M/s Hameln Pharma ltd, UK by performing all the quality tests.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

65.	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: 1162 Address: Ghazali Borthers19-SR-7, Campbel Street, Azzainab Court, 1st Floor, Karachi- Pakistan Validity: 28th Oct 2021 Status: Drug License by the way of Wholesale
	Name and address of marketing authorization holder (abroad)	**MAH Holder:** M/s Jiangsu Huayang Pharmacuticals CO., LTD., NO.21, ChangJiang Road, Si Yang County, P.R.China **EXPORTER:** M/s Shanghai Pharmaceutical CO., LTD., No.450 FENGLIN ROAD, shanghai 200032, China
	Name, address of manufacturer(s)	M/s Jiangsu Huayang Pharmacuticals CO., LTD., NO.21, ChangJiang Road, Si Yang County, P.R.China
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate) • Copy of GMP certificate No. JS20191088 valid till 27/06/2024 is submitted. • Original legalized CoPP issued by Jiangsu province Drug Administration Suqian Inspection Branch, China on 12/03/2020. The applied product is available in market of exporting country for free sale. The facilities sand operations conform to WHO-GMP.	
	Details of letter of authorization / sole agency agreement	

• Copy of agency agreement is submitted which is signed by the exporter, manufacturer and the importer (M/s Ghazali Brothers) whereby M/s Ghazali Brothers is declared as a solo agent for the exporter for registration, tender and marketing for Water for Injection 5ml.	
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. 7393 : 09-03-2021
Details of fee submitted	PKR 100,000/- : 06-08-2021
The proposed proprietary name / brand name	Sterile WFI (water for injection) 5ml
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains: Sterile Water for injection…..5ml
Pharmaceutical form of applied drug	Sterile water for injection
Pharmacotherapeutic Group of (API)	Water for injection/diluent/solvent
Reference to Finished product specifications	B.P
Proposed Pack size	10 ampoules (5ml) per box
Proposed unit price	As per SRO
The status in reference regulatory authorities	Sterile water for injection 5ml glass ampoule by M/s Pfizer, MHRA Approved.
For generic drugs (me-too status)	Water for injection 5ml by M/s GSK, Reg. No. 088255
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, batch analysis and justification of specification, reference standard, container closure system and stability studies of the product.
Name, address of drug substance manufacturer	N/A
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, 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)	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, 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 against Water for Injection By M/s Hameln Pharma Ltd., UK by performing all the tests mentioned in B.P.
	Analytical method validation/verification of product	N/A
	Container closure system of the drug product	Type I low borosilicate glass ampoule
	Stability study data of drug product, shelf life and storage conditions	Not submitted

Evaluation by PEC:

The official monograph for "water for injection in bulk" is present in B.P/Ph.Eur. which describes tests and specifications which are different from the tests and specifications as developed and set by the manufacturer for manufacturing of the applied product. Therefore, you are required to clarify by comparing the tests and specifications of B.P/Ph.Eur. and the in-house standards.	The firm has stated that, "The initial testing of performed on bulk is in-house. There is no active ingredient and its 100% water for injectiononly. Whereas the finished product is tested according to B.P.".
The validation/verification of analytical method has not been provided in the submitted dossier. Submit complete analytical method validation studies for the tests used for routine testing of "water for injection in bulk" and "sterile water for injection".	The testing of drug substance or drug product do not involve any analytical testing like HPLC or UV analysis. The testing only involves Impurities, pH, conductivity, microbiological sterility & Endotoxin etc which only requires a calibrated equipment and does not require performing validation or verification studies.
Please submit stability studies of ampoules containing 5ml WFI since the submitted stability is for 10ml WFI as per the following conditions; • Real time stability studies at 30ºC±2 and 65%RH±5% till claimed shelf lifeof 3 batches • Accelerated stability study conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches	• Real time stability studies have been conducted at 30ºC±2 and 65%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: 17100611, 17100711, 17100811

Decision: The Board deliberated that the testing on bulk water for injection is done according to the In-House specifications while the finished prouduct that is ampoules containing sterile water for injections is developed and tested according to British Pharmacopoeial monograph. Furthermore, the Board discussed that all the tests which are present in British Pharmacopoeial monograph of Bulk Water for Injection are also included in British Pharmacopoeial monograph of Sterile Water for Injection. Keeping in view th fact, The Board Approved the case as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

66.	Name, address of Applicant / Importer	M/S Excel Healthcare Laboratories Pvt Ltd., d-122, block-4 federal b area Karachi Pakistan
	Details of Drug Sale License of importer	**License No:** 001 **Address:** D-122 Block-4, Federal B Area Karachi.

	Godown: D-122 Block-4, Federal B Area Karachi. **Validity:** 08-08-2022. **Status:** License to sell drugs as distributor **Renewal:** N/A
Name and address of marketing authorization holder (abroad)	M/s AFT Pharmaceuticals Limited, PO box 33203, Takapuna, Auckland 0740, New Zealand
Name, address of manufacturer(s)	M/s S.M. Farmaceutici S.R.L. Zona Industriale, 85050 TITO , Italy
Name of exporting country	New Zealand

Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)

- Firm has submitted original, legalized CoPP certificate (No. 104098) dated 5th December 2019 issued by Ministry of Health New Zealand for Maxigesic IV Solution for Injection.
  The CoPP confirms free sale status of the product in exporting country.
- Firm has also provided GMP Certificate (N0. IT/138/H/2019) dated 23/7/2019 issued by AIFA Italian medicine Agency on the basis of inspection conducted on 29/03/2019.
- The firm has submitted copy of certificate of Suitability No. R1-CEP 1995-050-Rev 04 for Paracetamol. The certificate is verifiable from the website. The weblink is given below.

https://extranet.edqm.eu/4DLink1/4DCGI/Query_CEP?vSelectName=3&Case_TSE=none&vContains=1&vContainsDate=1&vtsubName=atabay+kimya+sanayi&vtsubDateBegin=&vtsubDateBtwBegin=&vtsubDateBtwEnd=&SWTP=1&OK=Search (accessed on 03/11/2021 at 12:33pm)

Details of letter of authorization / sole agency agreement

- Firm has submitted Original Legalized letter of distribution certificate from M/s AFT Pharmaceutical Ltd. The letter Confirms that the marketing authorization holder appoints M/s Excel Healthcare Laboratories (Pvt) Ltd to register their products in Pakistan for Maxigesic IV Solution for infusion to register, import, market, distribute, sell. The authorization letter is valid till 15th-01st-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. 1955: 02-03-2021
Details of fee submitted	PKR 50,000/-: 03-01-2021
The proposed proprietary name / brand name	Maxigesic IV Infusion 10mg/3mg
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Paracetamol……10mg Ibuprofen as sodium dihydrate…..3mg
Pharmaceutical form of applied drug	Clear and colourless solution for IV Infusion
Pharmacotherapeutic Group of (API)	Analgesic/Antipyretic
Reference to Finished product specifications	In house
Proposed Pack size	10 x 100ml vials

Proposed unit price	Rs. 700/- per vial
The status in reference regulatory authorities	Maxigesic IV Infusion by M/s AFT Pharmaceuticals, TGA Australia
For generic drugs (me-too status)	N/A
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 validation for drug substances as well as for the impurities, batch analysis and justification of specification, reference standard, container closure system and stability studies drug product. The firm has referred the certificate of suitability for Paracetamol.
Name, address of drug substance manufacturer	Ibuprofen Sodium Dihydrate: M/s Solara Active Pharma Sciences Limited, R.S.No:33 & 34, Mathur Road, Periyakalapet Puducherry 605014, India <u>Paracetamol:</u> M/s Atabay Kimya Sanayi Ve Ticaret AS Dilovasi Organize Sanayi Bolgesi 4. Kisim Sakarya Caddesi, No. 28 Gebze. Kocaeli 41400. Turkey.
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 validation for drug substances and impurities, batch analysis and justification of specification, detail of reference standard, container closure system and stability studies of Ibuprofen Sodium dihydrate. The firm has submitted copy of certificate of suitability for Paracetamol
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Ibuprofen Sodium Dihydrate: • Real time stability studies have been conducted at 30oC±2 & 65%RH±5% for 12 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: B3ISP160009, B3ISP160010, B3ISP160009.
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	Firm has submitted analytical method validation studies for the applied product.
Container closure system of the drug product	Type II glass vial with bromobutyl stopper & aluminium cap.
Stability study data of drug product, shelf	• Real time stability studies have been conducted at 30oC±2

	life and storage conditions	& 75%RH±5% for; 36 months of batches: C9280, C9281, C9282 & 24 months of batches: E0182, E0496 • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: C9280, C9281, C9282, E0182, E0496

Evaluation by PEC:

Observation	**Response**
Please submit S part of module II for Ibuprofen by providing relevant information under relevant section since you have referred to DMF and Module III for required information is different sections.	The firm has provided S part for Ibuprofen of QOS as per WHO-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 validation for drug substances as well as for the impurities, batch analysis and justification of specification, reference standard, container closure system and stability studies for Ibuprofen sodium.
Provide summary of analytical procedures in section 2.3.P.5.2 of QOS for drug product.	The firm has summarised the relevant information of analytical procedures in section 2.3.P.5.2.
Justification is required since the acceptance criteria for recovery is set from 95-105% for analytical validation studies of Accuracy parameter for impurities. Refer the guideline as well.	The acceptance criteria for impurities is set from 95-105% based on the experimental performances. The criteria 95-105% is set for unknown impurity. For the rest of the impurities the acceptance criteria is set from 98-102%. The firm has not referred any guideline for establishing the criteria.
Scientific justification is required since the assay results of 4-Aminophenol are out of specifications for all three batches of drug product at different timepoints of stability study data conducted at 30oC±2 & 75%RH±5% and 40oC±2 and 75%RH±5%.	"The product is designed as a hospital product and should be stored below 25ºC". "As described in Pharmaceutical Development, the product is temperature sensitive and stable for a shorter period (3 months) when stored at 40oC±2 and 75%RH±5% while at 30oC±2 and 75%RH±5% the stability profile is slightly longer from 12 to 18 months". "The hydrolysis of paracetamol producing impurity 4-aminophenol depends therefore on the factors pH, temperature and time. Hydrolysis is increased at higher pH, higher temperature and with time". "Nevertheless, the level of impurity 4-aminophenol at 25°C remains in compliance with the established specification of maximum 0.05% up to the end of shelf life (24 months). Therefore, the proposed shelf life is 24 months, when stored at or below 25°C, including transport".

Decision: The Board Deferred the case for;

- **Scientific justification since the assay results of 4-Aminophenol are out of specifications for all three batches of drug product at different timepoints of stability study data conducted at 30oC±2 & 75%RH±5% and 40oC±2 and 75%RH±5%.**
- **Furthermore, the Board directed the firm to provide indication of the applied product with respect to the dose of drug substances in the formulation.**

67.	Name, address of Applicant / Importer	M/s Biocare Pharmaceutica 807 Shadman-I, Lahore.
	Details of Drug Sale License of importer	DSL No.: 05-352-0063-032069D Address: Biocare pharamceutica 80 shadman-I district Lahore.

		Validity: 17/04/2022 Status: License to sell drugs as Distributor
	Name and address of marketing authorization holder (abroad)	M/s PT Dexa Medica, JI. Jend. Bambang Utoyo No. 138, Palembang, Indonesia
	Name, address of manufacturer(s)	M/s PT Ferron Par Pharmaceuticals, Kawasan Industri Jababeka I, JI. Jababeka VI Block J3, Cikarang, Bekasi, Indonesia.
	Exporting country	Indonesia
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. RG.01.05.32.321.08.19.0644) issued by National Agency of Drug and Food Control, Indonesia on 05/08/2019. The applied product is available in the market for free sale with a brand name of Levica. The facilities and operation conform to WHO-GMP.	
	Details of letter of authorization / sole agency agreement • The applicant has submitted copy of supply and distribution agreement signed by PT Dexa Medica and Biocar Pharmaceutica for Levobupivacaine 5mg/10ml infusion.	
	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 4077 Dated 04/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 30/12/2020
	The proposed proprietary name / brand name	L-Ascain solution for injection 50mg/10ml Alternate brand names: Levica L-Bup
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Levobupivacaine as hydrochloride monohydrate……..5mg
	Pharmaceutical form of applied drug	Intrathecal or epidural solution for injection
	Pharmacotherapeutic Group of (API)	Anesthetic
	Reference to Finished product specifications	In-house
	Proposed Pack size	1's×5 (50mg/10ml ampoule)
	Proposed unit price	Rs. 410/- per ampoule Rs. 2010/- per pack of 5 ampoules
	The status in reference regulatory authorities	Chircaine 5mg/ml infusion by M/s Abbvie Ltd., PL41042/0006, MHRA Approved.
	For generic drugs (me-too status)	N/A
	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.
	Name, address of drug substance manufacturer	M/s Pioneer Agro Industries (Pharmaceutical Division_ Plot No. 6,7,8,20 & 24 MIDC Industrial Area, Badlapur, Dist-Thane 421 503, Maharashtra State India.
	Module-III Drug Substance:	There are 02 polymorphic forms of Levobupivacaine hydrochloride. Stable polymorph is having a specific rotation of 14^{o} while the pseudopolymorph has a value of specific rotation equal to 6.5^{o}. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 66 months real time stability data at 30˚C ± 2˚C / 65% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches Batches: LBH/004/05/09, LBH/005/05/09, LBH/006/06/09
	Module-III Drug Product:	No compatibility studies are required since the qualitative composition of the drug product is similar to the reference product (Sodium Chloride, Hydrochloric acid, Sodium hydroxide, WFI). Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established against the innovator's product CHirocaine 5mg/ml injection by M/s Abbvie S.r.l Italy (batch no.: 1026457) by performing all the quality tests.
	Analytical method validation/verification of product	Validation studies of analytical method with satisfactory results of accuracy, specificity, linearity, precision etc are submitted.
	Container closure system of the drug product	Type I 10ml glass ampoule
	Stability study data of drug product, shelf life and storage conditions	• 24 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches Batches: 2971434, 2580972, 2781351 Batch Size: 4717 ampoules • 36 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches Batches: K-10427-00-F-SCU-1A,

		K-10427-00-F-PSC-1A, K-10427-00-F-PSC-2A Batch Size: 18,868 ampoules • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (Batches: 2971434, 2580972, 2781351, K-10427-00-F-SCU-1A, K-10427-00-F-PSC-1A, K-10427-00-F-PSC-2A) • In-Use stability of the applied product in Diluent (0.9% sodium chloride solution) with acceptable results till 7 days is submitted.

Evaluation by PEC-I:

Observations	**Response**
Product specific sole agency agreement is required.	The applicant has submitted copy of supply and distribution agreement signed by PT Dexa Medica and Biocare Pharmaceutica for Levobupivacaine 5mg/10ml infusion.
API used for manufacturing of the applied product is Levobupivacaine Hydrochloride Monohydrate while Levobupivacaine Hydrochloride is used for manufacturing the reference product, please clarify.	"Since the applied product is in solution for injection form manufactured by solubilizing the API in water for injection so the monohydrate that is previously bound with the API crystal will also become part of solution".
Justification is required since the titration method is adopted for analysis of drug substance as well as the applied product. However, HPLC method is adopted for identification test.	"Analytical method for drug substance is adopted from DMF and this titration method is similar to the assay method of Bupivacaine Hydrochloride given in USP monograph. However, the method used for analysis of drug product is HPLC method derived from the method present in USP for Ropivacaine Hydrochloride with slight modification of column dimension and flow rate'. "Identification of drug substance in drug product was taken from this assay procedure by HPLC". "The assay method for drug substance and drug product already validated as per ICH guidelines".
Justify the specification limit for R-enantiomer (impurity) that is 0.5% of the drug substance.	Since Levobupivacaine is the s-isomer of racemic Bupivacaine and the Biopharmaceutical review of Chirocaine (reference product) reveals the limit for R-enantiomer as 1.5%.

https://www.accessdata.fda.gov/drugsatfda_docs/nda/99/20997_CHIROCAINE_biopharmr.pdf (accessed on 08/11/2021 at 4:45pm).

2.0. PHYSICOCHEMICAL PROPERTIES & FORMULATION

Levobupivacaine HCL is a white crystalline solid that is soluble in water (>100 mg/mL). The partition coefficient (oleyl alcohol/water) is 1624 and the pKa is 8.09. The level of (R)-bupivacaine is controlled in the active ingredient specification to not more than 1.5%. Levobupivacaine Injection is a sterile, non-pyrogenic (pH 4.0-6.5) aqueous solution containing levobupivacaine hydrochloride equivalent to 2.5 mg/mL, 5.0 mg/mL, and 7.5 mg/mL of levobupivacaine base, sodium chloride for isotonicity, and Water for Injection. Sodium hydroxide and/or hydrochloric acid may be added to adjust the pH. Levobupivacaine Injection is preservative free and is available in 10 mL and 30 mL single dose vials.

Decision: The Board deferred the case for submission method of analysis for R-enantiomer (dextro rotatory) and limits for the estimated content.

68.	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	**DSL No.:** 05-352-0065-016174D **Address:** Himmel Pharmaceuticals (Pvt) Ltd 793 D, Block C,

		Faisal Town, District Lahore. **Godown: N/A** **Validity:** 06/02/2022 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. DA/6-110/2016/3284) issued by Directorate General of Drug Administration on 01/06/2020. The applied product is available in market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Copy of GMP certificate No. DA/6-11-/06/4950 dated 17/07/2019 on the basis of inspection conducted on 07/07/2018 (expired).	
	Details of letter of authorization / sole agency agreement • Copy of letter of authorization is submitted whereby M/s Himmel Pharmaceuticals is authorized to register and sell different products including Baricinix 2mg tablet.	
	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 4307 Dated 08/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 15/12/2020
	The proposed proprietary name / brand name	Baricinix 2mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Baricitinib……..2mg
	Pharmaceutical form of applied drug	Immediate release
	Pharmacotherapeutic Group of (API)	Antirheumatic/Immunosuppressant
	Reference to Finished product specifications	In-house
	Proposed Pack size	30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Olumiant tablet 2mg by M/s Eli Lilly, MHRA Approved.
	For generic drugs (me-too status)	N/A

	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.
	Name, address of drug substance manufacturer	M/s Beijing Mesochem Technology Co., Ltd., Floor 23, Building 9, Lippo Plaza, Economic and technological Development zone Beijing.(GMP certificate not provided)
	Module-III Drug Substance:	The API used belongs to BCS class III. The firm has submitted detail of the drug substance is classified in BCS Class IV. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25˚C ± 2˚C / 60% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (150522, 150825, 150718)
	Module-III Drug Product:	Batch analysis (3460009, 3460010, 3460011) Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has performed Pharmaceutical Equivalence against the reference product, Olumiant 2mg tablet by M/s Ely Lilly Nederland B.V, The Netherland (Batch number B123004) by performing quality tests. CDP (with acceptable results of f1 and f2) against the reference product Olumiant 2mg tablet by M/s Ely Lilly Nederland B.V, The Netherland. (Batch number B121901).
	Analytical method validation/verification of product	Data of analytical method validation is submitted including, specificity, accuracy, ruggedness, precision and linearity etc for assay of API and impurities as well.
	Container closure system of the drug product	White HDPE bottle with white screw cap containing 30 tablets and silica gel packed in a box of secondary package.
	Stability study data of drug product, shelf life and storage conditions	Batches: (3460009, 3460008, 3460007) Batch size: 18,333 tablets • 24 months real time stability data at 30˚C ± 2˚C /

		75% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

Observation	Response
Since the excipients used in the manufacturing of the product are different from the excipients use in manufacturing of reference product, therefore, compatibility of the excipients with API is required to be performed. The information should be presented under relevant section in module II and module III.	The firm has submitted that the excipients used are complying with current BP monograph except orange lake color Ph. Grade which complies with in-house specifications. These excipients are pharmaceutically inert substances. These excipients are used below "Inactive Ingredient Guide" limit of FDA. Extensive analysis of the product is done and satisfactory results of assay, dissolution and impurity profile are obtained.
As per available literature of the reference product, the dissolution specifications including dissolution medium and dissolution time are not same as selected for the dissolution testing of the applied product. The selected time point for dissolution testing of reference product is 30 minutes While the time point for dissolution testing is 45 minutes. Furthermore, 0.1N HCl solution is selected for applied product while the dissolution medium for the reference product is Acetate buffer (pH=4.5), please clarify.	"We have done dissolution test of Baricinix 2mg and 4mg tablets additionally by using dissolution medium pH 4.5 acetate buffer. We have used 18month passed controlled sample for Baricinix 2mg and 14 months passed controlled sample for Baricinix 4mg tablet and found following results; **Baricinix 2mg Tablet** **Test Batch** | **Dissolution medium** | **Time point** | **Result** B/N: 3460012 Mfg:Feb, 20 Exp:June, 22 | Acetate Buffer pH 4.5 | 30 mins | 85.4% **Baricinix 4mg Tablet** **Test Batch** | **Dissolution medium** | **Time point** | **Result** B/N: 3470006 Mfg: Jul, 20 Exp: June, 22 | Acetate Buffer pH 4.5 | 30 mins | 78.2%

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 for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021

69.	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	**DSL No.:** 05-352-0065-016174D **Address:** Himmel Pharmaceuticals (Pvt) Ltd 793 D, Block C, Faisal Town, District Lahore. **Godown: N/A** **Validity:** 06/02/2022 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Exporting country	Bangladesh

	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. DA/6-110/2016/3285) issued by Directorate General of Drug Administration on 01/06/2020. The applied product is available in market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Copy of GMP certificate No. DA/6-11-/06/4950 dated 17/07/2019 on the basis of inspection conducted on 07/07/2018 (expired).	
	Details of letter of authorization / sole agency agreement • Copy of letter of authorization is submitted whereby M/s Himmel Pharmaceuticals is authorized to register and sell different products including Baricinix 4mg tablet.	
	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 4307 Dated 08/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 15/12/2020
	The proposed proprietary name / brand name	Baricinix 4mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Baricitinib……..4mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Antirheumatic/Immunosuppressant
	Reference to Finished product specifications	In-house
	Proposed Pack size	30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Olumiant tablet 4mg by M/s Eli Lilly, MHRA Approved
	For generic drugs (me-too status)	N/A
	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.
	Name, address of drug substance manufacturer	M/s Beijing Mesochem Technology Co., Ltd., Floor 23, Building 9, Lippo Plaza, Economic and technological Development zone Beijing.

	Module-III Drug Substance:	The API used belongs to BCS class III. The firm has submitted detail of the drug substance is classified in BCS Class IV. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25˚C ± 2˚C / 60% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (150522, 150825, 150718)
	Module-III Drug Product:	Batch analysis (3470003, 3470004, 3470005) Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has performed Pharmaceutical Equivalence against the innovator's product, Olumiant 4mg tablet by M/s Ely Lilly Nederland B.V, The Netherland (Batch number B121701) by performing quality tests. CDP (with acceptable results of f1 and f2) against the innovator's product Olumiant 4mg tablet by M/s Ely Lilly Nederland B.V, The Netherland. (Batch number B121901).
	Analytical method validation/verification of product	Data of analytical method validation is submitted including, specificity, accuracy, ruggedness, precision and linearity etc for assay of API.
	Container closure system of the drug product	White HDPE bottle with white screw cap containing 30 tablets and silica gel packed in a box of secondary package.
	Stability study data of drug product, shelf life and storage conditions	Batches: (3470003, 3470004, 3470005) Batch size: 18,333 tablets • 24 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Remarks of Evaluator-I:

Observation	Response
Since the excipients used in the manufacturing of the product are different from the excipients use in manufacturing of reference product, therefore, compatibility of the excipients with API is required to be performed. The information should be presented under relevant section in module II and module III.	The firm has submitted that the excipients used are complying with current BP monograph except orange lake color Ph. Grade which complies with in-house specifications. These excipients are pharmaceutically inert substances. These excipients are used below "Inactive Ingredient Guide" limit of FDA. Extensive analysis of the product is done and satisfactory results of assay, dissolution and impurity profile are obtained.
As per available literature of the reference	"We have done dissolution test of Baricinix 2mg and

product, the dissolution specifications including dissolution medium and dissolution time are not same as selected for the dissolution testing of the applied product. The selected time point for dissolution testing of reference product is 30 minutes While the time point for dissolution testing is 45 minutes. Furthermore, 0.1N HCl solution is selected for applied product while the dissolution medium for the reference product is Acetate buffer (pH=4.5), please clarify.	4mg tablets additionally by using dissolution medium pH 4.5 acetate buffer. We have used 18month passed controlled sample for Baricinix 2mg and 14 months passed controlled sample for Baricinix 4mg tablet and found following results; **Baricinix 2mg Tablet** **Test Batch** | **Dissolution medium** | **Time point** | **Result** B/N: 3460012 Mfg: Feb, 20 Exp: June, 22 | Acetate Buffer pH 4.5 | 30 mins | 85.4% **Baricinix 4mg Tablet** **Test Batch** | **Dissolution medium** | **Time point** | **Result** B/N: 3470006 Mfg: Jul, 20 Exp: June, 22 | Acetate Buffer pH 4.5 | 30 mins | 78.2%

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 for revision of specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021

70.	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	**DSL No.:** 05-352-0065-016174D **Address:** Himmel Pharmaceuticals (Pvt) Ltd 793 D, Block C, Faisal Town, District Lahore. **Godown:** N/A **Validity:** 06/02/2022 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel,C/A Dhaka-1000, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. DA/6-110/2016/3288) issued by Directorate General of Drug Administration on 01/06/2020. The applied product is available in market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Copy of GMP certificate No. DA/6-11-/06/4950 dated 17/07/2019 on the basis of inspection conducted on 07/07/2018 (expired).	
	Details of letter of authorization / sole agency agreement • Copy of letter of authorization is submitted whereby M/s Himmel Pharmaceuticals is authorized to	

	register and sell different products including Cobazanix capsule (20mg & 80mg).	
	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 4311 Dated 08/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 10/12/2020
	The proposed proprietary name / brand name	Cabozanix 20mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Cobazanitinib as S-Malate……20mg
	Pharmaceutical form of applied drug	Immediate release hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In-house
	Proposed Pack size	90's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cometriq Capsule (20mg, 80mg) by Ipsen Pharma, EMA approved.
	For generic drugs (me-too status)	N/A
	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.
	Name, address of drug substance manufacturer	M/s Beijing Mesochem Technology Co., Ltd., Floor 23, Building 9, Lippo Plaza, Economic and technological Development zone Beijing (GMP certificate not provided).
	Module-III Drug Substance:	The API used belongs to BCS class II. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25˚C ± 2˚C / 60% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (150528, 150712, 150925)
	Module-III Drug Product:	Batch analysis (3590002, 3590003, 3590004) Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	CDP against the reference product, Cometric 20mg Capsule by M/s Ipsen Pharma, France (EMA Approved) is submitted with acceptable values of f1 and f2. (Batch number C22001).
	Analytical method validation/verification of product	Data of analytical method validation is submitted including, specificity, accuracy, ruggedness, precision and linearity etc for assay of API. (validation studies of analytical method for related substance have submitted as well.
	Container closure system of the drug product	HDPE pot with srew cap, induction sealable wad containing 90 capsules along with silica gel, packed in secondary outer carton.
	Stability study data of drug product, shelf life and storage conditions	Batches: (3590002, 3590003, 3590004) Batch size: 10,000 capsules • 24 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

The drug substance manufacturer is M/s Beijing Mesochem Technology Co., Ltd., China. The submitted GMP certificate is of M/s Kaifeng Pharmaceutical (group) Co., Ltd., China. The applicant has submitted a letter form M/s Beijing Mesochem Technology Co., Ltd., China stating;

"We Beijing Mesochem Technology Co., Ltd., certiifctae that Beijing Mesochem is a manufacturer. According to cooperation agreement currently, Beijing Mesochem tehnology Co., ltd., is manufacturing at Kaifeng Pharmaceutical (group) co., Ltd.,. as per the agreement enclosed. We guarantee the site equivalence and analytical/product equivalence".

Observation	**Response**
Since the excipients used in the manufacturing of the product are different from the excipients used in manufacturing of reference product, therefore, compatibility study of the excipients with API is required to be performed. The information should be presented under relevant section in module II and module III.	The excipients used comply to current pharmacopoeial monograph (BP). These excipients are pharmaceutically inert substances and These excipients are used below "Inactive Ingredient Guide" limit of FDA. Extensive analysis of the product is done and satisfactory results of assay, dissolution and impurity profile are obtained.
Test for Genotoxic impurities in addition to impurity profiling, is included in the final specifications of the reference product while the test is not included in the specifications of the applied product, please clarify.	Not responded
As per EMA assessment report of the innovator's product, the testing specification for Drug Substance include tests for malic acid content, organic volatile	Not responded

	impurities, genotoxic impurities, crystal form, particle size distribution and percentage purity as well while the testing specifications for Drug Substance used for the manufacturing of the applied product do not include the above-mentioned tests, please explain. Moreover, a discussion shall be provided on the inclusion of certain tests, evolution of tests, analytical procedures and acceptance criteria with reference to above query under relevant sections in Module II and Module III.	
	Pharmaceutical equivalence of the applied product is established against the innovator's product Cabometyx capsule by Ipsen Pharma France as per the submitted dossier, while Cabometyx by Ipsen Pharma, France is not actually Capsule dosage form. The mentioned brand name that is Cabometyx is film coated tablet as per the information provided on the official website of ANSM, France, please clarify.	The firm has submitted copy of clarification letter from M/s Beacon Pharmaceuticals Limited. **"**Cabometyx and Cometriq are two brand name drugs that both contain the same active ingredient of Cabozanitinib by Ipsen Pharma, France. While Cabometyx is film coated tablet and Cometriq is Capsule dosage form as per the information provided on EMc. During Bio-equivalence studies of Cabozanix 20mg Capsule, Cometriq Capsuel (B/NC21801) used as reference product".
	Scientific justification for the use of 1% overage in the formulation is required.	Not responded

Decision: Deferred for the following;

- **Submission of impurity profiling as per the innovator's product including the detail of testing of genotoxic impurities.**
- **Justification for not performing certain tests which include malic acid content, organic volatile impurities, genotoxic impurities, crystal form, particle size distribution and percentage purity for drug substance.**
- **Scientific justification for the use of 1% overage in the formulation**

71.	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	**DSL No.:** 05-352-0065-016174D **Address:** Himmel Pharmaceuticals (Pvt) Ltd 793 D, Block C, Faisal Town, District Lahore. **Godown:** N/A **Validity:** 06/02/2022 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel,C/A Dhaka-1000, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. DA/6-110/2016/3289) issued by Directorate General of Drug Administration on 01/06/2020. The applied product is available in market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Copy of GMP certificate No. DA/6-11-/06/4950 dated 17/07/2019 on the basis of inspection conducted on 07/07/2018 (expired).	

	Details of letter of authorization / sole agency agreement • Copy of letter of authorization is submitted whereby M/s Himmel Pharmaceuticals is authorized to register and sell different products including Cobazanix tablet 60mg.	
	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 4306 Dated 08/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 10/12/2020
	The proposed proprietary name / brand name	Cabozanix 60mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Cobazantinib as S-Malate……20mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In-house
	Proposed Pack size	30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cabometyx tablet (20mg, 40mg, 60mg) by M/s Ipsen Pharma EMA Approved.
	For generic drugs (me-too status)	N/A
	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.
	Name, address of drug substance manufacturer	M/s Beijing Mesochem Technology Co., Ltd., Floor 23, Building 9, Lippo Plaza, Economic and technological Development zone Beijing (GMP certificate not provided).
	Module-III Drug Substance:	The API used belongs to BCS class II. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25˚C ± 2˚C / 60% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches
	Module-III Drug Product:	Batch analysis (3850002, 3850003, 3850004) Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted. The dissolution specifications are as per USFDA dissolution method available online.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has performed Pharmaceutical Equivalence against the innovator's product, Cabometyx 60mg tablet by M/s Ipsen Pharma, France (EMA approved) (Batch number C91801). CDP against the reference product, Cabometyx 60mg tablet by M/s Ipsen Pharma, France (EMA Approved) is submitted. (Batch number C22001).
	Analytical method validation/verification of product	Data of analytical method validation is submitted including, specificity, accuracy, ruggedness, precision and linearity etc for assay of API. (validation studies of analytical method for related substance have submitted as well.
	Container closure system of the drug product	HDPE bottle with srew cap and induction sealable wad and silica gel containing 30 tablets packed in secondary outer packaging.
	Stability study data of drug product, shelf life and storage conditions	Batches: (3850002, 3850003, 3850004) Batch size: 6666 tablets • 24 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

The drug substance manufacturer is M/s Beijing Mesochem Technology Co., Ltd., China. The submitted GMP certificate is of M/s Kaifeng Pharmaceutical (group) Co., Ltd., China. The applicant has submitted a letter form M/s Beijing Mesochem Technology Co., Ltd., China stating;

"We Beijing Mesochem Technology Co., Ltd., certiifctae that Beijing Mesochem is a manufacturer. According to cooperation agreement currently, Beijing Mesochem tehnology Co., ltd., is manufacturing at Kaifeng Pharmaceutical (group) co., Ltd.,. as per the agreement enclosed. We guarantee the site equivalence and analytical/product equivalence".

Observation	**Response**
Since the qualitative composition of the applied product is different from the innovator/reference product, therefore, compatibility studies of the excipients with the drug substance is required. The information should be presented under relevant section in module II and module III.	The excipients used comply to current pharmacopoeial monograph (BP & USP). These excipients are pharmaceutically inert substances and These excipients are used below "Inactive Ingredient Guide" limit of FDA. Extensive analysis of the product is done and satisfactory results of assay, dissolution and impurity profile are obtained.
Justify the manufacturing process of the applied product	"As per Beacon's manufacturing process, Direct

since it is a type of direct compression method while the reference product is manufactured by wet granulation method.	compression method is used and the process is validated".
Test for Genotoxic impurities in addition to impurity profiling is including in the final specifications of the reference product while the test is not included in the specifications of the applied product, please clarify.	Not responded
As per EMA assessment report of the innovator's product, the testing specification for Drug Substance include tests for malic acid content, organic volatile impurities, crystal form, particle size distribution and percentage purity as well while the testing specifications for Drug Substance used for the manufacturing of the applied product do not include the above-mentioned tests, please explain. Moreover, a discussion shall be provided on the inclusion of certain tests, evolution of tests, analytical procedures and acceptance criteria with reference to above query under relevant sections in Module II and Module III.	Not responded

Decision: Deferred for the following;

- **Submission of impurity profiling as per the innovator's product including the detail of testing of genotoxic impurities.**
- **Justification for not performing certain tests which include malic acid content, organic volatile impurities, genotoxic impurities, crystal form, particle size distribution and percentage purity for drug substance.**
- **Submission of relevant data for drug substance as per the GUIDANCE DOCUMENT FOR SUBMISSION OF APPLICATION ON FORM 5-F FOR REGISTRATION OF PHARMACEUTICAL DRUG PRODUCTS FOR HUMAN USE available on the official website of DRUG REGULATORY AUTHORITY OF PAKISTAN.**
- **Clarification since the GMP certificate of M/s Kaifeng Pharmaceutical (group) Co., Ltd., China is submitted while as per submitted dossier the manufacturer of drug substance is M/s Beijing Mesochem Technology Co., Ltd., China and the relevant data related to drug substance is submitted from M/s Beijing Mesochem Technology Co., Ltd., China.**

72.	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	**DSL No.:** 05-352-0065-016174D **Address:** Himmel Pharmaceuticals (Pvt) Ltd 793 D, Block C, Faisal Town, District Lahore. **Godown: N/A** **Validity:** 06/02/2022 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. DA/6-110/2016/3299) issued by Directorate General of Drug Administration on 01/06/2020. The applied product is available in market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Copy of GMP certificate No. DA/6-11-/06/4950 dated 17/07/2019 on the basis of inspection conducted on 07/07/2018 (expired).	
	Details of letter of authorization / sole agency agreement • Copy of letter of authorization is submitted whereby M/s Himmel Pharmaceuticals is authorized to register and sell different products including Olaparib 150mg Capsule.	
	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 3566 Dated 01/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 14/12/2020
	The proposed proprietary name / brand name	Olaparix 150mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Olaparib……..150mg
	Pharmaceutical form of applied drug	Orange colored, oval shaped, film coated, Immediate release tablet
	Pharmacotherapeutic Group of (API)	Anticancer

	Reference to Finished product specifications	In-house
	Proposed Pack size	120's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lynparza film coated tablet 150mg by M/s Astrzazeneca, MHRA 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. 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.
	Name, address of drug substance manufacturer	M/s Shanghai Qingsong Pharmaceutical CO., Ltd., Suite No. 505, Building # 2, No. 3377 Kangxin Rd, Pudong New Area Shanghai, China.
	Module-III Drug Substance:	The drug substance is classified in BCS Class IV. Micronized Olaparib is used for manufacturing of the product. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25˚C ± 2˚C / 60% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (15050101,15101201, 1604130)
	Module-III Drug Product:	Batch analysis (3950003, 3950004, 3950005) Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has performed Pharmaceutical Equivalence and CDP (acceptable results for f1 and f2) against the reference product Lynparza 150mg film coated tablet by M/s Astrazeneca AB, Sweden. (Batch number L11118).
	Analytical method validation/verification of product	Data of analytical method validation is submitted including, specificity, accuracy, ruggedness, pricison and linearity etc for assay of API.
	Container closure system of the drug product	HDPE white bottle with white screw cap containing silica gel.

	Stability study data of drug product, shelf life and storage conditions	Batches: 3950003, 3950004, 3950005 Batch size: 7179 tablets • 24 months real time stability data at 30°C ± 2°C / 65% ± 5%RH of 03 batches • 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

Observation	**Response**
Since the excipients used in the manufacturing of the product are different from the excipients use in manufacturing of reference product, therefore, compatibility of the excipients with API is required to be performed. The information should be presented under relevant section in module II and module III.	The excipients used comply to current pharmacopoeial monograph (BP and USP). These excipients are pharmaceutically inert substances and These excipients are used below "Inactive Ingredient Guide" limit of FDA. Extensive analysis of the product is done and satisfactory results of assay, dissolution and impurity profile are obtained.
As per available literature of the reference product (150mg Tablet), the parameters for dissolution are; • First sample at 30mins. • Second sample at 60 minutes, While the selected time point for dissolution testing of the applied product is 60 minutes based on the information gained during development of the drug product and established from validation. Please provide scientific justification for selection of a single time point in contrast with the reference product supported by relevant data. Moreover, the apparatus used for dissolution testing of the reference product is USP Type I while USP type II apparatus has been selected for dissolution testing of applied product, justify scientifically. Furthermore, scientific justification is required for selection 1000ml volume for the said testing.	The firm is unable to provide scientific justification regarding the difference of dissolution parameters of reference and applied product. The firm has stated that they have used USFDA database for medium, apparatus, volume and timepoint, however, the referred parameters are for Olaparib Capsule (1000ml volume of dissolution medium, USP apparatus II etc).

Decision: Deferred for submission of;

- **Drug-excipient compatibility studies.**
- **Justification for not selecting the dissolution testing parameters / specifications and apparatus as recommended by the innovator.**

73.	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	**DSL No.:** 05-352-0065-016174D **Address:** Himmel Pharmaceuticals (Pvt) Ltd 793 D, Block C, Faisal Town, District Lahore. **Godown: N/A** **Validity:** 06/02/2022 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road, Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited, Office Address: 9/B/2, Toyenbee Circular road,

		Motijheel, Dhaka-1223, Bangladesh. Plant Address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. DA/6-110/2016/3298) issued by Directorate General of Drug Administration on 01/06/2020. The applied product is available in market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Copy of GMP certificate No. DA/6-11-/06/4950 dated 17/07/2019 on the basis of inspection conducted on 07/07/2018 (expired).	
	Details of letter of authorization / sole agency agreement • Copy of letter of authorization is submitted whereby M/s Himmel Pharmaceuticals is authorized to register and sell different products including Olaparib 50mg Capsule.	
	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 4309 Dated 08/02/2021
	Details of fee submitted	Rs. 50,000/- Dated 14/12/2020
	The proposed proprietary name / brand name	Olaparix 50mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Olaparib……50mg
	Pharmaceutical form of applied drug	Immediate release capsule
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	In-house
	Proposed Pack size	1×112's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lynparza capsule 50mg by M/s Aztrzeneca, MHRA Approved.
	For generic drugs (me-too status)	N/A
	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.
	Name, address of drug substance manufacturer	M/s Shanghai Qingsong Pharmaceutical CO., Ltd., Suite No. 505, Building # 2, No. 3377 Kangxin Rd, Pudong New Area Shanghai, China. (GMP certificate not provided)
	Module-III Drug Substance:	The drug substance is classified in BCS Class IV. Micronized Olaparib is used for manufacturing of the product. The firm as 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 of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25˚C ± 2˚C / 60% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (15050101,15101201, 1604130)
	Module-III Drug Product:	Batch analysis (3970002, 3970003, 3970004) Detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product is submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has performed Pharmaceutical Equivalence and CDP (acceptable results for f1 and f2) against the reference product Lynparza 50mg capsule by M/s Astrazeneca AB, Sweden. (Batch number L121801).
	Analytical method validation/verification of product	Data of analytical method validation is submitted including, specificity, accuracy, ruggedness, precision and linearity etc for assay of API.
	Container closure system of the drug product	HDPE white bottle with white screw cap containing silica gel.
	Stability study data of drug product, shelf life and storage conditions	Batches: 3970002, 3970003, 3970004 Batch size: 9230 capsules • 24 months real time stability data at 30˚C ± 2˚C / 65% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

Observation	**Response**
Since the excipients used in the manufacturing of the product are different from the excipients use in manufacturing of reference product, therefore, compatibility of the excipients with API is required to be performed. The information should be presented under relevant section in module II and module III.	The firm has not provided any justification for not performing the compatibility of excipients with the drug substance.
As per available literature of the reference product (50mg Capsule), the selected time point for dissolution testing is 45 minutes While the time point for dissolution testing is 60 minutes (NLT 70% in 60mins).	The firm is unable to provide scientific justification for different time point for dissolution testing.

Decision: Deferred for submission of;

- **Drug-excipients compatibility studies.**
- **Justification for not selecting the dissolution testing parameters / specifications and apparatus as recommended by the innovator.**

74.	Name, address of Applicant / Importer	M/s Fresenius Kabi Pakistan Private Limited First Floor, Tanwir Ahmed Medical Center (TAMC), MM Alam Road, 27-C/3, Gulberg-III, Lahore
	Details of Drug Sale License of importer	**License No:** 05-352-0065-019525D **Address:** Fresenius Kabi Pakistan Pvt. Ltd. Tanwir Ahmed Medical Centre (TAMC), first floor MM Alma road, 27-C/3, Gulberg III **Address of Godown:** Agility Logistics (pvt) Limited. RLC-2, 26-KM, Multan road, opposite Hussaini Darbar, near Shamshad Farm house, District Lahore. **Validity:** 21/12/2021 **Status:** License to sell drugs as a Distributor
	Name and address of marketing authorization holder (abroad)	M/s PT.Ethica Industri Farmasi (PT.Ethica). Kawasan Industri Jababeka Tahap V, Blok B1B1, Desa Jayamukti, Kecamatan Cikarang Pusat, Kabupaten Bekasi, Jawa Barat, Indonesia
	Name, address of manufacturer(s)	M/s PT.Ethica Industri Farmasi (PT.Ethica). Kawasan Industri Jababeka Tahap V, Blok B1B1, Desa Jayamukti, Kecamatan Cikarang Pusat, Kabupaten Bekasi, Jawa Barat, Indonesia
	Name of exporting country	Indonesia
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original Legalized CoPP (Certificate#. PN.01.05.31.313.04.18.0399) dated 16-04-2018 by National Agency of Drug and Food Control Indonesia declaring the free sale of applied product and GMP compliant status of the manufacturer.	
	Details of letter of authorization / sole agency agreement: Original Legalized Product Specific Letter of Authorization from Product License Holder 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 39264 Dated 29-11-2018
	Details of fee submitted	(Rs. 100,000/- Dated 29-11-2018)
	The proposed proprietary name / brand name	EPINOR 1mg/ml Injection (4mg/4ml)
	Strength / concentration of drug of Active	Each ml contains:

	Pharmaceutical ingredient (API) per unit	Norepinephrine bitartrate monohydrate eq. to Norepinephrine….1mg
	Pharmaceutical form of applied drug	Solution for IV injection
	Pharmacotherapeutic Group of (API)	Adrenergic and Dopaminergic agent
	Reference to Finished product specifications	USP
	Proposed Pack size	1's×
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	LEVOPHED® 4mg/4ml (USFDA)
	For generic drugs (me-too status)	Norepinephrine injection of M/s MTI Medical (Pvt) Ltd 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 product.
	Name, address of drug substance manufacturer	M/s Cambrex Profarmaco Milano S.r.I via Curiel, 34 20067 Paullo, Milano-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)	Not 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	Pharmaceutical equivalence is submitted against RAIVAS by M/s Ferron Pharmaceutical Indonesia by performing the quality tests.
	Analytical method validation/verification of product	The firm has submitted relevant data including analytical method validation for the drug product for assay method of drug substance, impurities and related substances.
	Container closure system of the drug product	Type I clear glass ampoule (4ml filled in 5ml ampoule)
	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 36 months of 3 batches • Accelerated stability studies is conducted at 40oC±2

		and 75%RH±5% for 6 months of 3 batches Batches: 9616J0004, 9616J0005, 9616J0006

Evaluation by PEC:

Observations	**Response**
Stability study data for drug substance is not submitted.	• Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 60 months of 7 batches Testing Frequency: 0, 12, 24, 36, 48, 60 Btaches:040101, 060101, 160101, 180304, 210102, 230102, 240104 • For Description, Solubilities and Impurities, the firm has submitted stability data of another 03 batches Testing frequency: 0, 3, 6, 9, 12, 24, 36, 48, 60 Conditions: (25oC±2 and 60%RH±5%) Batches: 010102, 010303, 020101 On the basis of above data, the firm has established the re-test period equal to 5 years.

Decision: Since the time points selected for real time stability studies' testing for drug substance are not same as recommended by ICH, therefore, the Board deferred the case for scientific justification of the same.

75.	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^{0}C, 75±5%RH • 6 months at 40^{0}C±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 and comparative dissolution profile 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: 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.

76.	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 693/20) 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 21790 Dated 24-10-2019
	Details of fee submitted	Rs. 100,000/- dated 21-08-2019
	The proposed proprietary name / brand name	LUTEINA 200mg vaginal tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vaginal tablet contains: Progesterone…..200mg
	Pharmaceutical form of applied drug	Vaginal Tablet
	Pharmacotherapeutic Group of (API)	Hormone
	Reference to Finished product specifications	In-house
	Proposed Pack size	Not provided
	Proposed unit price	Rs. 1347/- per pack
	The status in reference regulatory authorities	Could not be confirmed
	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	Not submitted.
	Analytical method validation/verification of product	The firm has submitted analytical method validation studies including linearity,
	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^{0}C, 65±5%RH • 6 months at 40^{0}C±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.

• The evidence of approval of the applied formulation could not be confirmed in RRAs.
Decision: • **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.** • **Deferred for evidence of approval of the applied formulation is Reference Regulatory Authorities as approved in 275th meeting of Registration Board.**

Deferred Cases:

77.	Name, address of Applicant / Importer	M/s Biocare Pharmaceutica 807 Shdman-I, Lahore.
	Details of Drug Sale License of importer	DSL No.: 05-352-0063-032069D Address: Biocare pharamceutica 80 shadman-I district Lahore. Validity: 17/04/2022 Status: License to sell drugs as Distributor
	Name and address of marketing authorization holder (abroad)	M/s Northeast Pharmaceutical Goup Shenyang No. 1 Pharmaceutical Co., Ltd., N0.8, Kunminghu street, Economic & Technological development zone, Shenyang, Liaoning
	Name, address of manufacturer(s)	M/s Northeast Pharmaceutical Group, Shenyang No. 1 Pharmaceutical Co., Ltd., No. 8, Kun Ming Hu street, Economic & Technological Development zone, Shenyang, Liaoning province, China.
	Exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. 20190073) issued by Liaoning Medical Products Administration valid till 29/07/2020. The product is available for free sale in the market of exporting country. The facilities and operations conform to Chinese-GMP. • Legalized GMP certificate (No. LN20180007) valid till 25/03/2023.	
	Details of letter of authorization / sole agency agreement • Copy of sole agency agreement is submitted whereby M/s Biocare pharmaceutica is appointed as a distributor 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 26048 Dated 005/10/2020
	Details of fee submitted	Rs. 50,000/- Dated 20/08/2020
	The proposed proprietary name / brand name	Fosofix Injection 2gm Alternate brand name: Fonyl Fosfix
	Strength / concentration of drug of Active	Each vial contains:

	Pharmaceutical ingredient (API) per unit	Fosfomycin as disodium……..2gm (equivalent to Fosfomycin disodium……2.64g)
	Pharmaceutical form of applied drug	Powder for solution for intravenous injection
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	In-house
	Proposed Pack size	1's
	Proposed unit price	Rs. 1000/-
	The status in reference regulatory authorities	Fosfomycin 20mg/ml powder for solution for infusion (2gm) by M/s Infectopharm, MHRA approved.
	For generic drugs (me-too status)	Could not be confirmed
	Module-II (Quality Overall Summary)	Submitted.
	Name, address of drug substance manufacturer	M/s Northeast Pharmaceutical Group Co., Ltd., 29 Shenxi Liudong road, Shenyang Economic and Technical Development zone, China. (GMP certificate No. LN20190041 valid till 15/07/2024)
	Module-III Drug Substance:	Submitted.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• 36 months real time stability data at 30˚C ± 2˚C / 65% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches
	Module-III Drug Product:	Submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established by conducting all the quality tests against the reference product, Fosmicn-S manufactured by M/s Meiji Seka Kaisha ltd, Japan.
	Analytical method validation/verification of product	Analyticl method validation studies are submitted.
	Container closure system of the drug product	Injection vials made up of molded soda lime glass, rubber stopper and aluminium -plastic laminated cap
	Stability study data of drug product, shelf life and storage conditions	• 24 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

- The product in reference country in approved with a primary packaging of 100ml glass bottle while the volume of vial of the applied product is 30ml.
- The firm has submitted Original, legalized and vlaid CoPP (certificate No. 20210024) issued by Liaoning Medical Products Administration valid till 07/01/2023. The product is available for free sale in the market of exporting country. The facilities and operations conform to Chinese-GMP.
- Analytical method verification studies for API performed by drug product manufacturer are not submitted. The firm has stated that the API testing was conducted as per Chinese Pharmacopoeia therefore verification studies are not required. Moreover, the official monograph for API is present in British Pharmacopoeia.

Decision of 308th meeting:

Deferred for of following points;

 Clarification since the product in reference country in approved with a primary packaging of 50ml glass bottle while the volume of vial of the applied product is 30ml.

 Submission of analytical method validation/verification studies of drug substance performed by drug product manufacturer**.**

Evaluation by PEC-I:

- The firm has provided the following reference of the product which is approved with 30ml volume of the

vial which is in-lined with the volume of the vial of the applied product.
Ivozfo (Fosfomycin for injection) (2g, 4g, 8g) by M/s Verity Pharmaceuticals, Ontario, Health Canada Approved.

IVOZFO™ (fosfomycin for injection) is supplied in clear type-I glass vials with a rubber stopper (bromobutyl rubber) and pull-off cap containing 2 g (in 30 mL vial), 4 g (in 30 mL vial) or 8 g (in 50 mL vial) of fosfomycin, respectively, in packs of 10 vials each.

https://health-products.canada.ca/dpd-bdpp/info.do?lang=en&code=97819 (accessed on 12/11/2021 at 7pm)

- As per MHRA, Water for Injections and Glucose Infusion 50 mg/ml (5 %) or Glucose Infusion 100 mg/ml (10 %) may be used as solvent for the reconstitution and dilution while according to HealthCanada, 5% dextrose solution must be used. Whereas both the authorities recommend that Sodium chloride containing solvents must not be used.
- Reconstitution: (MHRA, Ireland & Health Canada)
  Shake the vial prior to the reconstitution to loosen up the powder. Reconstitute the 2 g or 4 g vials with 20ml solvent.
- Dilution (MHRA, Ireland & Health Canada)
  Transfer the reconstituted contents of **2 g vials** into an infusion container with further **30 ml** of solvent.
  Transfer the reconstituted contents of **4 g vials** into an infusion container with further **80 ml** of solvent.
- The frim has submitted analytical method validation studies for Fosfomycin including precision, accuracy, linearity and specificity. The validation studies for impurities have also been submitted.
- As per the provided data, the in-use after reconstitution with 5% and 10% dextrose solution for 12 hours.
- The applied product is developed and tested according to In-House specifications while the official monograph of the product is available in J.P. The comparison of In-house and J.P specificaytions are given below.

Test	**Limits defined by J.P**	**In-house limits**
pH	6.5-8.5	6.5-8.5
Fosfomycin sodium diol (impurity A)	Test not performed	≤ 1%
Clarity of solution	Clear and colorless	Clear and colorless Should not be more pronounced than the reference suspension 1. Any color produced should not be more intense than reference solution yellow 1.
Water	≤ 4%	≤ 2%
Bacterial endotoxins	Less than 0.025EU/mg	Less than 0.033EU/mg
Visible particles	clear and free from foreign insoluble matters (foreign insoluble matter)	Absent
Particulate matter	≤ 6000/container (≥10um) ≤ 600/container (≥25um)	≤ 6000/container (≥10um) ≤ 600/container (≥25um)
Weight variation	Should meet the requirement <6.02>	±5%
Assay	90-110% Cylinder plate method Test Organism: Proteus Sp.	90-110% Cup plate method Test Organism: Micrococcus Luteus Nephelometry test (parallel lines method) Test Organism: Escheritia Coli

Decision: The Board deliberated tha the specifications limits as defined by Japanese Pharmacopoeia are more stringent and tighter than the established In-House specification as well as the method used for the testing of the applied product are also different from the method developed In-House. Therefore, the Board decided to defer the case and directed the firm to submitted all the relevant data according to the the monograph present in Japanese Pharmacopoeia.

78.	Name, address of Applicant / Importer	M/s Biocare Pharmaceutica 807 Shdman-I, Lahore.
	Details of Drug Sale License of importer	DSL No.: 05-352-0063-032069D Address: Biocare pharamceutica 80 shadman-I district Lahore. Validity: 17/04/2022 Status: License to sell drugs as Distributor

	Name and address of marketing authorization holder (abroad)	M/s Northeast Pharmaceutical Goup Shenyang No. 1 Pharmaceutical Co., Ltd., N0.8, Kunminghu street, Economic & Technological development zone, Shenyang, Liaoning
	Name, address of manufacturer(s)	M/s Northeast Pharmaceutical Group, Shenyang No. 1 Pharmaceutical Co., Ltd., No. 8, Kun Ming Hu street, Economic & Technological Development zone, Shenyang, Liaoning province, China.
	Exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (certificate No. 20190072) issued by Liaoning Medical Products Administration valid till 29/07/2020. The product is available for free sale in the market of exporting country. The facilities and operations conform to Chinese-GMP. • Legalized GMP certificate (No. LN20180007) valid till 25/03/2023.	
	Details of letter of authorization / sole agency agreement • Copy of sole agency agreement is submitted whereby M/s Biocare pharmaceutica is appointed as a distributor 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 30397 Dated 13/11/2020
	Details of fee submitted	Rs. 50,000/- Dated 20/08/2020 (1925409) Rs. 50,000/- dated 23/09/2020 (1925466)
	The proposed proprietary name / brand name	Fosofix Injection 4gm Alternate brand name: Fonyl Fosfix
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Fosfomycin as disodium……..4gm (equivalent to Fosfomycin disodium……5.28g)
	Pharmaceutical form of applied drug	Powder for solution for intravenous injection
	Pharmacotherapeutic Group of (API)	Antibacterial
	Reference to Finished product specifications	In-house
	Proposed Pack size	1’s
	Proposed unit price	Rs. 1700/-
	The status in reference regulatory authorities	Fosfomycin 40mg/ml powder for solution for infusion (4gm) by M/s Infectopharm, MHRA approved.
	For generic drugs (me-too status)	Fosfomycin injection 4gm by M/s Efroze KHI, R.No.004722
	Module-II (Quality Overall Summary)	Submitted.

	Name, address of drug substance manufacturer	M/s Northeast Pharmaceutical Group Co., Ltd., 29 Shenxi Liudong road, Shenyang Economic and Technical Development zone, China. (GMP certificate No. LN20190041 valid till 15/07/2024)
	Module-III Drug Substance:	Submitted
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• 36 months real time stability data at 30˚C ± 2˚C / 65% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches
	Module-III Drug Product:	Submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established by conducting all the quality tests against the reference product, Fosmicin-S manufactured by M/s Meiji Seka Kaisha ltd, Japan.
	Analytical method validation/verification of product	COAs: 10119030002, 10119030003, 10119030.
	Container closure system of the drug product	Injection vials made up of molded soda lime glass, rubber stopper and aluminium -plastic laminated cap
	Stability study data of drug product, shelf life and storage conditions	• 18 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches

Evaluation by PEC-I:

- The product in reference country in approved with a primary packaging of 100ml glass bottle while the volume of vial of the applied product is 30ml.
- The firm has submitted Original, legalized and vlaid CoPP (certificate No. 20210027) issued by Liaoning Medical Products Administration valid till 07/01/2023. The product is available for free sale in the market of exporting country. The facilities and operations conform to Chinese-GMP.
- Analytical method verification studies for API performed by drug product manufacturer are not submitted. The firm has stated that the API testing was conducted as per Chinese Pharmacopoeia therefore verification studies are not required. Moreover, the official monograph for API is present in British Pharmacopoeia.

Decision of 308th meeting:

Deferred for of following points;

 Clarification since the product in reference country in approved with a primary packaging of 50ml glass bottle while the volume of vial of the applied product is 30ml.

 Submission of analytical method validation/verification studies of drug substance performed by drug product manufacturer**.**

 Submission of real time stability study data according to the conditions of zone IV-A of 03 batches till shelf life since the submitted data is of 18 months only.

Evaluation by PEC-I:

- The firm has provided the following reference of the product which is approved with 30ml volume of the vial which is in-lined with the volume of the vial of the applied product.
  Ivozfo (Fosfomycin for injection) (2g, 4g, 8g) by M/s Verity Pharmaceuticals, Ontario, Health Canada Approved.
  IVOZFO™ (fosfomycin for injection) is supplied in clear type-I glass vials with a rubber stopper (bromobutyl rubber) and pull-off cap containing 2 g (in 30 mL vial), 4 g (in 30 mL vial) or 8 g (in 50 mL vial) of fosfomycin, respectively, in packs of 10 vials each.
  https://health-products.canada.ca/dpd-bdpp/info.do?lang=en&code=97819 (accessed on 12/11/2021 at 7pm)
- As per MHRA, Water for Injections and Glucose Infusion 50 mg/ml (5 %) or Glucose Infusion 100 mg/ml (10 %) may be used as solvent for the reconstitution and dilution while according to HealthCanada, 5% dextrose solution must be used. Whereas both the authorities recommend that Sodium chloride containing solvents must not be used.
- Reconstitution: (MHRA, Ireland & Health Canada)

Shake the vial prior to the reconstitution to loosen up the powder. Reconstitute the 2 g or 4 g vials with 20ml solvent.

- Dilution (MHRA, Ireland & Health Canada)
  Transfer the reconstituted contents of **2 g vials** into an infusion container with further **30 ml** of solvent.
  Transfer the reconstituted contents of **4 g vials** into an infusion container with further **80 ml** of solvent.
- The firm has submitted analytical method validation studies for Fosfomycin including precision, accuracy, linearity and specificity. The validation studies for impurities have also been submitted.
- The firm has submitted stability data with the following details;
  24 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches
  06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches
  Batches: 4190406, 4190407, 4190408
- As per the provided data, the in-use after reconstitution with 5% and 10% dextrose solution for 12 hours.
- The applied product is developed and tested according to In-House specifications while the official monograph of the product is available in J.P. The comparison of In-house and J.P specificaytions are given below.

Test	**Limits defined by J.P**	**In-house limits**
pH	6.5-8.5	6.5-8.5
Fosfomycin sodium diol (impurity A)	Test not performed	≤ 1%
Clarity of solution	Clear and colorless	Clear and colorless Should not be more pronounced than the reference suspension 1. Any color produced should not be more intense than reference solution yellow 1.
Water	≤ 4%	≤ 2%
Bacterial endotoxins	Less than 0.025EU/mg	Less than 0.033EU/mg
Visible particles	clear and free from foreign insoluble matters (foreign insoluble matter)	Absent
Particulate matter	≤ 6000/container (≥10um) ≤ 600/container (≥25um)	≤ 6000/container (≥10um) ≤ 600/container (≥25um)
Weight variation	Should meet the requirement <6.02>	±5%
Assay	90-110% **Cylinder plate method** Test Organism: Proteus Sp.	90-110% **Cup plate method** Test Organism: Micrococcus Luteus **Nephelometry test (parallel lines method)** Test Organism: Escheritia Coli

Decision: The Board deliberated tha the specifications limits as defined by Japanese Pharmacopoeia are more stringent and tighter than the established In-House specification as well as the method used for the testing of the applied product are also different from the method developed In-House. Therefore, the Board decided to defer the case and directed the firm to submitted all the relevant data according to the the monograph present in Japanese Pharmacopoeia.

Case No. 3: Registration applications Imported products submitted on Form 5A (Human)
New Cases:

79.	**Name and address of Applicant**	M/s Fresenius Kabi Pakistan Private Limited First Floor, Tanwir Ahmed Medical Center (TAMC), MM Alam Road, 27-C/3, Gulberg-III, Lahore
	Detail of Drug Sale License	License No: 05-352-0065-019525D Address: Fresenius Kabi Pakistan Pvt. Ltd. Tanwir Ahmed Medical Centre (TAMC), first floor MM Alma road, 27-C/3, Gulberg III Address of Godown: Agility Logistics (pvt) Limited. RLC-2, 26-KM, Multan road, opposite Hussaini Darbar, near Shamshad Farm house, District Lahore. Validity: 21/12/201

		Status: License to sell drugs as a Distributor
	Manufacturer & Product License Holder	Manufacturer and Product License Holder: M/s PT.Ethica Industri Farmasi (PT.Ethica). Kawasan Industri Jababeka Tahap V, Blok B1B1, Desa Jayamukti, Kecamatan Cikarang Pusat, Kabupaten Bekasi, Jawa Barat, Indonesia
	Name of exporting country	Indonesia
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No 44226 Dated 28-12-2018
	Fee including differential fee	Rs. 100,000/- Dated 28-12-2018
	Brand Name +Dosage Form + Strength	Ketorolac Kabi Injection 30mg/ml
	Composition	Each ml contains: Ketorolac Tromethamine…..30mg
	Finished Product Specification	USP
	Pharmacological Group	NSAID
	Shelf life	36 Months
	Pack size & Demanded Price	5 ampoules (1ml each) & As per SRO
	International availability	Ketorolac Tromethamine Injection USP 30mg/1ml vial by M/s Pfizer Canada Inc. DIN 02390582, Health Canada Approved.
	Me-too status	Tolek injection 30mg/1ml ampoule by M/s Regal Pharmaceuticals, Reg. no. 082006
	Stability studies	• Real time stability studies have been conducted at 30oC±2 and 75%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: 9616F0001, 9616F0002, 9616F0012
	Detail of certificates attached	• Original Legalized CoPP (Certificate#. PN.01.05.31.313.10.18.0965) dated 16-10-2018 issued by National Agency of Drug and Food Control Indonesia declaring the free sale of applied product and GMP compliant status of the manufacturer. • Original Legalized Product Specific Letter of Authorization from M/s PT. Ethica Industri Farmasi (PT.Ethica). M/s Fresenius Kabi Pakistan Pvt. Ltd. Will be responsible for all matters pertaining to the registration of Ketorolac Kabi injection 30mg/ml.
	Remarks of the Evaluator.	
	Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.	
80.	Name and address of Applicant	M/s Himmel Pharmaceuticals Pvt. Limited 793-D Block C Faisal Town Lahore Pakistan
	Product License Holder & Manufacturer	M/s BEACON Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office Address: 9/B/2, Toyenbee Circular Road, Motijheel Dhaka, Bangladesh
	Name of exporting country	Bangladesh
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No 7363 Dated 20-02-2019
	Fee including differential fee	Rs. 100,000/- Dated 20-02-2019
	Brand Name +Dosage Form + Strength	Lapanix 250mg Tablet
	Composition	Each film coated tablet contains: Lapatinib Ditosylate INN 398mg eq. to Lapatinib….250mg
	Finished Product Specification	In-house
	Pharmacological Group	Anti-cancer

	Shelf life	24 Months
	Pack size & Demanded Price	150's & As per SRO
	International availability	Tyverb® 250 mg film-coated tablets (UK)
	Me-too status	TYKERB TABLETS 250MG of M/s Gsk Karachi
	Stability studies	Firm has submitted long term (24 months) at 30+2oC, 65+5%RH & accelerated (06 months) stability data at 40+ 2oC, 75+ 5% RH for three batches.
	Detail of certificates attached	Original Legalized CoPP (Certificate#. DA/6-110/2016/22466 issued on 14-10-2018 by Govt. of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration declaring the free sale of applied product and GMP compliant status of the manufacturer i.e., M/s BEACON Pharmaceuticals Limited. Original product specific letter of authorization from product license holder is submitted.
	Remarks of the Evaluator.	Reference formulation Each film-coated tablet contains lapatinib ditosylate monohydrate, equivalent to 250 mg lapatinib while applied Each film coated tablet contains: Lapatinib Ditosylate INN 398mg eq. to Lapatinib….250mg
	Decision of 293rd meeting: Deferred for revision of composition as per reference product along with submission of requisite fee for the revision. Submission by the firm: The firm has submitted several references from RRAs confirming the monohydrate for of the salt of the applied product that is Lapatinib Ditosylate monhydrtae. Hoever, the API used for manufacturing of the applied product is Lpatinib Ditosylate.	
	Decision of 308th meeting: The Board deferred the case for clarification since the reference product contains Lapatinib Ditosylate Monohydrate while the applied product is manufactured by using Lapatinib Ditosylate. Submission by the firm: The firm has submitted attested copy of declaration from the API manufacturer stating that the API manufacturer had provided the API as Lapatinib Ditosylate to M/s Beacon Pharmaceuticals ltd Bangladesh (the drug product manufacturer).	
	Decision of 312th meeting: The Board deferred the case for further deliberation since the API used for manufacturing of reference product is lapatinib ditosylate monohydrate while the applied product is manufactured by using lapatinib ditosylate. Submission by the firm: The firm has submitted that the drug substance used for the manufacturing of the applied product is Lapatinib Ditosylate. A declaration letter from Drug Substance manufacturer is also submitted stating that the drug substance which has been supplied to finished product manufacturer is Lapatinib Ditosylate. It is worthy to bring the fact before the Board that the drug substance falls in BCS Class II (low solubility/high permeability) (Sourse: USFDA Biopharamceutical review of the innovator's product).	
	Decision: The Board deferred the case for further deliberation since the API used for manufacturing of reference product is lapatinib ditosylate monohydrate while the applied product is manufactured by using lapatinib ditosylate.	

Case No. 4: Registration applications Imported products submitted on Form 5A (Veterinary)

81.	Name and address of Applicant	M/s Saadat International 117 Habitat Flat Shadman II Jail Road Lahore
	Name and address of manufacturer	Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (QC and Batch Release) 48 Vasil Petleshkov Str Peshtera 4550,Bulgaria (Manufacture)

	Name and address of Product License Holder	Huvepharma AD, 3a Nikolay Haytov street, 1113 Sofia Bulgaria
	Exporting Country	Bulgaria
	Brand Name+Dosage Form +Strength	Vetmulin 450mg/g Water soluble granules
	Diary No. Date of R& I & fee	Dy No. 336 : 09-06-2015 PKR 100,000/- : 09-06-2015
	Composition	Each gram contains Tiamulin hydrogen fumarate ……450 mg
	Target Specie	Chicken, Turkey
	Pharmacological Group	ATC Vet Code: QJ01XQ01 Antibacterials for systemic use, Pleuromutilins
	Type of Form	Form 5-A
	Finished Product Specification	In-house
	Shelf life	2 years (supported by accelerated and real time stability data)
	Pack size & Demanded Price	1 kg sachet
	Approval status of product in Reference Regulatory Authorities.	Vetmulin (Denmark Approved) HPRA Approved
	Me-too status	006846 TIAMUTIN 45% HILTON KARACHI
	CoPP/GMP status	Original, legalized certificate of origin and free sale issued on 20-03-2014 by Ministry of Agriculture and Food, Bulgarian Food Safety Agency confirms its free sale Copy of GMP certificate (No. 31/2013/GMP) issued on 27-12-2013 by Ministry of Agriculture and Food, Bulgarian Food Safety Agency confirms the GMP of Biovet but the address written on certificate is different from that provided in Form 5-A as well as in free sale certificate. Authority letter M/s Saadat International 117 Habitat Flat Shadman II Jail Road Lahore & Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria Dated : 13 June 2017 Biovet Joint Stock Company is subsidiary of Huvepharma Eood Located in 3 A ,Nikolay haytov Street, Sofia, 1113 , Bulgaria
	Remarks of the Evaluator.	Withdrawal Period: Chickens Meat and offal: 3 days Eggs: Zero days Turkeys Meat and offal: 5 days ● The address of manufacturing site on GMP certificate is "39, Petar Rakov St. 48 Vasil Petleshkov Str Peshtera 4, Pazardjik, Bulgaria" which is different from that provided on Form 5-A . ● The free sale certificate mentions the product license holder is Biovet Joint Stock Company whereas Form 5 A mentions Huvepharma AD. ● Clarify 1 Kg sachet or bag.
	Previous Decision (M-282)	Deferred for the following reasons: ● Clarification for type of container whether you have applied for sachet or bag. ● The address of manufacturing site mentioned on Form 5A is different from the address mentioned on GMP certificate. Clarification is required with documented evidence. ● The product license holder mentioned on free sale certificate is different from the product license holder

	mentioned on Form 5A. Clarification is required.

Fresh Evaluation:

a. Clarification for type of container whether you have applied for sachet or bag.

1 Kg sachet

b. The address of manufacturing site mentioned on Form 5A is different from the address mentioned on GMP certificate. Clarification is required with documented evidence.

(QC and Batch Release+Headquarter)

Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria

(Manufactures)

48 Vasil Petleshkov Str Peshtera 4550,Bulgaria

c. The product license holder mentioned on free sale certificate is different from the product license holder mentioned on Form 5A. Clarification is required.

Firm has submitted that product license holder is Biovet Joint Stock Company 39, Petar Rakov St. 4550 Peshtera, Bulgaria and the same has been mentioned on Free sale certificate.

Decision of 285th meeting of Registration Board:

"Deferred for above clarifications"

Now the firm has submitted the following documents:

a. Vetmulin 450mg/g
   It is a 1kg sachet.
b. Original Legalized CoPP (Certificate#. BG 6/2019) issued on 29-01-2019 by Bulgarian Food Safety Agency Ministry of Agriculture, Food and Forestry 15 Pencho Slaveikov Blvd. Sofia 1606, Bulgaria declaring the free sale of applied product and GMP compliant status of the manufacturer i.e., BIOVET Joint Stock Company, 39 Petar Rakov Str. /48 Vasil Petleshkov Str., Peshtera 4550, Bulgaria. Product License Holder of applied product is M/s Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium.
   (Revised form-5A showed that Address of QC, Batch release and Headquarter: 39, Petar Rakov Street, 4550 Peshtera, Bulgaria while address of manufacturing site is 48 vasil Petleshkov street, Peshtera 4550, Bulgaria)
c. The firm has submitted original and legalized letter of authorization for the following products;
   Hydrodoxx 500mg
   Vetmulin 450mg
   Tilmovet 250mg

Decision of 296th meeting:

Deferred for confirmation whether the applicant has applied same addresses of manufacturing sites as per CoPP.

Evaluation by PEC:

The addresses of MAH (abroad) and manufacturer as mentioned in revised Form 5A are different from the addresses mentioned in initially submitted Form 5A along with the dossier.

The firm has submitted Rs. 5,000/- vide challan number 0590987 dated 26/03/2021for change of address of manufacturer and MAH (abroad). Following are the details;

Address of QC, Batch release and Headquarter: BIOVET Joint Stock Company 39, Petar Rakov Street, 4550 Peshtera, Bulgaria

manufacturing site: BIOVET Joint Stock Company 48 vasil Petleshkov street, Peshtera 4550, Bulgaria

Product license holder: Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium.

Decision of 308th meeting:

The Board deferred the case for clarification of addresses of manufacturing site in previously submitted dossier, CoPP and revised form 5A.

Evaluation by PEC:

- Initially the firm had not mentioned the addresses of MAH (abroad) and manufacturing facility in Form 5A. However, the address of QC/Batch releasing sit was mentioned on Form 5A. The submitted data in the dossier is from the relevant sites.
- The firm, later on, submitted the revised Form 5A along with fee of Rs. 5,000/- mentioning correct addresses of MAH (abroad), manufacturing site and QC/Batch releasing site, the detail of which is given below;

  Address of QC, Batch release and Headquarter: BIOVET Joint Stock Company 39, Petar Rakov Street, 4550 Peshtera, Bulgaria

  Manufacturing site: BIOVET Joint Stock Company 48 vasil Petleshkov street, Peshtera 4550,

	Bulgaria **Product license holder:** Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium. Furthermore, the firm has submitted copy of clarification letter from M/s *HuvePharma EOOD, 3a Nikolay Haytov street 1113 Sofia, Bulgaria* which states that *Huvepharma NV, Belgium (MAH) and Biovet Joint Stock Company, Bulgaria* (including QC/Batch releasing site & Manufacturing sites) are subsidiaries of HuvePharma EOOD, Bulgaria.	
	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 full fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021	
82.	Name and address of Applicant	M/s Saadat International 117 Habitat Flat Shadman II Jail Road Lahore
	Name and address of manufacturer	Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (QC and Batch Release) 48 Vasil Petleshkov Str Peshtera 4550,Bulgaria (Manufactures)
	Name and address of Product License Holder	Huvepharma AD, 3a Nikolay Haytov street, 1113 Sofia Bulgaria
	Exporting Country	Bulgaria
	Brand Name +Dosage Form + Strength	Tilmovet 250mg/ml Concentrate for oral solution
	Diary No. Date of R& I & fee	Dy No. 337 : 09-06-2015 PKR 100,000/- : 09-06-2015
	Composition	Each ml contains Tilmicosin ……250 mg
	Target Specie	Chicken (Broiler, pullets), Turkey and Calves
	Pharmacological Group	Antimicrobials for systemic use, macrolides ATC vet code: QJ01FA91
	Type of Form	Form 5-A
	Finished Product Specification	In-House
	Shelf life	2 years
	Stability studies	Firm has submitted long term (24 months) at 30±2ºC RH 65%± 5%± 5% & accelerated (06 months) stability data at 40± 2ºC, 75± 5% RH for three batches.
	Pack size & Demanded Price	960 ml is presented in a white high density polyethylene bottle with white polypropylene or , tamper-evident cap, 240 ml is presented in high density polyethylene (HDPE) bottle with a closure made of PET. 60 mL PET vials with closure of PET/PE
	Approval status of product in Reference Regulatory Authorities.	HPRA Approved
	Me-too status	044909 HICOS 250 ORAL SOLUTION HILTON PHARMA (PVT) LTD., KARACHI.
	CoPP/GMP status	Original, legalized certificate of origin and free sale issued on 20-03-2014 by Ministry of Agriculture and Food, Bulgarian Food Safety Agency confirms its free sale Copy of GMP certificate (No. 31/2013/GMP) issued on 27-12-2013 by Ministry of Agriculture and Food, Bulgarian Food Safety Agency confirms the GMP of Biovet but the address written on certificate is different from that provided in Form 5-A as well as in free sale certificate
	Remarks of the Evaluator.	Withdrawal Period: Calves: 42 days. Chickens: 12 days

		Turkeys: 19 days Eggs: Not authorized for use in birds producing eggs for human consumption. ● The address of manufacturing site on GMP certificate is 39, Petar Rakov St. 48 Vasil Petleshkov Str Peshtera 4, Pazardjik, Bulgaria which is different from that provided on Form 5-A . ● The free sale certificate mentions the product license holder is Biovet Joint Stock Company whereas Form 5 A mentions Huvepharma AD.
	Previous Decision (M-282)	Deferred for the following reasons: ● Clarification for type of container whether you have applied for sachet or bag. ● The address of manufacturing site mentioned on Form 5A is different from the address mentioned on GMP certificate. Clarification is required with documented evidence. ● The product license holder mentioned on free sale certificate is different from the product license holder mentioned on Form 5A. Clarification is required.
	Fresh Evaluation: a. Clarification for type of container whether you have applied for sachet or bag. 960 ml is presented in a white high density polyethylene bottle with white polypropylene or , tamper evident cap, 240 ml is presented in high density polyethylene (HDPE) bottle with a closure made of PET.60 mL PET vials with closure of PET/PE. b. The address of manufacturing site mentioned on Form 5A is different from the address mentioned on GMP certificate. Clarification is required with documented evidence. (QC and Batch Release+Headquarter) Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (Manufactures) 48 Vasil Petleshkov Str Peshtera 4550,Bulgaria c. The product license holder mentioned on free sale certificate is different from the product license holder mentioned on Form 5A. Clarification is required. Firm has submitted that product license holder is Biovet Joint Stock Company 39, Petar Rakov St. 4550 Peshtera, Bulgaria and the same has been mentioned on Free sale certificate. Decision of 285th meeting of Registration Board: "Deferred for above clarifications" Now the firm has submitted the following documents: a. Tilmovet 250mg/ml concentrate for oral solution is packed in 3 container types and sizes: High density polyethylene (HDPE) bottles of 960ml with vertically see-through bar and a graduated scale provided with white tamper evident closure made of PP with white foamed sealing disk. High-density polyethylene (HDPE) bottles of 240ml with a closure made of polyethylene terephthalate (PET). Polyethylene terephthalate (PET) vials of 60ml with a closure made of polyethylene terephthalate/polyethylene (PET/PE). **(**Provided stability data is of only 240ml bottle) b. Original Legalized CoPP (Certificate#. BG 7/2019) issued on 29-01-2019 by Bulgarian Food Safety Agency Ministry of Agriculture, Food and Forestry 15 Pencho Slaveikov Blvd. Sofia 1606, Bulgaria declaring the free sale of applied product and GMP compliant status of the manufacturer i.e., BIOVET Joint Stock Company, 39 Petar Rakov Str. /48 Vasil Petleshkov Str., Peshtera 4550, Bulgaria. Product License Holder of applied product is M/s Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium. (Revised form-5A showed that Address of QC, Batch release and Headquarter: 39, Petar Rakov Street, 4550 Peshtera, Bulgaria while address of manufacturing site is 48 vasil Petleshkov street,	

	Peshtera 4550, Bulgaria) c. The firm has submitted original and legalized letter of authorization for the following products; Hydrodoxx 500mg Vetmulin 450mg Tilmovet 250mg Decsion of 296th meeting: Deferred for confirmation whether the applicant has applied same addresses of manufacturing sites as per CoPP. Evaluation by PEC: The addresses of MAH (abroad) nad manufacturer as mentioned in revised Form 5A are different from the addresses mentioned in initially submitted Form 5A along with the dossier. The firm has submitted Rs. 5,000/- vide challan number 0590986 dated 26/03/2021for change of address of manufacturer and MAH (aboad). Following are the details; Address of QC, Batch release and Headquarter: BIOVET Joint Stock Company 39, Petar Rakov Street, 4550 Peshtera, Bulgaria manufacturing site: BIOVET Joint Stock Company 48 vasil Petleshkov street, Peshtera 4550, Bulgaria Product license holder: Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium.	
	Decision of 308th meeting: The Board deferred the case for clarification of addresses of manufacturing site in previously submitted dossier, CoPP and revised form 5A. **Evaluation by PEC:** • Initially the firm had not mentioned the addresses of MAH (abroad) and manufacturing facility in Form 5A. However, the address of QC/Batch releasing sit was mentioned on Form 5A. The submitted data in the dossier is from the relevant sites. • The firm, later on, submitted the revised Form 5A along with fee of Rs. 5,000/- mentioning correct addresses of MAH (abroad), manufacturing site and QC/Batch releasing site, the detail of which is given below; **Address of QC, Batch release and Headquarter:** BIOVET Joint Stock Company 39, Petar Rakov Street, 4550 Peshtera, Bulgaria **Manufacturing site:** BIOVET Joint Stock Company 48 vasil Petleshkov street, Peshtera 4550, Bulgaria **Product license holder:** Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium. Furthermore, the firm has submitted copy of clarification letter from M/s *HuvePharma EOOD, 3a Nikolay Haytov street 1113 Sofia, Bulgaria* which states that *Huvepharma NV, Belgium (MAH) and Biovet Joint Stock Company, Bulgaria* (including QC/Batch releasing site & Manufacturing sites) are subsidiaries of HuvePharma EOOD, Bulgaria.	
	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 full fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021	
83.	Name address of Applicant	M/s Saadat International, 117 Habitat Flat Shadman II Jail Road Lahore
	Drug Sale License	Address: 117 Habitat Flat Shadman II Jail Road Lahore Lahore Validity: 12-06-2020 Status: License to sell drugs as a Distributor
	Name and address of manufacturer	Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (QC and Batch Release) 48 Vasil Petleshkov Str Peshtera 4550,Bulgaria (Manufacturer)
	Name and address of Product License Holder	Huvepharma AD, 3a Nikolay Haytov street, 1113 Sofia Bulgaria
	Exporting Country	Bulgaria
	Brand Name +Dosage Form + Strength	HydroDoxx 500mg/g Powder for use in drinking water
	Diary No. Date of R& I & fee	Dy No. 335 : 09-06-2015

		PKR 100,000/- : 09-06-2015
	Composition	Each gram contains Doxycycline (as hyclate) ……500 mg
	Pharmacological Group	ATC Vet Code: QJ01AA02.: Antibacterial for systemic use; tetracyclines Tetracycline
	Type of Form	Form 5-A
	Finished Product Specification	In-House
	Target Specie	Chicken Broiler
	Shelf life	3 years (supported by accelerated and real time stability data) Shelf-life of the veterinary medicinal product as packaged for sale: 36 months(HPRA)
	Pack size & Demanded Price	1kg sachet
	Approval status of product in Reference Regulatory Authorities.	Ireland Approved HPRA
	Me-too status	023470 Doxyveto- 50 S Soluble Powder Vmd Pakistan Rawalpindi
	CoPP/GMP status	Original, legalized certificate of origin and free sale issued on 20-03-2014 by Ministry of Agriculture and Food, Bulgarian Food Safety Agency confirms its free sale. Copy of GMP certificate (No. 64/2017/GMP) issued on 01-13-2017 by Ministry of Agriculture and Food, Bulgarian Food Safety Agency confirms the GMP of Biovet but the address written on certificate is different from that provided in Form 5-A as well as in free sale certificate. Authority letter M/s Saadat International 117 Habitat Flat Shadman II Jail Road Lahore & Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria Dated : 13 June 2017 Biovet Joint Stock Company is subsidiary of Huvepharma Eood Located in 3 A ,Nikolay haytov Street, Sofia, 1113 ,Bulgaria
	Remarks of the Evaluator.	Withdrawal Period: Meat and offal: Chicken : 6 days Not authorized for use in laying birds producing eggs for human consumption Do not use within 4 weeks of onset of the laying period. ● The address of manufacturing site on GMP certificate is 39, Petar Rakov St. 48 Vasil Petleshkov Str Peshtera 4, Pazardjik, Bulgaria which is different from that provided on Form 5-A . ● The free sale certificate mentions the product license holder is Biovet Joint Stock Company whereas Form 5 A mentions Huvepharma AD. ● Clarify 1 Kg sachet or bag
	(M-282)	Deferred for the following reasons: ● Clarification for type of container whether you have applied for sachet or bag. ● The address of manufacturing site mentioned on Form 5A is different from the address mentioned on GMP certificate. Clarification is required with documented evidence. ● The product license holder mentioned on free sale certificate is different from the product license holder mentioned on Form 5A. Clarification is required.

Fresh Evaluation:
a. Clarification for type of container whether you have applied for sachet or bag.
1 Kg sachet
b. The address of manufacturing site mentioned on Form 5A is different from the address mentioned on GMP certificate. Clarification is required with documented evidence.
(QC and Batch Release+Headquarter)
Biovet Joint Stock Company
39, Petar Rakov St. 4500 Peshtera, Bulgaria
(Manufactures)
48 Vasil Petleshkov Str Peshtera 4550,Bulgaria
c. The product license holder mentioned on free sale certificate is different from the product license holder mentioned on Form 5A. Clarification is required.
Firm has submitted that product license holder is Biovet Joint Stock Company 39, Petar Rakov St. 4550 Peshtera, Bulgaria and the same has been mentioned on Free sale Certificate.

Decision of 285th meeting of RB: Deferred for above clarifications
Now the firm has submitted the following documents:

a. It is a 1kg sachet
b. Original Legalized CoPP (Certificate#. BG 5/2019) issued on 29-01-2019 by Bulgarian Food Safety Agency Ministry of Agriculture, Food and Forestry 15 Pencho Slaveikov Blvd. Sofia 1606, Bulgaria declaring the free sale of applied product and GMP compliant status of the manufacturer i.e., BIOVET Joint Stock Company**,** 39 Petar Rakov Str. /48 Vasil Petleshkov Str., Peshtera 4550, Bulgaria.
   Product License Holder of applied product is M/s Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium.
   (Revised form-5A showed that Address of QC, Batch release and Headquarter: 39, Petar Rakov Street, 4550 Peshtera, Bulgaria while address of manufacturing site is 48 vasil Petleshkov street, Peshtera 4550, Bulgaria)
c. The firm has submitted original and legalized letter of authorization for the following products;
   Hydrodoxx 500mg
   Vetmulin 450mg
   Tilmovet 250mg

Decsion of 296th meeting:
Deferred for confirmation whether the applicant has applied same addresses of manufacturing sites as per CoPP.
Evaluation by PEC:
The addresses of MAH (abroad) nad manufacturer as mentioned in revised Form 5A are different from the addresses mentioned in initially submitted Form 5A along with the dossier.
The firm has submitted Rs. 5,000/- vide challan number 0590985 dated 26/03/2021for change of address of manufacturer and MAH (aboad). Following are the details;
Address of QC, Batch release and Headquarter: BIOVET Joint Stock Company 39, Petar Rakov Street, 4550 Peshtera, Bulgaria
manufacturing site: BIOVET Joint Stock Company 48 vasil Petleshkov street, Peshtera 4550, Bulgaria
Product license holder: Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium.

Decision of 308th meeting:
The Board deferred the case for clarification of addresses of manufacturing site in previously submitted dossier, CoPP and revised form 5A.
Evaluation by PEC:

- Initially the firm had not mentioned the addresses of MAH (abroad) and manufacturing facility in Form 5A. However, the address of QC/Batch releasing sit was mentioned on Form 5A. The submitted data in the dossier is from the relevant sites.
- The firm, later on, submitted the revised Form 5A along with fee of Rs. 5,000/- mentioning correct addresses of MAH (abroad), manufacturing site and QC/Batch releasing site, the detail of which is given below;
  Address of QC, Batch release and Headquarter: BIOVET Joint Stock Company 39, Petar Rakov Street, 4550 Peshtera, Bulgaria
  Manufacturing site: BIOVET Joint Stock Company 48 vasil Petleshkov street, Peshtera 4550, Bulgaria

	Product license holder: Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium. Furthermore, the firm has submitted copy of clarification letter from M/s *HuvePharma EOOD, 3a Nikolay Haytov street 1113 Sofia, Bulgaria* which states that *Huvepharma NV, Belgium (MAH) and Biovet Joint Stock Company, Bulgaria* (including QC/Batch releasing site & Manufacturing sites) are subsidiaries of HuvePharma EOOD, Bulgaria.
	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 full fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021

Case No. 5: Registration applications for local manufacturing submitted on Form 5(Human)
New Cases:

84.	Name and address of manufacturer / Applicant	M/s. High-Q Pharmaceuticals, B 64, KDA-1, Karsaz Road, Karachi
	Brand Name +Dosage Form + Strength	Telmas Tablet 40mg+10mg
	Composition	Each bilayer tablet contains: Telmisartan …..40mg Amlodipine as besylate…10mg
	Diary No. Date of R& I & fee	Dy. No. 1376, 24-11-2016 , Rs.20,000/- (23-10-2016)
	Pharmacological Group	Angiotensin II Receptor Antagonist; Calcium Channel Blocker
	Type of Form	Form-5
	Finished product Specification	Manufacturer
	Pack size & Demanded Price	10's,14's, 20's,30's As per leader price
	Approval status of product in Reference Regulatory Authorities.	Telmisartan and amlodipine 40/10mg Tablet by M/s. Lupin Ltd, USA
	Me-too status	Amtas Tablet by M/s Getz Pharma. Karachi.
	GMP status	30-06-2020 Renewal of DML.
	Remarks of the Evaluator.V	• Brand name resemblance with Telmas of Global Pharma. New brand name Elsart -AM. • Evidence of bilayer machine. DML renewal inspection report mentions Double layer rotary compression machine is newly installed with a capacity of around 50000 tablets per hour. Approved in USFDA with box warning.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
85.	Name and address of manufacturer / Applicant	M/s. High-Q Pharmaceuticals, B 64, KDA-1, Karsaz Road, Karachi
	Brand Name +Dosage Form + Strength	Telmas Tablet 80mg+5mg
	Composition	Each bilayer tablet contains: Telmisartan …..80mg Amlodipine as besylate…5mg
	Diary No. Date of R& I & fee	Dy. No. 1377, 24-11-2016 , Rs.20,000/- (23-10-2016)
	Pharmacological Group	Angiotensin II Receptor Antagonist; Calcium Channel Blocker
	Type of Form	Form-5
	Finished product Specification	Manufacturer
	Pack size & Demanded Price	10's,14's, 20's,30's As per leader price
	Approval status of product in Reference Regulatory Authorities.	Telmisartan and amlodipine 80/5mg Tablet by M/s. Lupin Ltd, USA
	Me-too status	Amtas Tablet by M/s Getz Pharma. Karachi.
	GMP status	30-06-2020 Renewal of DML.
	Remarks of the Evaluator.V	• Brand name resemblance with Telmas of Global Pharma. New brand name Elsart -AM.

		• Evidence of bilayer machine. DML renewal inspection report mentions Double layer rotary compression machine is newly installed with a capacity of around 50000 tablets per hour. Approved in USFDA with box warning.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
86.	Name and address of manufacturer / Applicant	M/s. High-Q Pharmaceuticals, B 64, KDA-1, Karsaz Road, Karachi
	Brand Name +Dosage Form + Strength	Telmas Tablet 40mg+5mg
	Composition	Each bilayer tablet contains: Telmisartan …..40mg Amlodipine as besylate…5mg
	Diary No. Date of R& I & fee	Dy. No. 1372, 24-11-2016 , Rs.20,000/- (23-10-2016)
	Pharmacological Group	Angiotensin II Receptor Antagonist; Calcium Channel Blocker
	Type of Form	Form-5
	Finished product Specification	Manufacturer
	Pack size & Demanded Price	10's,14's, 20's,30's As per leader price
	Approval status of product in Reference Regulatory Authorities.	Telmisartan and amlodipine 40/5mg Tablet by M/s. Lupin Ltd,USA.
	Me-too status	Amtas Tablet by M/s Getz Pharma. Karachi.
	GMP status	30-06-2020 Renewal of DML.
	Remarks of the Evaluator.V	• Brand name resemblance with Telmas of Global Pharma. New brand name Elsart -AM. • Evidence of bilayer machine. DML renewal inspection report mentions Double layer rotary compression machine is newly installed with a capacity of around 50000 tablets per hour. Approved in USFDA with box warning.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
87.	Name and address of manufacturer / Applicant	M/s. High-Q Pharmaceuticals, B 64, KDA-1, Karsaz Road, Karachi
	Brand Name +Dosage Form + Strength	Telmas Tablet 80mg+10mg
	Composition	Each bilayer tablet contains: Telmisartan …..80mg Amlodipine as besylate…10mg
	Diary No. Date of R& I & fee	Dy. No. 1372, 24-11-2016 , Rs.20,000/- (23-10-2016)
	Pharmacological Group	Angiotensin II Receptor Antagonist; Calcium Channel Blocker
	Type of Form	Form-5
	Finished product Specification	Manufacturer
	Pack size & Demanded Price	10's,14's, 20's,30's As per leader price
	Approval status of product in Reference Regulatory Authorities.	Telmisartan and amlodipine 40/5mg Tablet by M/s. Lupin Ltd,USA.
	Me-too status	Amtas Tablet by M/s Getz Pharma. Karachi.
	GMP status	30-06-2020 Renewal of DML.
	Remarks of the Evaluator.V	• Brand name resemblance with Telmas of Global Pharma. New brand name Elsart -AM. • Evidence of bilayer machine. DML renewal inspection report mentions Double layer rotary compression machine is newly installed with a capacity of around 50000 tablets per hour. Approved in USFDA with box warning.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	

88.	Name and address of manufacturer / Applicant	M/s. High-Q Pharmaceuticals, B 64, KDA-1, Karsaz Road, Karachi
	Brand Name +Dosage Form + Strength	Telmath Tablet 40mg+12.5mg
	Composition	Each bilayer tablet contains: Telmisartan….40mg Hydrochlorthiazide….12.5mg
	Diary No. Date of R& I & fee	Dy. No.1375, 24-11-2014 , Rs.20,000/- (23-11-2014)
	Pharmacological Group	Calcium Antagonist: Diuretic
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's,14's,28's: As per brand leader
	Approval status of product in Reference Regulatory Authorities.	Micardis HCT USFDA Approved
	Me-too status	Velmon H by Martin Dow
	GMP status	30-06-2020 Renewal of DML.
	Remarks of the Evaluator.V	• Brand name resemblance with Telmas of Global Pharma. New brand name Co- Elsart . • Evidence of bilayer machine. DML renewal inspection report mentions Double layer rotary compression machine is newly installed with a capacity of around 50000 tablets per hour. • Approved in USFDA with box warning.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
89.	Name and address of manufacturer / Applicant	M/s. High-Q Pharmaceuticals, B 64, KDA-1, Karsaz Road, Karachi
	Brand Name +Dosage Form + Strength	Telmath Tablet 80mg+12.5mg
	Composition	Each bilayer tablet contains: Telmisartan….80mg Hydrochlorthiazide….12.5mg
	Diary No. Date of R& I & fee	Dy. No.1370, 24-11-2014 , Rs.20,000/- (23-11-2014)
	Pharmacological Group	Calcium Antagonist: Diuretic
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's,14's,28's: As per brand leader
	Approval status of product in Reference Regulatory Authorities.	Micardis HCT USFDA Approved
	Me-too status	Velmon H by Martin Dow
	GMP status	30-06-2020 Renewal of DML.
	Remarks of the Evaluator.V	• Brand name resemblance with Telmas of Global Pharma. New brand name Co- Elsart . • Evidence of bilayer machine. DML renewal inspection report mentions Double layer rotary compression machine is newly installed with a capacity of around 50000 tablets per hour. • Approved in USFDA with box warning.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	

Deferred Cases:

90.	Name and address of manufacturer / Applicant	M/s Unisa Pharmaceuticals Industries, G.T Road Adamzai, Akora, Khattak, Nowshehra, KPK
	Brand Name +Dosage Form + Strength	Unilyte-M 500ml Infusion (5% Dextrose & Electrolytes)
	Composition	Each 100ml contains: Dextrose anhydrous……5g Calcium Chloride dihydrate……0.022g Potassium Chloride……...0.150g Sodium Chloride……...0.216g Sodium Acetate Trihydrate……..0.313g Water for injection…….q.suff.
	Diary No. Date of R& I & fee	Dy. No.4234; 29-12-2016; Rs.20,000/- (23-12-2016)
	Pharmacological Group	Electrolytes and carbohydrates
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	500ml & as recommended by PRC (MOH)
	Approval status of product in Reference Regulatory Authorities.	Not provided
	Me-too status	Medilyte-M of M/s MediPak limited
	GMP status	Last GMP inspection conducted on 22-09-2017 and the report concludes that the overall GMP compliance of the firm was found good.
	Remarks of the Evaluator	The approved drug could not be verified in the reference authorities.
	Decision of 278th meeting: Deferred for evidence of approval of applied formulation in LDPE packaging material by reference regulatory authorities/agencies which were declared/approved by the Registration Board. **Submission by the firm:** The firm has submitted following; • GMP inspection report dated 11/01/2019 concludes that the firm is operating at satisfactory level of GMP. • The firm has submitted following RRA reference Dextrose 5% in Acetated Ringer's in plastic Container by M/s B Braun, USFDA Approved. Calcium chloride, Potassium Chloride, Sodium Acetate, Sodium Chloride, Dextrose (20mg/100ml, 30mg/100ml, 380mg/100ml, 600mg/100ml, 5gm/100ml) • The product is discontinued in USFDA.	
	Decision: Deferred for the evidence of approval of the applied formulation by reference regulatory authorities as approved by Regisrtation Board in 275th meeting.	

Case No. 6: Registration applications for local manufacturing submitted on Form 5 (veterinary)

Deferred Cases:

91.	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 100 gm Contains :- Paracetamol……..20 gm Vitamin C……..5 gm Potassium Carbonate…….12.5 gm Sodium Bicarbonate……..12.5 gm Vitamin E……..1.25 gm
	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, 2.5 kg, 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 100 gm Contains :- Paracetamol……..20 gm Vitamin C……..5 gm Potassium Carbonate…….12.5 gm Sodium Bicarbonate……..12.5 gm Vitamin E……..12.5 gm* *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.	
	Decision: Since the formulation is under review the expert working group on veterinary drugs, therefore, the Board deferred the case till finalisation of the fate of the applied product by expert working group.	
92.	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	DOXYCOL-T POWDER
	Composition	Each 100 gm Contains:- Tylosin Tartrate……..10 gm Doxycycline HCL……..20 gm Colistin Sulphate……3 gm Bromhexine HCL……...1 gm
	Diary No. Date of R& I & fee	Dy. No. 11641; 06-03-2019; Rs. 20,000/- (01-03-2019)
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Firm has claimed In-house specification
	Pack size & Demanded Price	100gm, 500gm, 1Kg, 2.5 kg, 5 kg, 25 kg : Decontrolled
	Me-too status	BIOSIN TD by Leads Pharma (Reg. No. 044951)
	GMP status	New License (Inspection Date: 04-10-2018 & 05-11-2018). DML issued on 05.03.19
	Remarks of the Evaluator	Firm mentioned different strength on label claim and Master Formula, Firm was asked to Clarify/Justify. Firm in reply submitted revised form 5 but which is not as per Me-too
	Decision of 289th meeting: "Deferred for submission of fee for revision of formulation" **Submission by the firm:** Now the firm has submitted the fee Rs. 5000/- while composition of me-too is not same as applied product. In generic/me-too product Bromohexine HCl is 10gm/100gm while applied is 1gm/100gm. **Decision of 293rd meeting:** Deferred for evidence of applied formulation/drug already approved by DRAP (generic / metoo status) along with registration number, brand name and name of firm. **Submission by the firm:** • 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 100 gm Contains :- Tylosin Tartrate……..10 gm Doxycycline HCL……..20 gm Colistin Sulphate……3 gm Bromhexine HCL……...10 gm* *Strength of Bromhexine HCl is changed from 1gm to 10gm. • Me too: BIOSIN TD POWDER by M/s Leads Pharma, Reg. no. 044951	
	Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of applicable fee as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021	

Agenda of Evaluator PEC-XIV

Case No. 1: Registration applications of Priority applications:

a) Registration applications of Import Human drugs submitted on Form-5F (CTD)

93.	Name, address of Applicant / Importer	M/s AJM Pharma (Pvt) Ltd. 1st Floor, Shafi Court, Merewether Road, Civil Lines, Karachi. **Address of the godown:** 2nd Floor, Shafi Court, Merewether Road, Civil Lines, Karachi.
	Details of Drug Sale License of importer	**Address:** 1st Floor Shafi Court Civil Lines, Merewether Road, Karachi **Validity:** 23-03-2023 **Status:** Drug license by the way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Chia Tai Tianqing Pharmaceutical Group Co., Ltd., No. 369 South Yuzhou Road, Haizhou District, Lianyungang, Jiangsu Province, China.
	Name, address of manufacturer(s)	M/s Chia Tai Tianqing Pharmaceutical Group Co., Ltd., No. 369 South Yuzhou Road, Haizhou District, Lianyungang, Jiangsu Province, China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted legalized CoPP certificate (No. JS20200392) issued by Jiangsu Drug Administration, Jiangsu Province, China for Fulvestrant for Injection 250mg/5ml. 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 12-02-2022.
	Details of letter of authorization / sole agency agreement	Firm has submitted a copy of letter of authorization M/s Chia Tai Tianqing Pharmaceutical Group Co., Ltd., No. 369 South Yuzhou Road, Haizhou District, Lianyungang, Jiangsu Province, 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 Chia Tai Tianqing Pharmaceutical Group Co., Ltd. for importation and distribution in the territory of Pakistan. The letter was issued on 25-11-2020 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 of 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	Form-5F Dy.No 23855 dated 31-08-2021
	Details of fee submitted	PKR 100,000/-: 15-03-2021
	Proposed proprietary name / brand name	Fulvestrant Injection 250mg / 5ml
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Fulvestrant……50mg
	Pharmaceutical form of applied drug	Solution for Injection
	Pharmacotherapeutic Group of (API)	Estrogen receptor antagonist (ATC code: L02BA03)
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	Two prefilled syringes (5ml each) / pack
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Faslodex 250 mg/5 mL (50 mg/mL) vial of AstraZeneca UK Limited Macclesfield, Cheshire, England
	For generic drugs (me-too status)	Femistra injection by Rotex 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, manufacture, description of manufacturing process and controls, 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 Lianyungang Runzhong Pharmaceutical Co., Ltd. No. 16 Jinqiao Rd., Dapu Industrial Park, Economic Technology Development Zone, Lianyungang, Jiangsu, 222069, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacture, description of manufacturing process and controls, 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 API at accelerated and real time conditions. The real time stability

<table>
<tr><td></td><td></td><td>data were conducted at 5±3°C for 36 months and accelerated stability data were conducted at 25±2°C for 6 months.</td></tr>
<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>The firm has submitted pharmaceutical equivalence data of three batches of Fluvestrant Injection 250mg / 5ml with reference listed drug (RLD, Batch # NB345). The quality tests include appearance, identification, related susbstances, Residual solvents, sterility, bacterial endotoxins, visible particulates, particulate matter, tightness of the syringe body and assay.</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>The firm has submitted validation results of assay method, related substances, of Fulvestrant Injection, 250mg/5ml.</td></tr>
<tr><td></td><td>Container closure system of the drug product</td><td>Prefilled Syringe: HYPAK BSCF 5ml RE PRTCFM27 with Luer Tip and Tip Cap.
Fluoropolymer coated bromobutyl rubber plunger (5mL): HYPAK BSCF5ML 4023/50GR FLUROTEC DHB.</td></tr>
<tr><td></td><td>Stability study data of drug product, shelf life and storage conditions</td><td>Firm has submitted stability study data of 3 batches with horizontal, upright and inverted orientation:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>170422185</td><td>5000 Syringes</td><td>22-04-2017</td></tr>
<tr><td>170509185</td><td>10000 Syringes</td><td>09-05-2017</td></tr>
<tr><td>170511185</td><td>10000 Syringes</td><td>11-05-2017</td></tr>
</table>
The firm has performed accelerated stability study at 40°C ± 2°C / 75% ± 5% RH for 6 months and real time stability study at 30 °C ±2 °C / 75 % ± 5%RH for 36 months.</td></tr>
<tr><td colspan="3">Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.</td></tr>
<tr><td>94.</td><td>Name, address of Applicant / Importer</td><td>M/s Amgomed Office # 4, First Floor Ghausia Plaza, Jinnah Avenue Blue Area Islamabad.</td></tr>
<tr><td></td><td>Details of Drug Sale License of importer</td><td>License No: 002-ICT/2013
Address: Office No. 4, 1st Floor Ghousia Plaza, Main Jinnah Avenue, Blue Area Islamabad.
Address of Godown: Office No. 5, first Floor, Rose-I Plaza, I-8 Markaz Islamabad.
Validity: 30-01-2022.
Status: License to sell drugs in a whole sale distributor</td></tr>
<tr><td></td><td>Name and address of marketing authorization holder (abroad)</td><td>PT Fonko International Pharmaceuticals Kawasan Industri Jababeka II, JI. Industri Selatan V, Block PP No. 7, Cikarang Selatan, Bekasi, Jawa Barat. Indonesia.</td></tr>
<tr><td></td><td>Name, address of manufacturer(s)</td><td>PT Fonko International Pharmaceuticals Kawasan Industri Jababeka II, JI. Industri Selatan V, Block PP No. 7, Cikarang Selatan, Bekasi, Jawa Barat. Indonesia.</td></tr>
<tr><td></td><td>Name of exporting country</td><td>Indonesia</td></tr>
</table>

	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted legalized CoPP certificate (No. RG.01.05.32.321.03.21.2589) issued by Badan Pengawas Obat dan Makanan (Google translation name: National Agency of Drug and Food Control) for Fonkozomib 3.5mg Injection. 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 2 years.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of authorization from Fonko International Pharmaceuticals. The letter specifies that the manufacturer appoints M/s Amgomed Islamabad to register their products in Pakistan. Authorization letter is issued on 24-09-2020.
	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 of 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	Form-5F Dy.No 25922 dated 17-09-2021
	Details of fee submitted	PKR 150,000/-: 06-09-2021
	Proposed proprietary name / brand name	FONKOZOMIB 3.5mg Injection
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Bortezomib…..……3.5mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Antineoplastic and immunomodulating agent (ATC code: L01XG01)
	Reference to Finished product specification	In-house Specifications
	Proposed Pack size	1's vial
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	VELCADE for injection 3.5mg per vial of Millenium pharms (USFDA approved)
	For generic drugs (me-too status)	3.5mg Bortezomib Lyophilized Powder for injection of M/s. Revive Pharma (Reg # 090738)
	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 Hetero Labs Limited, Unit-I, Survey No. 10, I.D.A, Gaddapotharam Village, Jinnaram Mandal, Sangareddy District -502319, Telangana, India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacture, description of manufacturing process & controls, characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system & 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. It was concluded that Bortezomib is stable upto 6 months under accelerated conditions (5±3°C) & 60 months under long term conditions (-20°C) and also stable up to 6 months under accelerated conditions (25°C ± 2°C / 60% ± 5% RH) and 60 months under long term 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 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	The firm has submitted pharmaceutical equivalence of Velcade® 3.5mg powder for solution for injection (batch # BILS000) of M/s Jassen Pharmaceutica NV with Bortezomib lyophilized powder for Injection 3.5mg (batch # E0009EB, F0011CA, F0079AA).
	Analytical method validation/verification of product	Firm has submitted validation of HPLC method for identification of Bortezomib in Bortezomib 3.5mg powder for Solution for injection. Analytical methods were developed and transferred PT Fonko International Pharmaceuticals. The analytical method validation was established to determine the Assay (By HPLC), Tertiary butyl alcohol (By HPLC), Related substance (By HPLC), in drug product validated as per the ICH.
	Container closure system of the drug product	**Vial size and type:** Type-I clear Glass vial, 10ml clear with 20 mm neck **Rubber stopper:** Bromobutyl grey rubber stopper 20 mm **Flip off seal:** White flip off seal 20 mm.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of Bortezomib 3.5mg Powder for solution for injection of 10ml vial (Upright):

Batch No.	Batch size	Mfg. Date	Initiation date
D0009	2619 vials	02-2017	April-2017
E0009	2619 vials	01-2018	Feb-2018
F0011	2619 vials	02-2019	Feb-2018

REMARKS OF EVALUATOR		
Pharmaceutical equivalence of the applied drug with the reference product should include results of all the quality tests of the developed formulation and the reference product. Submit stability study data of 3 batches of Bortezomib 3.5mg Injection 10ml vial in horizontal and inverted position.		
Decision: Deferred for following submissions: • **Performance of pharmaceutical equivalence data of applied drug with the innovator product including results of all the quality tests.** • **Stability study data of 3 batches of Bortezomib 3.5mg Injection 10ml vial in horizontal and inverted position.**		
95.	Name, address of Applicant / Importer	M/s GRATON PHARMA, Office # 501, 502, 5th Floor Plot # 42C/2, Lane # 08, Bukhari Commercial, DHA phase - VI, Karachi
	Details of Drug Sale License of importer	**Address:** Office no. 501,502 ,5th floor Plot no IV 42c/2 Lane 08, Bukhari Commercial Phase, D.H.A Karachi **Validity:** 22-10-2021 **Status:** Drug license by the way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s JODAS EXPOIM PVT. LTD., Plot No. 55, Phase-III, Biotech Park, Karkapatla (v), Markook (Mandal), Siddipet District, Telangana-502279, India.
	Name, address of manufacturer(s)	M/s JODAS EXPOIM PVT. LTD., Plot No. 55, Phase-III, Biotech Park, Karkapatla (v), Markook (Mandal), Siddipet District, Telangana-502279, 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.2750 /E1/2020) dated 19 Nov 2020 issued by Drugs Control Administration Hyderabad india for Abiraterone Tablet 250mg. 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. Furthermore, the CoPP was valid till 26-02-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of distribution certificate from Jodas Expoim Pvt Ltd, India. The letter species that the manufacturer appoints M/s Graton Pharma, to register their products in Pakistan. The authorization letter is valid till 31-12-2025.
	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
	Dy. No. and date of submission	Form-5F Dy.No. 27702 dated 06-10-2021
	Details of fee submitted	PKR 75,000/-: 14 July 2021

	Proposed proprietary name / brand name	**XABITON Tablet 250mg**
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Abiraterone Acetate…….250mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	Hormone antagonists and related agents (ATC code: L02BX03)
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	Bottle Pack: 60's Tablets are packed in one HDPE bottle
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zytiga® Tablet 250mg of M/s Janssen-Cilag international NV Turnhoutseweg 30, B-2340 Beerse Belgium **(USFDA Approved**).
	For generic drugs (me-too status)	Not 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. 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 Mac Chem Products (India) Pvt. Ltd. 304, Town centre, Andheri – Kurla Road, Andheri (East), Mumbai – 400 059, India.
	Module-III Drug Substance:	The firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacture, characterization, control of API, analytical procedures and its validation, batch analyses, 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 conditions (40°C ± 2°C/ 75% ± 5% RH) for 6 months and at real time conditions (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.

<table>
<tr><td></td><td>Pharmaceutical Equivalence and Comparative Dissolution Profile</td><td>The firm has submitted comparative dissolution profile data of developed formulation Abiraterone acetate 250mg tablet with reference product Zytiga tablet 250mg in three BCS media</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Firm has submitted analytical method validation studies for the applied product.</td></tr>
<tr><td></td><td>Container closure system of the drug product</td><td>PVC / PE/PVdC-Alu Blister Pack:
10 tablets are packed in one PVC/PE/PVdC-Alu blister
HDPE Bottle pack:
60 tablets are packed in one HDPE bottle.</td></tr>
<tr><td></td><td>Stability study data of drug product, shelf life and storage conditions</td><td>Firm has submitted stability study data of 3 batches:
<table>
<tr><td>Batch No.</td><td>Batch size</td><td>Mfg. Date</td></tr>
<tr><td>ON-E18019</td><td>12,000 Tablets</td><td>12-2018</td></tr>
<tr><td>ON-E18020</td><td>12,000 Tablets</td><td>12-2018</td></tr>
<tr><td>ON-E18021</td><td>12,000 Tablets</td><td>12-2018</td></tr>
</table>
The firm has performed accelerated stability study at 40 ºC±2ºC/75%±5%RH for 6 months and real time stability study at 30 ºC±2 ºC/75%±5%RH for 12 months.</td></tr>
<tr><td colspan="3">Details of batches of developed formulation and reference product Zytiga 250mg tablet used in comparative dissolution profile should be provided.
Pharmaceutical equivalence of the applied drug with the reference product should include results of all the quality tests of the developed formulation and the reference product.
Specify the container closure system in which the final product will be imported.
Submit stability study data (real time) in relevant container closure system till claimed shelf life under conditions of Zone- IVA.
The submitted copy of drug sale license has expired therefore the updated copy of drug sale license is required.</td></tr>
<tr><td colspan="3">Decision: Decision: Deferred for following submissions:
• Performance of pharmaceutical equivalence data of applied drug with the innovator product including results of all the quality tests.
• Details of batches of developed formulation and reference product Zytiga 250mg tablet used in comparative dissolution profile.
• Stability study data (real time) in relevant container closure system till claimed shelf life under conditions of Zone- IVA.
• Updated copy of drug sale license of importer.</td></tr>
</table>

Case no. 02 Registration applications for local manufacturing of (Human) drugs

a. Deferred cases

96.	Name and address of manufacturer / Applicant	M/s. Lisko Pakistan, L-10-D, Block No 21, Shaheed Rashid Minhas Road, FB Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Albezole Suspension (200mg/5ml)
	Composition	Each 5ml contains: Albendazole……100mg
	Diary No. Date of R& I & fee	686, 25-04-2016, Rs. 20,000/- (25-04-2016)
	Pharmacological Group	Benzimidazole anthelmintic
	Type of Form	Form-5
	Finished product Specifications	BP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed.
	Me-too status	Nenzole Suspension of M/s Nenza Pharma (Reg# 025891)
	GMP status	23-01-2017, Good
	Previous remarks of the Evaluator.	
	Previous Decision	Deferred for evidence of approval of applied formulation in

		reference regulatory authorities/agencies which were declared/ approved by the Registration Board in 249th meeting (M-274).
	Evaluation by PEC	Applicant has submitted that h applied is approved in EMA. Approval authority name: EMA Product Name: Zentel 100mg/5ml Generic: albendazole National Authorization Number: 10/0173/85-C/S MAH of Product in member state: GSK The product monograph is present in USP.
	Decision: Approved with innovator's specifications. 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.	
97.	Name and address of manufacturer / Applicant	M/s Saibins Pharmaceuticals, Plot 316, Industrial Triangle Kahuta Road Islamabad
	Brand Name +Dosage Form + Strength	SAIFLOX 750mg tablet
	Composition	Each film coated tablet contains: Levofloxacin (as hemihydrate)…….750mg
	Diary No. Date of R& I & fee	Dy. No.432; 21-03-2016; Rs.20,000/- (18-03-2016)
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	1 × 10's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in USFDA
	Me-too status	Tevoflox Tablets 750 mg of M/s Pearl Pharmaceuticals (068560)
	GMP status	Last GMP inspection report dated 02-01-2017 confirms good compliance to GMP
	Previous remarks of the Evaluator.	Coating ingredients not mentioned in the master formulation.
	Previous Decision	Deferred for clarification of dosage form whether coated or uncoated as coating ingredients were not mentioned in the master formulation (M-274). Deferred for submission of fee for revision of formulation (M-291).
	Evaluation by PEC	The firm has submitted revised master formulation with film coating composition. The firm has submitted fee challan of Rs. 7500/- (Slip # 352440397150) dated 27-09-2021 for revision of formulation. The firm is granted GMP certificate based on inspection conducted on 24-12-2018 valid till 23-12-2021.
	Decision: Approved.	
98.	Name and address of manufacturer / Applicant	M/s Saibins Pharmaceuticals, Plot 316, Industrial Triangle Kahuta Road Islamabad
	Brand Name +Dosage Form + Strength	RIBAN 10mg tablets
	Composition	Each film coated tablet contains: Rivaroxaban……10mg
	Diary No. Date of R& I & fee	Dy. No.303; 16-03-2016; Rs.20,000/- (15-03-2016)
	Pharmacological Group	Anticoagulant
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	1 × 14's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved by MHRA of UK
	Me-too status	Xarelto of M/s Bayer Health Care (Reg.# 059057)
	GMP status	Last GMP inspection report dated 02-01-2017 confirms good compliance to GMP

	Previous remarks of the Evaluator.	Coating ingredients not mentioned in the master formulation. No USP or BP monograph is available for applied formulation
	Previous Decision	Deferred for clarification of dosage form whether coated or uncoated as coating ingredients were not mentioned in the master formulation (M-274). Deferred for submission of fee for revision of formulation (M-291).
	Evaluation by PEC	The firm has submitted revised master formulation with film coating composition. The firm has submitted fee challan of Rs. 7500/- (Slip # 9138090740) dated 27-09-2021 for revision of formulation. The firm is granted GMP certificate based on inspection conducted on 24-12-2018 valid till 23-12-2021.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
99.	Name and address of manufacturer / Applicant	M/s Saibins Pharmaceuticals, Plot 316, Industrial Triangle Kahuta Road Islamabad
	Brand Name +Dosage Form + Strength	RIBAN 15mg tablets
	Composition	Each film coated tablet contains: Rivaroxaban……15mg
	Diary No. Date of R& I & fee	Dy. No.304; 16-03-2016; Rs.20,000/- (15-03-2016)
	Pharmacological Group	Anticoagulant
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	1 × 14's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved by MHRA of UK
	Me-too status	Xarelto of M/s Bayer Health Care (Reg.# 072549)
	GMP status	Last GMP inspection report dated 02-01-2017 confirms good compliance to GMP
	Previous remarks of the Evaluator.	Coating ingredients not mentioned in the master formulation. No USP or BP monograph is available for applied formulation.
	Previous Decision	Deferred for clarification of dosage form whether coated or uncoated as coating ingredients were not mentioned in the master formulation (M-274). Deferred for submission of fee for revision of formulation (M-291).
	Evaluation by PEC	The firm has submitted revised master formulation with film coating composition. The firm has submitted fee challan of Rs. 7500/- (Slip # 3450289611) dated 27-09-2021 for revision of formulation. The firm is granted GMP certificate based on inspection conducted on 24-12-2018 valid till 23-12-2021.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
100.	Name and address of manufacturer / Applicant	M/s Saibins Pharmaceuticals, Plot 316, Industrial Triangle Kahuta Road Islamabad
	Brand Name +Dosage Form + Strength	RIBAN 20mg tablets
	Composition	Each film coated tablet contains: Rivaroxaban……20mg
	Diary No. Date of R& I & fee	Dy. No.305; 16-03-2016; Rs.20,000/- (15-03-2016)
	Pharmacological Group	Anticoagulant
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	1 × 14's: As per SRO
	Approval status of product in Reference	Approved by MHRA of UK

	Regulatory Authorities	
	Me-too status	Xarelto of M/s Bayer Health Care (Reg.# 072550)
	GMP status	Last GMP inspection report dated 02-01-2017 confirms good compliance to GMP
	Previous remarks of the Evaluator.	Coating ingredients not mentioned in the master formulation. No USP or BP monograph is available for applied formulation.
	Previous Decision	Deferred for clarification of dosage form whether coated or uncoated as coating ingredients were not mentioned in the master formulation (M-274). Deferred for submission of fee for revision of formulation (M-291).
	Evaluation by PEC	The firm has submitted revised master formulation with film coating composition. The firm has submitted fee challan of Rs. 7500/- (Slip # 38624683) dated 27-09-2021 for revision of formulation. The firm is granted GMP certificate based on inspection conducted on 24-12-2018 valid till 23-12-2021.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
101.	Name and address of manufacturer / Applicant	"M/s Surge Laboratories Pvt Ltd. 10 km, Faisalabad Road, Bikhi, District Sheikhupura"
	Brand Name +Dosage Form + Strength	Surgidex 25% Injection
	Composition	"Each ml Contains: Dextrose……250mg"
	Diary No. Date of R& I & fee	Dy. No. 34293 dated 16-10-2018 Rs.20,000/-
	Pharmacological Group	Electrolyte
	Type of Form	Form-5
	Finished product Specifications	BP specifications
	Pack size & Demanded Price	10's; 20ml
	Approval status of product in Reference Regulatory Authorities	Dextrose Injection (25% & 50%) by M/s Hospira, USFDA Approved.
	Me-too status	Dextrose 25% Injection (20ml) by M/s Zafa, Reg. No. 57804
	GMP status	Date: 22-02-2018 & 04-05-2018 Recommendations: Based on the physical inspection of the unit, the technical personal met and documents evaluated, the panel concluded that the firm M/s Surge Labs Sheikhupura has maintained a fair level of GMP compliance as per Schedule B-II of Drug (Lic, Reg & Adv) Rules 1976 on the day of inspection.
	Previous remarks of the Evaluator.	Evidence of reference product packed in polypropylene ampoule.
	Previous Decision	Deferred for the following (M-295): Evidence of reference product packed in polypropylene ampoule. Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.
	Evaluation by PEC	The firm has submitted that it was wrongly communicated that the product "Surgidex 25% Injection" will be supplied in polypropylene ampoule. In this connection, we would like to submit that we will supply the product "Surgidex 25% Injection" 20ml in Low density polyethylene (LDPE), twist-off, plastic ampoule. We regret for the inconvenience caused to you in this regard. Approval status of applied formulation is confirmed in USFDA.
	Discussion: Registration Board discussed that 25% dextrose infusion is not available in 20ml fill volume in	

	any reference regulatory authority. It was discussed that there is no difference in composition and packaging material and that 20ml fill volume is already available in Pakistan. **Decision: Keeping in view above discussion, the Board decided to approve the registration of Surgidex 25% Injection.** **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
102.	Name and address of manufacturer / Applicant	M/s Sunshine Pharmaceuticals, Emanabad, G.T. Road, Gujranwala.
	Brand Name +Dosage Form + Strength	Cobol 500mcg Tablets
	Composition	Each tablet contains: Mecobalamin……...500mcg
	Diary No. Date of R& I & fee	Dy No:2534, 12-10-2010, Rs 12,000/- Rs 8,000/-
	Pharmacological Group	Vitamin B12 analogue
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	10 x 10's; Rs 75 per 10 tablets
	Approval status of product in Reference Regulatory Authorities	PMDA approved.
	Me-too status	Mecovis 500mcg by Global
	GMP status	GMP inspection report dated 20-01-2021 concluded that firm has made lot of improvements and up-gradations as per GMP guidelines.
	Previous remarks of the Evaluator.	
	Previous Decision (M-307)	Deferred for revision of formulation as per reference product along with submission of requisite fee for change of formulation.
	Evaluation by PEC	The firm has submitted revised master formulation with sugar coating composition as per reference. Each sugar-coated tablet contains: Mecobalamin……500mcg Fee challan of Rs. 7500/- (slip # 60357575581) dated 13-08-2021 for revision of formulation as per reference.
	Decision: Deferred for confirmation of requirement of JP monograph regarding storage and testing of drug substance and container closure system of drug product.	
103.	Name and address of manufacturer / Applicant	M/s Sunshine Pharmaceuticals, Emanabad, G.T. Road, Gujranwala.
	Brand Name +Dosage Form + Strength	Montikast 10mg tablet
	Composition	Each tablet contains: Montelukast as sodium…….....10mg
	Diary No. Date of R& I & fee	Dy No:2530, 12-10-2010, Rs 12,000/- Rs 8,000/-
	Pharmacological Group	Anti-histamine
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	2 x 10's; Rs 440 per 20 tablets
	Approval status of product in Reference Regulatory Authorities	SINGULAIR 10 mg Film coated Tablets (USFDA)
	Me-too status	Montiget 10mg Tablet by M/s Getz Pharma
	GMP status	GMP inspection report dated 20-01-2021 concluded that firm has made lot of improvements and up-gradations as per GMP guidelines.
	Previous remarks of the Evaluator.	
	Previous Decision (M-307)	Deferred for revision of formulation as per reference product along with submission of requisite fee for change of formulation.
	Evaluation by PEC	The firm has submitted revised master formulation with film coating composition as per reference. Each film coated tablet contains:

		Montelukast as sodium……10mg Fee challan of Rs. 7500/- (slip # 160582682) dated 13-08-2021 for revision of formulation as per reference.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
104.	Name and address of manufacturer / Applicant	M/s Sunshine Pharmaceuticals, Emanabad, G.T. Road, Gujranwala.
	Brand Name +Dosage Form + Strength	Sunsaid 100mg tablet
	Composition	Each tablet contains: Flurbiprofen……...100mg
	Diary No. Date of R& I & fee	Dy No:874, 12-10-2010, Rs 12,000/- Rs 8,000/-
	Pharmacological Group	NSAID
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	3 x 10's; Rs 7.1 per tablet, Rs 213 per 30 tablet
	Approval status of product in Reference Regulatory Authorities	ANSM approved.
	Me-too status	Ansaid 100mg tablet
	GMP status	GMP inspection report dated 20-01-2021 concluded that firm has made lot of improvements and up-gradations as per GMP guidelines.
	Previous remarks of the Evaluator.	
	Previous Decision (M-307)	Deferred for revision of formulation as per reference product along with submission of requisite fee for change of formulation.
	Evaluation by PEC	The firm has submitted revised master formulation with film coating composition as per reference. Each film coated tablet contains: Flurbiprofen……100mg Fee challan of Rs. 7500/- (slip # 8698438585) dated 13-08-2021 for revision of formulation as per reference.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
105.	Name and address of manufacturer / Applicant	M/s Sunshine Pharmaceuticals, Emanabad, G.T. Road, Gujranwala.
	Brand Name +Dosage Form + Strength	Xysun 10mg tablets
	Composition	Each tablet contains: Levocetrizine……..…..10mg
	Diary No. Date of R& I & fee	Dy No:874, 12-10-2010, Rs 12,000/- Rs 8,000/-
	Pharmacological Group	Anti-histamine
	Type of Form	Form-5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	1 x 10's; Rs 55 per 10 tablets
	Approval status of product in Reference Regulatory Authorities	Not Provided
	Me-too status	Alergocit 5mg tablet by M/s Global Pharma
	GMP status	GMP inspection report dated 20-01-2021 concluded that firm has made lot of improvements and up-gradations as per GMP guidelines.
	Previous remarks of the Evaluator.	
	Previous Decision (M-271)	Deferred for the followings: a) Submission of latest GMP inspection report conducted within a year. b) Evidence of approval status of formulation in the reference

		regulatory authorities and me-too status
	Evaluation by PEC	The firm has revisd the composition of the product from 10mg film coated tablet to 5mg film coated tablet as per reference: Each film coated tablet contains: Levocetirizine dihydrochloride……5mg Me-too status: Evocin Tablets of M/s Skims Pharmaceuticals (Reg # 091477). International reference: XYZAL (levocetirizine dihydrochloride) film coated tablets, (USFDA approved). Fee challan of Rs. 30,000/- (slip # 1064562565) dated 10-08-2021 for revision of formulation as per reference.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
106.	Name and address of manufacturer / Applicant	M/s Brookes Pharma (Private) Limited, 58 & 59, Sector 15, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Misonil 75mg Tablet
	Composition	Each tablet contains: Diclofenac sodium…….75mg Misoprostol (HPMC dispersion 1%)……...200mcg
	Diary No. Date of R & I & fee	2142, 16-01-2018, 20,000/-, 12-01-2018
	Pharmacological Group	NSAID with prostaglandin analogue
	Type of Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	20's; As per brand leader price
	Approval status of product in Reference Regulatory Authorities	Arthrotec 75 of GD Searle (USFDA approved)
	Me-too status	Cytopan-75 Tablets by Getz Pharma (Reg#024014)
	GMP status	GMP inspection dated 11-10-2017 and 16-10-2017 concluded that the firm is considered to be operating at satisfactory level of compliance.
	Previous remarks of the Evaluator.	Master formulation shows that the tablet consists of an enteric coated core containing 75mg of diclofenac sodium surrounded by an outer mantle containing 200mcg misoprostol.
	Previous Decision (M-288)	Deferred for the clarification of manufacturing outline as in reference regulatory authorities the approved drug is multilayered tablet, while the applied drug is mono layered tablet and submission of double layer compression machine.
	Evaluation by PEC	The firm has submitted manufacturing flowchart and master to elaborate the process and layering of the product. This shows that the product consists of an "inner enteric coated core and outer core mantle covering" of misoprostol, which is called Tablet in Tablet or Bi-Layered Tablet. Last inspection report dated 15-07-2019 concludes as under: "Based on the above observations the panel unanimously recommends the firm for the grant of GMP Certificate for export purpose." Evidence of bi-layered machine
	Decision: Deferred for evidence of availability of bilayered machine for manufacturing of applied drug product.	
107.	Name and address of manufacturer / Applicant	M/s Saydon Pharmaceutical Industries Pvt Ltd., 77-A, Hayatabad Industrial Estate, Peshawar
	Brand Name +Dosage Form + Strength	Met-Sit 1000/50 mg Tablets
	Composition	"Each Film Coated Tablet Contains: Metformin hydrochloride…1000mg Sitagliptin (as phosphate monohydrate)…….50mg"

	Diary No. Date of R & I & fee	Dy No. 16640; 27-04-18: Rs.20,000
	Pharmacological Group	Anti-diabetic
	Type of Form	Form-5
	Finished product Specifications	USP specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in USFDA
	Me-too status	Gliptin Plus Tablet of Genix Pharma Karachi
	GMP status	GMP inspection was conducted on 13-02-2018 with following conclusions & recommendations. **Conclusion:** "Overall the firm was in good working condition and following the cGMP guidelines as per Drugs Act, 1976 and rules framed there under. Based on the area inspected the people met and document reviewed and considering the findings of Inspection of M/s Say don Pharmaceuticals Pvt. Ltd Peshawar is considered at acceptable level of compliance with cGMP guidelines as per Drugs Act, 1976 and rules framed under."
	Previous remarks of the Evaluator.	
	Previous Decision (M-290)	Deferred for GMP status of firm from QA &LT Division.
	Evaluation by PEC	The firm has submitted copy of inspection report conducted on 28-07-2020 which concluded that the firm may be considered at acceptable level of GMP compliance.
	Decision: Approved with innovator's specifications. **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
108.	Name and address of manufacturer / Applicant	M/s Vega Pharmaceuticals (PVT) LTD. Plot No.4, Pharma city Sunder 30KM Multan road Lahore.
	Brand Name +Dosage Form + Strength	MOMAT Nasal spray (50mcg/spray)
	Composition	Each spray contains: Mometasone furoate……..50mcg
	Diary No. Date of R & I & fee	Dy.No. 33945 dated 12/10/2018 PKR 20,000/-
	Pharmacological Group	Coticosteroid
	Type of Form	Form-5
	Finished product Specifications	BP specifications
	Pack size & Demanded Price	Price Rs.300/- per bottle of 20ml
	Approval status of product in Reference Regulatory Authorities	APO-MOMETASONE aqueous nasal spray by M/s Apotex Inc. Health Canada approved
	Me-too status	Memocart nasal spray by M/s Platinum Pharma Karachi, Reg no. 36585
	GMP status	Last inspection report dated 17/07/2017 concluded that the firm has maintained good level of GMP compliance. The firm has Eye Drops (Steroidal) Section.
	Previous remarks of the Evaluator.	
	Previous Decision	Deferred for confirmation of required manufacturing facility / section Nasal Spray from Licensing Division (M-293).
	Evaluation by PEC	The firm as submitted that we have two eye drops sections for general and steroid products. Nasal drops are manufactured in the same facility of eye drops, as their manufacturing process is same. No separate facility is required for nasal sprays. We have already four registered products of nasal sprays, one product Fluni nasal spray is steroid while other three are non-antibiotic nasal sprays. Non-antibiotic nasal sprays are manufactured in general eye drops section and steroid nasal sprays are manufactured in steroid eye drop section. The panel of inspectors recommends grant of renewal of DML

		based on inspection conducted on on 10-11-2020 and some changes in nomenclature of existing sections are also suggested* as given below: Tablet Section (General) Capsule Section (General) Eye, Ear & Nasal Section (General)* Eye, Ear & Nasal Section (Steroid)* Capsules (Cephalosporin) Oral dry powder for suspension (Cephalosporin) Dry powder for Injection (Cephalosporin)
	Decision: Deferred and advised to deliberate with Licensing Division regarding manufacturing requirements of applied formulation in eye and ear section.	

Case no. 03 Registration applications for local manufacturing of (Veterinary) drugs

a. Deferred cases

109.	Name and address of manufacturer / Applicant	M/s Mylab Pvt Ltd., Khankah Sharif, Bahawalpur
	Brand Name +Dosage Form + Strength	Tetramide Spray
	Composition	Each 100gm Contains: Chlortetracycline……..367000IU Sulphanilamide……..…5.963mg
	Diary No. Date of R& I & fee	Dy.No 2024 dated 16-01-2018 Rs. 20,000 Dated 15-01-2018
	Pharmacological Group	Insecticide/hormonal analogue
	Type of Form	Form-5
	Finished product Specification	In house
	Pack size & Demanded Price	210 ml; Decontrolled
	Me-too status	Orospray External Spray (Reg # 027453)
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator.	• The firm has provided Aerosol vet section.
	Previous decision(s) (M-296)	Deferred for clarification of manufacturing of powder formulation in aerosol section (M-288). Deferred for further deliberation regarding clarification of manufacturing of powder formulation in aerosol section.
	Evaluation by PEC	The firm has submitted that finished product aerosol spray is not in powder form rather it is in liquid form. QC procedures are carried out by taking weight of contents of finished product because after filling liquid and propellant sealing is performed and after that container cannot be opened. Hence final filled volume is quantified by weight. The firm has submitted that "Aerosol dosage form is a suspension of fine solid drug particles or liquid drug droplets in a carrier gas/propellant and the design of such delivery system is intended to release measured mass and appropriate quantity of the active pharmaceutical ingredient upon each actuation." Therefore, we had represented the composition of our aerosol pharmaceutical product in terms of mass (grams), rather than in terms of volume.
	Decision: The Board deferred the case for confirmation whether appled product is spray or aerosol and then required manufacturing facility including filling of carrier / propellant gas for aerosol formulation.	
110.	Name and address of manufacturer / Applicant	M/s Mylab Pvt Ltd., Khankah Sharif, Bahawalpur
	Brand Name +Dosage Form + Strength	Roximax Topical Spray
	Composition	Each 170 gm Bottle Contains: Rifaximin…….0.5gm

	Diary No. Date of R& I & fee	Dy.No 2008 dated 16-01-2018 Rs. 20,000 Dated 15-01-2018
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	In house
	Pack size & Demanded Price	170gm; Decontrolled
	Me-too status	Fatroximin Topical Spray (Reg#021263)
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator.	• The firm has provided Aerosol vet section.
	Previous decision(s) (M-296)	Deferred for clarification of manufacturing of powder formulation in aerosol section (M-288). Deferred for further deliberation regarding clarification of manufacturing of powder formulation in aerosol section.
	Evaluation by PEC	The firm has submitted that finished product aerosol spray is not in powder form rather it is in liquid form. QC procedures are carried out by taking weight of contents of finished product because after filling liquid and propellant sealing is performed and after that container cannot be opened. Hence final filled volume is quantified by weight. The firm has submitted that "Aerosol dosage form is a suspension of fine solid drug particles or liquid drug droplets in a carrier gas/propellant and the design of such delivery system is intended to release measured mass and appropriate quality of the active pharmaceutical ingredient upon each actuation." Therefore, we had represented the composition of our aerosol pharmaceutical product in terms of mass (grams), rather than in terms of volume.
	Decision: The Board deferred the case for confirmation whether the applied product is spray or aerosol and accordingly required manufacturing facility including filling of carrier / propellant gas for aerosol formulation.	
111.	Name and address of manufacturer / Applicant	M/s Mylab Pvt Ltd., Khankah Sharif, Bahawalpur
	Brand Name +Dosage Form + Strength	Anti-Mastitis Spray
	Composition	Each 15gm Contains: Rifaximin…….……0.100gm Cefacetrile Sodium…..…0.200gm
	Diary No. Date of R& I & fee	Dy.No 2006, 16-01-2018 Rs. 20,000, 15-01-2018
	Pharmacological Group	Anti-Mastitis
	Type of Form	Form-5
	Finished product Specification	In house
	Pack size & Demanded Price	4×15gm can; Decontrolled
	Me-too status	Cefaximin-l Anti Mastitis Spray (Reg # 019906)
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator.	• The firm has provided Aerosol vet section.
	Previous decision(s) (M-296)	Deferred for clarification of manufacturing of powder formulation in aerosol section (M-288). Deferred for further deliberation regarding clarification of manufacturing of powder formulation in aerosol section.
	Evaluation by PEC	The firm has submitted that finished product aerosol spray is not in powder form rather it is in liquid form. QC procedures are carried out by taking weight of contents of finished product because after filling liquid and propellant sealing is performed and after that container cannot be opened. Hence final filled volume is quantified by weight. The firm has submitted that "Aerosol dosage form is a

		suspension of fine solid drug particles or liquid drug droplets in a carrier gas/propellant and the design of such delivery system is intended to release measured mass and appropriate quality of the active pharmaceutical ingredient upon each actuation." Therefore, we had represented the composition of our aerosol pharmaceutical product in terms of mass (grams), rather than in terms of volume.
	Decision: Deferred for following submission: • **Confirmation whether the applied product is spray or aerosol and accordingly required manufacturing facility including filling of carrier / propellant gas for aerosol formulation..** • **Rationale for application of topical spray dosage form for the treatment of Mastitis.**	
112.	Name and address of manufacturer / Applicant	M/s Mylab Pvt Ltd., Khankah Sharif, Bahawalpur
	Brand Name +Dosage Form + Strength	Alspray
	Composition	Each gm Contains: Aluminium Powder…….40mg
	Diary No. Date of R& I & fee	Dy. No. 2005, 16-01-2018 Rs. 20,000 dated 15-01-2018
	Pharmacological Group	Antiseptic
	Type of Form	Form-5
	Finished product Specification	In house
	Pack size & Demanded Price	210 ml; Decontrolled
	Me-too status	Aluspray Pressurized suspension (Reg # 028560)
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator.	• The firm has provided Aerosol vet section.
	Previous decision(s) (M-296)	Deferred for clarification of manufacturing of powder formulation in aerosol section (M-288). Deferred for further deliberation regarding clarification of manufacturing of powder formulation in aerosol section
	Evaluation by PEC	The firm has submitted that finished product aerosol spray is not in powder form rather it is in liquid form. QC procedures are carried out by taking weight of contents of finished product because after filling liquid and propellant sealing is performed and after that container cannot be opened. Hence final filled volume is quantified by weight. The firm has submitted that "Aerosol dosage form is a suspension of fine solid drug particles or liquid drug droplets in a carrier gas/propellant and the design of such delivery system is intended to release measured mass and appropriate quality of the active pharmaceutical ingredient upon each actuation." Therefore, we had represented the composition of our aerosol pharmaceutical product in terms of mass (grams), rather than in terms of volume.
	Decision: Deferred for following submission: • **Confirmation whether the applied product is spray or aerosol and accordingly required manufacturing facility including filling of carrier / propellant gas for aerosol formulation.** • **Confirmation of aluminium salt to be used in the applied formulation.**	
113.	Name and address of manufacturer / Applicant	M/s Mylab Pvt Ltd., Khankah Sharif, Bahawalpur
	Brand Name +Dosage Form + Strength	Roximax Intrauterine Foam
	Composition	Each 13.4gm Bottle Contains: Rifaximin……..0.10gm
	Diary No. Date of R& I & fee	Dy.No 2009 dated 16-01-2018 Rs. 20,000 Dated 15-01-2018
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	In house

	Pack size & Demanded Price	13.4g; Decontrolled
	Me-too status	Fatroximin Intrauterine Foam. (Reg#048129)
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator.	• The firm has provided Aerosol vet section.
	Previous decision(s) (M-296)	Deferred for clarification of manufacturing of powder formulation in aerosol section (M-288). Deferred for further deliberation regarding clarification of manufacturing of powder formulation in aerosol section.
	Evaluation by PEC	The firm has submitted that finished product aerosol spray is not in powder form rather it is in liquid form. QC procedures are carried out by taking weight of contents of finished product because after filling liquid and propellant sealing is performed and after that container cannot be opened. Hence final filled volume is quantified by weight. The firm has submitted that "Aerosol dosage form is a suspension of fine solid drug particles or liquid drug droplets in a carrier gas/propellant and the design of such delivery system is intended to release measured mass and appropriate quality of the active pharmaceutical ingredient upon each actuation." Therefore, we had represented the composition of our aerosol pharmaceutical product in terms of mass (grams), rather than in terms of volume.
	Decision: Registration Board deferred the case for confirmation/clarification of required manufacturing facility for intrauterine foam.	
114.	Name and address of Applicant/ Manufacturer	M/s Prix Pharmaceutica (Pvt.) Ltd. Plot#5 Pharma city 30th Km Multan Road Lahore
	Type of Form	Form-5
	Diary No. & Date of R& I	Dy. No 16908 Dated 08-05-2018
	Fee including differential fee	Rs. 20,000/- Dated 08-05-2018
	Brand Name +Dosage Form + Strength	PRIDOX 50 Water soluble powder
	Composition	Each gram water soluble powder contains: Doxycycline hyclate……500mg (Equivalent to 450.30mg doxycycline base)
	Finished Product Specification	Firm claim manufacturer specification
	Pharmacological Group	Antibiotic
	Demanded Price	Decontrolled
	Pack size	100gm, 500gm, 1000gm sachet/jar/Bag
	Me-too status	DOXYTOX 50% WATER SOLUBLE POWDER by M/s Rotass universal, Reg. no. 034562
	GMP status	DML by way of formulation dated 16-10-2015 and panel inspection recommendation for renewal of DML dt: 13-6-2018, 10-10-2018 & 11-12-2018 Oral powder section (general) is approved.
	Remarks of the Evaluator-1	
	Decision of 297th meeting: Deferred for confirmation of required manufacturing facility whether it is for jar, poly bags or sachet from Licensing division.	
	Firm's response: Firm has submitted copy of renewal of DML letter dated 06-03-2019 wherein following sections have been mentioned: i. Oral general Powder section (Veterinary) ii. Oral Powder section (General antibiotic) Firm has also submitted copy of GMP inspection report dated 31-07-2013 wherein availability of PLC controlled semi-automatic jar filling machine has been mentioned for both oral powder sections.	
	Decision: Approved with innovator's specifications in jar packing. **Registration letter shall be issued after submission of applicable fee for revision of specifications in**	

Case No.04: Registration applications of drugs for which stability study data is submitted

a. Verification of stability study data

115.	Name and address of manufacturer / Applicant	M/s Pacific Pharmaceuticals Limited, 30km Multan road Lahore
	Brand Name +Dosage Form + Strength	ESMELIN TABLET 15mg
	Composition	Each Prolonged Release tablet contains: Darifenacin (as hydrobromide) ……..15mg
	Diary No. Date of R& I & fee	Duplicate, 20,000/-, 04-12-2018, 30,000/-, 27-02-2020
	Pharmacological Group	Drug for urinary frequency and incontinence
	Type of Form	Form-5D
	Finished Product Specification	Manufacturer's specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved in USFDA (Enablex 15 extended release tablet of APIL)
	Me-too status	N/A
	GMP status	The firm is granted GMP certificate base on evaluation conducted on 07-03-2019.
	Remarks of Evaluator	•

STABILITY STUDY DATA			
Drug	ESMELIN TABLET 15mg		
Name of Manufacturer	M/s Pacific Pharmaceuticals Limited, 30km Multan road Lahore		
Manufacturer of API	M/s Megafine pharma (Pvt.) Ltd, Plot No. 31 to 35 & 48 to 51, 5,26 &K/201, Lakhmapur, Tal Dindori, Dist. Nashik -422 202, Maharashtra, India		
API Lot No.	DB1804002		
Description of Pack (Container closure system)	Alu-Alu Blister		
Stability Storage Condition	Accelerated: 40ºC ± 2ºC/75%±5% RH Real Time: 30ºC ± 2ºC/65%±5% RH		
Time Period	Accelerated: 06 (months) Real Time: 06 (months)		
Frequency	Accelerated: 0,1,2,3,4,6 (06 months) Real Time: 0,3,6 (06 months)		
Batch No.	P000106O	P000206O	P000406O
Batch Size	8000 Tablets	8000 Tablets	8000 Tablets
Manufacturing Date	18-07-2019	18-07-2019	18-07-2019
Date of Initiation	20-07-2019	20-07-2019	20-07-2019
No. of Batches	03		
Date of Submission	(02-03-2020)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr.#	**Documents To Be Provided**	**Status**
1.	COA of API.	Copy of COA of API (batch # DLP363) from M/s Megafine Pharma, Maharashtra, India is submitted.
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.	The firm has submitted copy of GMP certificate for M/s Megafine Pharma (P) Ltd, India issued from Food and Drug Administration, Maharashtra, India. It is valid till 12-2-2022.

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.	The firm has submitted invoice for import of Darifenacin hydrobromide (0.5Kg) attested by Assistant Director (I & E), DRAP, Lahore dated 29-10-2018. Invoice No: NX18190203
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

REMARKS OF EVALUATOR

- The firm has submitted 06 months Accelerated and 06 months Real Time Stability Data for 03 Batches.

Decision: Registration Board decided to consider the case after onsite inspection by the panel to be constituted by Chairman Registration Board for verification of authenticity of submitted stability study data.

1.1 General Information.

Name of Manufacturer	M/s Pacific Pharmaceuticals, Limited.
Physical Address	30km Multan Road, Lahore.
Drug Manufacturing License No. and validity	DML No 000295 by way of formulation
Date of Inspection.	10-08-2020
Purpose of Inspection	Verification of Authenticity of Stability Data for Purpose of Registration of Drugs with reference DRAP's letter No. F.1-2/2020-PEC (Pt)dated 29-12-2020.
Name of Inspector	i. Mr. Iftikhar Ch., (Member DRB) ii. Mr. Ajmal Sohail Asif, FID, DRAP, Lahore. iii. Ms. Maham Misbah, Assistant Director, DRAP, Lahore.
Name of firm Representatives	i. Mr. Ghazi Mustansar Riaz, Head of Quality Assurance ii. Mr. Muhammad Ali Asghar, Quality Control Incharge. iii. Mr. Ali Mir, Deputy Manager, Quality Assurance iv. Mr. Muaz Daud, Deputy Manager, Production

Focus of Inspection:

The inspection was focused on a thorough evaluation of data for stability studies of following product:

Sr. No.	Name / Composition of Drugs
1.	Esmelin Tablet 15mg Each Prolonged release tablet contains: Darifenacin (as Hydrobromide) ……15mg

OBSERVATIONS:

Q.#	Questions	Observation by panel
1.	Do you have documents confirming the import of Darifenacin Hydrobromide including approval from DRAP?	The firm had imported Darifenacin Hydrobromide raw material vide invoice no. NX18190203 dated 28-09-2018 from M/s. Megafine Pharma Pvt, Ltd, India and got DRAP approval vide no. 13410/2018 DRAP dated 24-10-2018.

2.	What was the rationale behind selecting the particular manufacturer of API?	The firm informed that they selected the API manufacturer based on their vendor evaluation mechanism, desktop audit and testing of advance sample sent by the manufacturer.
3.	Do you have documents confirming the import of reference standard and impurity standards?	The firm's representative informed that they had imported Darifenacin Hydrobromide working standard from the manufacturer along with the API. Impurity standards were not imported by the firm, as informed by the firm's representative.
4.	Do you have certificate of Analysis of the API, reference standards and impurity standards?	The firm had certificates of analysis for API and working standard. CoAs of impurity standards were not available.
5.	Do you have GMP certificate of API manufacturer issued by regulatory authority of country of origin?	Yes
6.	Do you use API manufacturer's method of testing for testing API?	Firm had not conducted the tests for X-Ray diffraction, impurities and residual solvents. The firm was advised to perform complete testing as per manufacturer's testing method.
7.	Do you have stability studies reports on API?	Yes, reports were shown to the panel for real time and accelerated stability studies.
8.	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	Tests for Related substances and impurities had been done, as per reports shown to the panel.
9.	Do you have method for quantifying the impurities in the API?	The firm had testing method to quantify the impurities as provided by raw material manufacturer.
10.	Do you have some remaining quantities of the API, its reference standard and impurities standards?	The firm had some remaining quantities of the API and working standard only. Remaining quantity of API as verified from SAP was 43.74grams.
11.	Have you used pharmaceutical grade excipients?	The firm had used following four excipients: Dibasic calcium phosphate (Vendor's CoA did not indicate the specifications, whether BP/USP or other) Methocel Magnesium stearate Opadry II white Other three excipients given above were pharma-grade.
12.	Do you have documents confirming the import of the used excipients?	The firm had imported the following three excipients: Methocel, Opadry IIwhite and Magnesium stearate. Clearance certificates from DRAP were available.
13.	Do you have test reports and other records on the excipients used?	The firm had Certificates of Analysis of all excipients.
14.	Do you have written and authorized protocols for the development of Darifenacin Hydrobromide Tablets?	The firm had written and authorized protocols for the development of Darifenacin hydrobromide Prolonged release Tablet 15mg.
15.	Have you performed Drug-excipient compatibility studies?	The firm had performed drug-excipients compatibility studies at 30°C ± 2°C / 65% ± 5% RH for four weeks.
16.	Have you performed comparative dissolution studies?	The firm had performed comparative dissolution studies for Darifenacin Prolonged Release Tablet 15mg with Emselex Prolonged Release Tablet 15mg, manufactured by M/s Merus Labs, Netherlands at 1,2,4,8,16 & 24 hours intervals using Paddle apparatus at 75RPM in three media i.e. 0.01N HCl, Buffer pH 4, Buffer pH 6.8.

17.	Do you have product development (R&D) section	The firm had product development (R&D) section. However, it was advised to equip it with necessary equipment, install proper work station and ensure proper ventilation in the section.
18.	Do you have necessary equipment available in product development section for development of Darifenacin Hydrobromide Tablets?	It was advised to upgrade the PD section and install all necessary equipment.
19.	Are the equipment in product development section qualified?	Firm did not have equipment qualification documents of production equipment in the PD section.
20.	Do you have proper maintenance / calibration / re-qualification program for the equipment used in PD section?	Advised to develop proper maintenance / calibration / re-qualification program for the equipment used in product development section.
21.	Do you have qualified staff in product development section with proper knowledge and training in product development?	Yes, however, the firm was advised to strengthen the PD section.
22.	Have you manufactured three stability batches for the stability studies of Darifenacin Hydrobromide Tablets as required?	The firm had manufactured three stability batches for the stability studies of Darifenacin hydrobromide Prolonged Release Tablets 15mg with following batch numbers: P000106O, P000206O, P000406O. Batch size of each of the three batches was 5000 tablets.
23.	Do you have any criteria for fixing the batch size of stability batches?	The firm had followed in-house SOP for fixing the batch size of stability batches in the light of DRAP guidelines.
24.	Do you have complete record of production of stability batches?	The firm had record of production of stability batches.
25.	Do you have protocols for stability testing of stability batches?	The firm had protocols for stability testing of stability batches.
26.	Do you have developed and validated the method for testing of stability batches?	The firm had developed testing method in house and validated it. (Validation report No. DE-MV-19-01SR dated 25-04-2019)
27.	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Not Applicable.
28.	Do you have documents confirming the qualification of equipment / instruments being used in the test and analysis of Darifenacin HBR API and the finished drug?	The firm had proper documents confirming the qualification of equipment / instruments being used in the test and analysis of Darifenacin API and the finished drug.
29.	Do your method of analysis stability indicating?	The firm's method of testing for finished product was not stability indicating.
30.	Do your HPLC software 21CFR Compliant?	Yes.
31.	Can you show Audit trail reports on Darifenacin Hydrobromide testing?	Log of data was available in the HPLCs. The data was also checked through hard copies of chromatograms.
32.	Do you have some remaining quantities of degradation products and stability batches?	Degradation products were not identified or tested. The firm had remaining quantities of stability batches kept on stability testing which are as follows: Batch no. Remaining quantity P000106O 60 tablets P000206O 60 tablets P000406O 60 tablets
33.	Do you have stability batches kept on stability testing?	The firm had stability batches kept on real time stability testing.
34.	Do you have valid calibration status for the	The firm had valid calibration status for the

	equipment used in Darifenacin HBr tablets production and analysis?	equipment used in Darifenacin testing and analysis. It was advised to qualify the production equipment in PD section.
35.	Do proper and continuous monitoring and control are available for stability chamber?	Adequate monitoring and control were available for stability chamber. The firm was advised to improve the alarm system.
36.	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Last inspection to check cGMP compliance status of the firm was conducted in 2021 and it was concluded that firm was operating at a satisfactory level of cGMP compliance in general tablet section.

In addition to the above, the panel also had the following observations/advices:

i. It was advised to calculate yield of stability batches and document it in the respective BMRs.
ii. The stability batches were placed in stability chamber in blisters. It was advised to place batches for stability testing in the final container/closure system for marketing, as per ICH guidelines.

Conclusion:

In the light of above observations, scrutiny of documents and records, the panel verified that firm conducted the accelerated and real time stability studies for intended product.

Report of the panel is submitted for consideration and further necessary action by the Drug Registration Board, please.

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.

Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5D as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

b. Exemption from onsite verification of stability data

116.	Name and address of manufacturer / Applicant	M/s Horizon Healthcare (Pvt) Ltd., Plot No.33, Sundar Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Empazon XR 25mg/1000mg Tablet
	Composition	Each Extended Release Tablet Contains: Empagliflozin…….25mg Metformin hydrochloride……1000mg
	Diary No. Date of R& I & fee	Dy. No. 5818, 11-02-2019, Rs.20,000/-, dated 07-02-2019, 30,000/- dated 14-01-2020.
	Pharmacological Group	Anti-diabetic
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	As per PRC
	Approval status of product in Reference Regulatory Authorities	Synjardy XR 25mg / 1000mg (USFDA Approved)
	Me-too status	Xenglu Met XR 25/1000mg of M/s Hilton Pharma
	GMP status	GMP inspection was conducted on 17-01-2019 and the report concludes that the firm was found to be operating at satisfactory level of GMP compliant at the time of inspection.
	Remarks of the Evaluator	

STABILITY STUDY DATA	
Name of Manufacturer	M/s Horizon Healthcare (Pvt) Ltd., Plot No.33, Sundar Industrial Estate, Lahore, Pakistan
Manufacturer of API	Empagliflozin: M/s Anhui Youcare Kaiyue Pharmaceutical Co.,Ltd, Industrial Avenue area A, Economic Development Zone Taihe Country, Anhui Province, China. Metformin Hydrochloride: M/s Aarti Drugs Limited, Plot No.211-213 Road no.2, G.I.D.C Sarigam,Tal.Umbergaon, Dist :Valsad,Gujarat, India
API Lot No.	Empagliflozin: 20181001002

	Metformin HCl: MEF/18010041		
Description of Pack (Container closure system)	Alu Alu Blister, 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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 6 months Real Time: 0,1,3,6 months		
Empazon XR 25mg/1000mg Tablet			
Batch No.	EMXRL-001	EMXRL-002	EMXRL-003
Batch Size	1000 Tablets	1000 Tablets	1000 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		
Date of Submission	28-07-2020 (Dy. No.63581)		

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 of 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. Following points were reported in the report: i. The HPLC software is 21 CFR compliant. ii. Audit trail on the testing reports was available
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has submitted certificate of analysis from both API manufacturer and drug product manufacturer.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** The firm has submitted methods used for analysis of API from both API manufacturer and drug product manufacturer. **Metformin hydrochloride:** The firm has submitted methods used for analysis of API from both API manufacturer and drug product manufacturer.
4.	Stability study data of API from API manufacturer.	**Empagliflozin:** The firm has submitted 6 months accelerated and 24 months real time stability study data of 3 batches of API. **Metformin hydrochloride:** The firm has submitted 6 months accelerated and 36 months real time stability study data of 3 batches of API.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by regulatory authority of country of origin.	**Empagliflozin:** The firm has submitted copy of GMP Certificate for M/s Anhui Youcare Kiayue Pharmaceutical Co.,Ltd, Industrial Avenue area A Economic Development Zone Taihe Country, Anhui Province, China issued by China Food and Drugs Administration. It is valid upto 07-04-2023. **Metformin hydrochloride:** The firm has submitted copy of GMP certificate in the name Aarti Drugs Limited, Plot No. 211-213 Road no.2, G.I.D.C Sarigam,Tal.Umbergaon, Dist: Valsad, Gujarat, India

6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** The firm has submitted copy of invoice for the purchase of Empagliflozin (200g), attested by Assistant Director (I & E) DRAP, Lahore dated 02-01-2019. **Metformin hydrochloride:** The firm has submitted copy of invoice for the purchase of metformin hydrochloride (4Kg), attested by Assistant Director (I & E) DRAP, Islamabad dated 06-03-2019.
7.	Protocols followed for conduction of stability study	The firm has submitted protocols for conduction of stability studies.
8.	Method used for analysis of FPP	The firm has submitted copy of method used for analysis of finished Product "Empazon XR 25/1000mg Tablet".
9.	Drug-excipients compatibility studies (where applicable)	The firm has not performed Drug-excipients compatibility studies and stated that the qualitative composition of their product is similar to that of innovator's product tablet and also stability studies have not shown any incompatibility or significant degradation.
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted photocopies of complete batch Manufacturing records s of following 03 Batches:

Batch No.	Batch Size	Mfg. Date
EMXRL-001	1000 Tablets	05-2019
EMXRL-002	1000 Tablets	06-2019
EMXRL-003	1000 Tablets	06-2019

11.	Record of comparative dissolution data (where applicable)	Firm has submitted CDP studies against the reference product of Synjardy XR 25mg tablets (Batch # 3176671) in three dissolution media of pH 1.2, 4.5, 6.8, with acceptable f_2 values.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted stability study data of 03 batches alongwith chromatograms, raw data sheets, COA, and summary data sheet.
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted audit trail reports of applied product.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted photocopies of data logger record for chambers used in Real Time & Accelerated stability studies of applied product

- The firm has submitted 06 months Accelerated and 06 months Real Time Stability Data for 03 Batches.

Sr. No.	Observations	Response of the firm
1.	Evidence of import of API including copy of commercial invoice cleared by DRAP field office.	**Empagliflozin:** The firm has submitted copy of invoice for the purchase of Empagliflozin (200g), attested by Assistant Director (I & E) DRAP, Lahore dated 02-01-2019. **Metformin hydrochloride:** The firm has submitted copy of invoice for the purchase of metformin hydrochloride (4Kg), attested by Assistant Director (I & E) DRAP, Islamabad dated 06-03-2019.
2.	Submit approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Anhui Youcare Kaiyue Pharmaceutical Co., Ltd. China issued by China Food and Drugs Administration. It is valid upto 03-01-2020.
3.	Copy of certificate of analysis of API from API manufacturer needs to be submitted.	The firm has submitted copy of certificate of analysis of API from M/s Aarti Drugs Limited, India.

4.	Protocols followed for conduction of stability study and details of tests.	The firm has submitted protocols for conduction of stability study and details of tests.
5.	Raw data sheets in the stability study data of 03 batches need to be submitted.	Submitted.
6.	Justification is required for using UV method is dissolution testing of metformin hydrochloride while in assay testing HPLC method has been used for analysis of API.	The firm has submitted that dissolution method of metformin hydrochloride is performed through UV by following USP method of metformin hydrochloride extended release tablet which is UV method.
7.	You have not performed uniformity of dosage unit by content uniformity (HPLC), as recommended by the USP general chapter <905> since contents of Empagliflozin in the formulation are less than 25%. Clarification is required.	The firm has submitted results of test of uniformity of dosage unit by content uniformity for determination of Empagliflozin in the formulation.
8.	Justify dissolution test conditions and dissolution specifications NLT 80% in 3 min since innovator product (Jardiance) has mentioned dissolution limits NLT Q in 15 min.	The firm has submitted data with revised dissolution conditions i.e., NLT 80% in 15 min of initial and one-month time point at accelerated and real time stability conditions for 2 batches as per decision of 293rd meeting of Registration Board.

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.

Case No.5 Registration applications for local manufacturing of human drugs submitted on CTD format (New License)

On the recommendations of panel of experts, the CLB in its 273rd meeting held on 15th January, 2020 has considered and approved the grant of Drug Manufacturing License by way of formulation with following four sections:

Name of Section	Considered till 312th RB meeting		Freshly applied	
	No of molecules	No of products	No of molecules	No of products
Tablet Section (General)	01	02	03	03
Capsule Section (General)	04	09	-	-
Sachet Section (General)	00	00	-	-
Dry powder injection section (pre-lyophilized) vial	03	03		

117.	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)
	GMP status of the firm	The firm was granted New DML (000914) on the recommendations of CLB in its 273rd meeting held on 15th January, 2020
	Evidence of approval of manufacturing facility	The firm has provided Tablet section (General) vide letter No. F. 1-1/2016-Lic of licensing division.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23339: 26-08-2021
	Details of fee submitted	PKR 30,000/-: 17-06-2021
	The proposed proprietary name / brand name	MOXIVAR 400mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Moxifloxacin hydrochloride eq. to Moxifloxacin……400mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	Quinolone antibiotic (ATC Code: J01MA14)
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Avelox 400mg Tablet of M/s Bayer Pharms. (USFDA approved)
	For generic drugs (me-too status)	Moxiget 400mg Tablet of M/s Getz Pharma (Reg.#047117)
	Name and address of API manufacturer.	M/s SHREE JEE LABORATORY Pvt. Ltd. C-24 & 25, RIICO Indl. Area, Sotanala, Behror-301701, 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, 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. 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:	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 6 months accelerated and 36 months real time data of 3 batches of drug substance.
	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 study of trial formulation (B # T-001) with comparator product MOXIGET 400mg Tablet (B # 205F31) of M/s GETZ pharma. The results of the quality tests of both products fall within the specifications and are comparable. The firm has performed comparative dissolution profile in pH 1.2, acetate buffer pH 4.5 and phosphate buffer 6.8. The results showed that similarity factor *f2* was above 50 in three media.
	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 SHREE JEE LABORATORY Pvt. Ltd. C-24 & 25, RIICO Indl. Area, Sotanala, Behror-301701, District. Alwar (Rajasthan.) India.		
API Lot No.	MXYST008		
Description of Pack (Container closure system)	5's Tablets in 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: 0,1,3,6 (Months) Real Time: 0, 3, 6 (Months)		
MOXIVAR 400mg Tablet			
Batch No.	T-001	T-002	T-003
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	08-2020	08-2020	09-2020
Date of Initiation	02-09-2020	06-09-2020	09-09-2020
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 (if any)	N/A
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. Shree Jee Laboratory Pvt. Ltd., Rajasthan, India issued by Drugs Control Organisation. It is valid till 06-02-2022.
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 Moxifloxacin hydrochloride (3.00Kg) attested by AD (I & E) DRAP Lahore dated 05-05-2020.
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.	The firm has submitted audit trail reports of testing of applied 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.#	Observations communicated	Response by the firm
1.	Pharmaceutical equivalence and CDP 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.	The firm has submitted pharmaceutical equivalence and CDP of the applied drug with Avelox 400mg Tablet of M/s Bayer and results of the quality tests have been submitted.
2.	Justify how the performance of Repeatability and Reproducibility parameters in method validation studies were carried out and how % RSD was calculated.	Repeatability: It was calculated from the results of six consecutive determinations. To check repeatability, six samples were drawn and test solutions were prepared and tested according to the test procedure. Reproducibility: To evaluate this parameter, two sets of five samples equivalent to 100% of label claim were prepared and assayed by two analysts individually.
3.	Weight of samples taken at different concentrations of accuracy parameter corresponding to 80%, 100% and 120% were not rational. Clarification is required.	The accuracy of test method has been determined by Spiked placebo method. However, clarification of weight of samples corresponding to 80%, 100% and 120% concentration was submitted.
4.	The table of Pharmaceutical equivalence contain dissolution test performance at three pH. Clarification is required how the dissolution test at three pH can be performed as routine quality test.	The firm has submitted pharmaceutical equivalence against Avelox 400mg Tablet of M/s Bayer (Batch: BXJFHS1) with results of dissolution test as quality test. Moreover, CDP performance has been submitted at three BCS media and calculated f_2 factor.

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.**

118.	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)
	GMP status of the firm	The firm was granted New DML (000914) on the recommendations of CLB in its 273rd meeting held on 15th January, 2020.
	Evidence of approval of manufacturing facility	The firm has provided Tablet section (General) vide letter No. F. 1-1/2016-Lic of licensing division.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No.25213: 10-09-2021
	Details of fee submitted	PKR 30,000/-: 26-03-2021
	proposed proprietary name / brand name	PIXIVAR 20mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Piroxicam beta cyclodextrin eq. to. Piroxicam……20mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	NSAID (WHO ATC Code: M02AC01)
	Reference to Finished product specification	Innovator's specification
	Proposed Pack size	20's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Approved by ANSM of France
	For generic drugs (me-too status)	Achway Tablets of M/s Getz Pharma (Reg.#047355)
	Name and address of API manufacturer.	M/s Nantong Jinghua Pharmaceutical Co., Ltd., No. 20, 3 Haibin Road, Yenhai Economic Development Zone, Rudong, Nantong, Jiangsu, 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, 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.
	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 6 months accelerated and 36 months real time data of 3 batches of drug substance.
	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 study of trial formulation (B # T-001) with reference product Brexin 20mg Tablet (B # 1095831) of M/s Chiesi pharma. The results of the

		quality tests of both products fall within the specifications and are comparable. The Firm has performed comparative dissolution profile in pH 1.2, acetate buffer pH 4.5 and phosphate buffer 6.8. The results showed that similarity factor *f2* was above 50 in three media.
	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 Nantong Jinghua Pharmaceutical Co., Ltd., No. 20, 3 Haibin Road, Yanhai Economic Development Zone, Rudong, Nantong, Jiangsu, China.
API Lot No.	20200901
Description of Pack (Container closure system)	20's Tablets in 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: 0,1,3,6 (Months) Real Time: 0, 3, 6 (Months)

PIXIVAR 20mg Tablet

Batch No.	T-001	T-002	T-003
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	15-02-2021	16-02-2021	16-02-2021
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 (if any)	N/A
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 for M/s Nantong Jinghua Pharmaceutical Co., Ltd. China issued by China Food and Drug Administration. It is valid till 31-5-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice for the purchase of Piroxicam beta-cyclodextrin (2Kg) attested by AD (I & E) DRAP Lahore dated 04-12-2020.
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.	The firm has submitted audit trail reports of testing of applied product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability

	chambers (real time and accelerated).	chambers.

REMARKS OF EVALUATOR

Sr.#	Observations communicated	Response by the firm
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.	Firm has submitted pharmaceutical equivalence study of trial formulation (B # T-001) with reference product Brexin 20mg Tablet (B # 1095831) of M/s Chiesi pharma. The results of the quality tests of both products fall within the specifications and are comparable.
2.	Justify how the performance of Repeatability and Reproducibility parameters in method validation studies were carried out and how % RSD was calculated.	Repeatability: It was calculated from the results of six consecutive determinations. To check repeatability, six samples were drawn and test solutions were prepared and tested according to the test procedure. Reproducibility: To evaluate this parameter, two sets of five samples equivalent to 100% of label claim were prepared and assayed by two analysts individually.
3.	Clarification is required whether dissolution and assay tests were performed by UV or HPLC method in the stability studies.	The firm has submitted that dissolution test has been performed on UV-visible spectrophotometer. While the assay test was performed on HPLC using a validated method for assay testing of drug product. Accordingly, the reports of UV spectra and chromatograms were arranged.
4.	The results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f_2 shall be submitted in module 2.	The results of CDP data have been submitted in tabulated form in module 2.
5.	Weight of samples taken at different concentrations of accuracy parameter corresponding to 80%, 100% and 120% were not rational. Clarification is required.	The accuracy of test method has been determined by Spiked placebo method. However, clarification of weight of samples corresponding to 80%, 100% and 120% concentration was 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.**

119.	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)
	GMP status of the firm	The firm was granted New DML (000914) on the recommendations of CLB in its 273rd meeting held on 15th January, 2020
	Evidence of approval of manufacturing facility	The firm has provided Tablet section (General) vide letter No. F. 1-1/2016-Lic of licensing division.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.23542: 27-08-2021
	Details of fee submitted	PKR 30,000/-: 13-07-2021
	The proposed proprietary name / brand name	V-MONT 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Montelukast sodium eq. to Montelukast……10mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	Leukotriene receptor antagonist (ATC Code: R03DC03)
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Singulair 10mg Tablet of M/s Merck & Co., Inc. (USFDA approved)
	For generic drugs (me-too status)	Myteka 10mg Tablet of M/s Hilton Pharma (Reg.#030051)
	Name and address of API manufacturer.	M/s Zhejiang Tianyu Pharmaceutical Co., Ltd. No. 15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou 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, 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.
	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 6 months accelerated and 24 months real time data of 3 batches of drug substance.
	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 study of trial formulation (B # T-001) with comparator product Myteka 10mg Tablet (B # 137136) of M/s Hilton pharma. The results of the quality tests of both products fall within the specifications and are comparable. The firm has performed comparative dissolution profile in pH 1.2, acetate buffer pH 4.5 and phosphate buffer 6.8. The results showed that similarity factor *f2* was above 50 in three media.
	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 Zhejiang Tianyu Pharmaceutical Co., Ltd. No. 15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, China.
API Lot No.	11001-200509
Description of Pack (Container closure system)	14's Tablets in 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: 0,1,3,6 (Months) Real Time: 0, 3, 6 (Months)

V-MONT 10mg Tablet

Batch No.	T-001	T-002	T-003
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	15-10-2021	17-10-2021	17-10-2021
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 (if any)	N/A
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 Zhejiang Tianyu Pharmaceutical Co., Ltd. China issued by China Food and Drug Administration. It is valid till 14-03-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice for the purchase of Montelukast sodium (200g) attested by AD (I & E) DRAP Lahore dated 23-07-2020.
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	The firm has submitted audit trail reports of testing of applied

	21CFR & audit trail reports on product testing.	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.#	Observations communicated	Response by the firm
1.	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.	The firm has submitted analytical method verification studies of Montelukast sodium performed by drug product manufacturer. The parameters include Linearity, Precision, Accuracy and Robustness studies.
2.	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.	Firm submitted pharmaceutical equivalence study of trial formulation (B # T-001) with Floaid 10mg Tablet (B # 212050) of M/s Abbott Pharma. The results of the quality tests of both products fall within the specifications and are comparable. The firm has performed comparative dissolution data with two products in pH 1.2, acetate buffer pH 4.5 and phosphate buffer 6.8. The results showed that similarity factor f_2 was above 50 in three media.
3.	Justify how the performance of Repeatability and Reproducibility parameters in method validation studies were carried out and how % RSD was calculated.	Repeatability: It was calculated from the results of six consecutive determinations. To check repeatability, six samples were drawn and test solutions were prepared and tested according to the test procedure. Reproducibility: To evaluate this parameter, two sets of five samples equivalent to 100% of label claim were prepared and assayed by two analysts individually.
4.	Weight of samples taken at different concentrations of accuracy parameter corresponding to 80%, 100% and 120% were not rational. Clarification is required.	The accuracy of test method has been determined by Spiked placebo method. However, clarification of weight of samples corresponding to 80%, 100% and 120% concentration was 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.**

Case no. 06: Registration applications of locally manufacturing drugs (human) submitted on CTD format

a. New cases

120.	Name, address of Applicant / Marketing Authorization Holder	M/s Nawan Laboratories (Pvt) Ltd, 136, Sector 15, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot # 145 Industrial Triangles, kahua Road, Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) The firm has submitted copy of agreement between M/s Nawan Laboratories (Pvt) Ltd and M/s Bio-Labs (Pvt.) Ltd, Islamabad made on 21-01-2020.

	GMP status of the firm	**M/s Nawan laboratories:** The firm is granted GMP certificate based on inspection conducted on 01-02-2020. **M/s Bio-Labs:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	The manufacturer has provided 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. 6957: 02-03-2021
	Details of fee submitted	PKR 50,000/-: 15-02-2021
	The proposed proprietary name / brand name	Oltrix Injection 40mg IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole……40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s Sandoz Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 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, 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. 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:	The 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)	The firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API as per Zone-IV 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 and 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	The firm has performed pharmaceutical equivalence of their developed formulation Delka 40mg IV Injection (B # L 289) with comparator product Risek 40mg Injection IV (B # 788P06) of M/s GETZ Pharma, Karachi. Quality tests of both products including description, identification, pH, assay, Sterility and bacterial endotoxins were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 Rajesthan, India		
API Lot No.	AOSS19032		
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)		
Delka 40mg IV Injection			
Batch No.	L-140	L-163	L-197
Batch Size	25000 vials	20,000 vials	15,000 vials
Manufacturing Date	03-2018	06-2018	11-2018
Date of Initiation	10-03-2018	15-06-2018	13-12-2018
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 (if any)	NA
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	The firm has submitted copy of invoice for the import of Omeprazole sodium.

	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 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 on testing reports of product 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.

S.#	Observations communicated	Response by the firm
1.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.	The firm has submitted that API lot used in stability studies procured from Rajasthan Antibiotics while provided DMF was from Metrochem. We are submitting DMF from Rajasthan antibiotics and COAs accordingly.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required.	Revised pharmaceutical equivalence report has been submitted.
3.	Data of commercial batches with different batch numbers was given in process validation reports, batch analysis of finished product and stability studies.	We do not perform process validation on all manufactured batches. We performed stability study and process validation on different batches however we are submitting revised batch analysis of stability batches.
4.	Pharmaceutical equivalence of the applied drug shall be established with the innovator 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 product should be submitted and discussed as per requirements of section 3.2.P.2.	The firm has submitted we used market leader product (Risek 40mg Injection) of GETZ pharma which was approved by DRAP.
5.	Justification is required for using UV spectrophotometric method in place of HPLC method for assay testing of Delka 40mg Injection IV.	The firm has submitted that since product is of in-house specifications and in-house validated method is applied for testing which is UV-visible spectrophotometer. Validation of analytical method is provided in module 3.
6.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Response not submitted against this point.
7.	Evidence of procurement of drug substance with approval from DRAP is required.	Response not submitted against this point.

Decision: Deferred for following submissions:

- **Scientific justification of manufacturing of applied formulation by way of lyophilization using pre-lyophilized omeprazole sodium from M/s Rajasthan Antibiotics, India.**
- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Approval of API/ DML/GMP certificate of API manufacturer (Rajasthan antibiotics) issued by concerned regulatory authority of country of origin.**
- **Evidence of procurement of drug substance with approval from DRAP.**

	Name, address of Applicant / Marketing Authorization Holder	M/s Islam Pharmaceuticals., 7 km, Pasrur Road, Sialkot.
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot # 145 Industrial Triangles, kahuta Road, Islamabad.

	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) The firm has submitted copy of agreement between M/s Islam Pharmaceuticals and M/s Bio-Labs (Pvt.) Ltd, Islamabad made on 21-01-2020.
	GMP status of the firm	**M/s Islam Pharmaceuticals:** The firm is granted GMP certificate based on inspection conducted on 01-02-2020. **M/s Bio-Labs Pvt Ltd:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	The manufacturer has provided 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. 7168: 04-03-2021
	Details of fee submitted	PKR 50,000/-: 18-01-2021
	The proposed proprietary name / brand name	Mozole Injection 40mg IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole……40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s Sandoza Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 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, 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. 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:	The 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)	The firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API as per Zone-IV 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 and 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	The firm has performed pharmaceutical equivalence of their developed formulation Delka 40mg IV Injection (B # L 289) with comparator product Risek 40mg Injection IV (B # 788P06) of M/s GETZ Pharma, Karachi. Quality tests of both products including description, identification, pH, assay, Sterility and bacterial endotoxins were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA			
Manufacturer of API	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 Rajesthan, India		
API Lot No.	AOSS19032		
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)		
Delka 40mg IV Injection			
Batch No.	L-140	L-163	L-197
Batch Size	25000 vials	20,000 vials	15,000 vials
Manufacturing Date	03-2018	06-2018	11-2018
Date of Initiation	10-03-2018	15-06-2018	13-12-2018
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 (if any)	N/A
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).	The firm has submitted copy of invoice for the import of Omeprazole sodium.
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 on testing reports of product 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.

S.#	Observations communicated	Response by the firm
1.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.	The firm has submitted that API lot used in stability studies procured from Rajasthan Antibiotics while provided DMF was from Metrochem. We are submitting DMF from Rajasthan antibiotics and COAs accordingly.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required.	Revised pharmaceutical equivalence report has been submitted.
3.	Data of commercial batches with different batch numbers was given in process validation reports, batch analysis of finished product and stability studies.	We do not perform process validation on all manufactured batches. We performed stability study and process validation on different batches however we are submitting revised batch analysis of stability batches.
4.	Pharmaceutical equivalence of the applied drug shall be established with the innovator 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 product should be submitted and discussed as per requirements of section 3.2.P.2.	The firm has submitted we used market leader product (Risek 40mg Injection) of GETZ pharma which was approved by DRAP.
5.	Justification is required for using UV spectrophotometric method in place of HPLC method for assay testing of Delka 40mg Injection IV.	The firm has submitted that since product is of in-house specifications and in-house validated method is applied for testing which is UV-visible spectrophotometer. Validation of analytical method is provided in module 3.
6.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Response not submitted against this point.
7.	Evidence of procurement of drug substance with approval from DRAP is required.	Response not submitted against this point.

Decision: Deferred for following submissions:

- **Scientific justification of manufacturing of applied formulation by way of lyophilization using pre-lyophilized omeprazole sodium from M/s Rajasthan Antibiotics, India.**

• **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.** • **Approval of API/ DML/GMP certificate of API manufacturer (Rajasthan antibiotics) issued by concerned regulatory authority of country of origin.** • **Evidence of procurement of drug substance with approval from DRAP.**		
121.	Name, address of Applicant / Marketing Authorization Holder	M/s Bio-Next Pharmaceuticals., Plot No. 50, Street No. S-10, RCCI, Rawat
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot # 145 Industrial Triangles, kahuta Road, Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) The firm has submitted copy of agreement between M/s Islam Pharmaceuticals and M/s Bio-Labs (Pvt.) Ltd, Islamabad made on 21-01-2020.
	GMP status of the firm	**M/s Bio-Next Pharmaceuticals:** The firm is granted GMP certificate based on inspection conducted on 01-02-2020. **M/s Bio-Labs Pvt Ltd:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	The manufacturer has provided 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. 7097: 03-03-2021
	Details of fee submitted	PKR 50,000/-: 19-11-2020
	The proposed proprietary name / brand name	Omepranext Injection 40mg IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole…….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s Sandoza Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 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, 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. 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:	The 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)	The firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API as per Zone-IV 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 and 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	The firm has performed pharmaceutical equivalence of their developed formulation Delka 40mg IV Injection (B # L 289) with comparator product Risek 40mg Injection IV (B # 788P06) of M/s GETZ Pharma, Karachi. Quality tests of both products including description, identification, pH, assay, Sterility and bacterial endotoxins were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA			
Manufacturer of API	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, RICO Industrial Area Bhiwadi-301019 Rajasthan, India		
API Lot No.	AOSS19032		
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)		
Delka 40mg IV Injection			
Batch No.	L-140	L-163	L-197

Batch Size	25000 vials	20,000 vials	15,000 vials
Manufacturing Date	03-2018	06-2018	11-2018
Date of Initiation	10-03-2018	15-06-2018	13-12-2018
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 (if any)	The firm has submitted reference of already conducted inspection dated……for registration application of ……..approved in 291st meeting of RB.
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 of M/s Metrochem API (Pvt) Ltd, India issued by Food & Drugs administration, Maharashtra state, India. The certificate is valid till 13 April, 2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Omeprazole sodium.
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 on testing reports of product submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time & accelerated).	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Sr.#	Observations communicated	Response by the firm
1.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.	The firm has submitted that API lot used in stability studies procured from Rajasthan Antibiotics while provided DMF was from Metrochem. We are submitting DMF from Rajasthan antibiotics and COAs accordingly.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required.	Revised pharmaceutical equivalence report has been submitted.
3.	Data of commercial batches with different batch numbers was given in process validation reports, batch analysis of finished product and stability studies.	We do not perform process validation on all manufactured batches. We performed stability study and process validation on different batches however we are submitting revised batch analysis of stability batches.
4.	Pharmaceutical equivalence of the applied drug shall be established with the innovator 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 product should be submitted and discussed as per requirements of section 3.2.P.2.	The firm has submitted we used market leader product (Risek 40mg Injection) of GETZ pharma which was approved by DRAP.
5.	Justification is required for using UV spectrophotometric method in place of HPLC method for assay testing of Delka 40mg Injection IV.	The firm has submitted that since product is of in-house specifications and in-house validated method is applied for testing which is UV-visible spectrophotometer. Validation of analytical method is provided in module 3.

6.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Response not submitted against this point.
7.	Evidence of procurement of drug substance with approval from DRAP is required.	Response not submitted against this point.

Decision: Deferred for following submissions:

- **Scientific justification of manufacturing of applied formulation by way of lyophilization using pre-lyophilized omeprazole sodium from M/s Rajasthan Antibiotics, India.**
- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Approval of API/ DML/GMP certificate of API manufacturer (Rajasthan antibiotics) issued by concerned regulatory authority of country of origin.**
- **Evidence of procurement of drug substance with approval from DRAP.**

122.	Name, address of Applicant / Marketing Authorization Holder	M/s Cherwel Pharmaceuticals (Pvt) Ltd., Plot No. 20, Phase 4, Hattar Industrial Estate Hattar
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot # 145 Industrial Triangles, kahuta Road, Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) The firm has submitted copy of agreement between M/s Islam Pharmaceuticals and M/s Bio-Labs (Pvt.) Ltd, Islamabad made on 21-01-2020.
	GMP status of the firm	**M/s Cherwel Pharmaceuticals:** The firm is granted GMP certificate **M/s Bio-Labs Pvt Ltd:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	The manufacturer has provided 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. 7457: 08-03-2021
	Details of fee submitted	PKR 50,000/-: 24-02-2021
	The proposed proprietary name / brand name	Nifzole Injection 40mg IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole…….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s Sandoza Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan

	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 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, 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. 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:	The 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)	The firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API as per Zone-IV 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 and 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	The firm has performed pharmaceutical equivalence of their developed formulation Delka 40mg IV Injection (B # L 289) with comparator product Risek 40mg Injection IV (B # 788P06) of M/s GETZ Pharma, Karachi. Quality tests of both products including description, identification, pH, assay, Sterility and bacterial endotoxins were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 Rajesthan, India
API Lot No.	AOSS19032
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)		
Delka 40mg IV Injection			
Batch No.	L-140	L-163	L-197
Batch Size	25000 vials	20,000 vials	15,000 vials
Manufacturing Date	03-2018	06-2018	11-2018
Date of Initiation	10-03-2018	15-06-2018	13-12-2018
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 (if any)	The firm has submitted reference of already conducted inspection dated……for registration application of ……..approved in 291st meeting of RB.
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 of M/s Metrochem API (Pvt) Ltd, India issued by Food & Drugs administration, Maharashtra state, India. The certificate is valid till 13 April, 2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Omeprazole sodium.
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 on testing reports of product 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.

S.#	Observations communicated	Response by the firm
1.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.	The firm has submitted that API lot used in stability studies procured from Rajasthan Antibiotics while provided DMF was from Metrochem. We are submitting DMF from Rajasthan antibiotics and COAs accordingly.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required.	Revised pharmaceutical equivalence report has been submitted.
3.	Data of commercial batches with different batch numbers was given in process validation reports, batch analysis of finished product and stability studies.	We do not perform process validation on all manufactured batches. We performed stability study and process validation on different batches however we are submitting revised batch analysis of stability batches.
4.	Pharmaceutical equivalence of the applied drug shall be established with the innovator product and results of all the quality tests (mentioned in any	The firm has submitted we used market leader product (Risek 40mg Injection) of GETZ pharma which was approved by DRAP.

	official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator product should be submitted and discussed as per requirements of section 3.2.P.2.	
5.	Justification is required for using UV spectrophotometric method in place of HPLC method for assay testing of Delka 40mg Injection IV.	The firm has submitted that since product is of in-house specifications and in-house validated method is applied for testing which is UV-visible spectrophotometer. Validation of analytical method is provided in module 3.
6.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Response not submitted against this point.
7.	Evidence of procurement of drug substance with approval from DRAP is required.	Response not submitted against this point.

Decision: Deferred for following submissions:

- **Scientific justification of manufacturing of applied formulation by way of lyophilization using pre-lyophilized omeprazole sodium from M/s Rajasthan Antibiotics, India.**
- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Approval of API/ DML/GMP certificate of API manufacturer (Rajasthan antibiotics) issued by concerned regulatory authority of country of origin.**
- **Evidence of procurement of drug substance with approval from DRAP.**

123.	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 # 145 Industrial Triangles, kahuta Road, Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) The firm has submitted copy of agreement between M/s Islam Pharmaceuticals and M/s Bio-Labs (Pvt.) Ltd, Islamabad made on 21-01-2020.
	GMP status of the firm	**M/s Alliance Pharmaceuticals:** The firm is granted GMP certificate **M/s Bio-Labs Pvt Ltd:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	The manufacturer has provided 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. 13167: 06-05-2021
	Details of fee submitted	PKR 50,000/-: 07-04-2021
	proposed proprietary name / brand name	Allomep 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole…….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product	Innovator's specifications

	specification	
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s Sandoza Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 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, 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. 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:	The 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)	The firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API as per Zone-IV 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 and 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	The firm has performed pharmaceutical equivalence of their developed formulation Delka 40mg IV Injection (B # L 289) with comparator product Risek 40mg Injection IV (B # 788P06) of M/s GETZ Pharma, Karachi. Quality tests of both products including description, identification, pH, assay, Sterility and bacterial endotoxins were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.
STABILITY STUDY DATA		
Manufacturer of API	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area	

	Bhiwadi-301019 Rajesthan, India		
API Lot No.	AOSS19032		
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)		
Delka 40mg IV Injection			
Batch No.	L-140	L-163	L-197
Batch Size	25000 vials	20,000 vials	15,000 vials
Manufacturing Date	03-2018	06-2018	11-2018
Date of Initiation	10-03-2018	15-06-2018	13-12-2018
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 (if any)	The firm has submitted reference of already conducted inspection dated……for registration application of ……..approved in 291st meeting of DRB.
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 of M/s Metrochem API (Pvt) Ltd, India issued by Food & Drugs administration, Maharashtra state, India. The certificate is valid till 13 April, 2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Omeprazole sodium.
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 on testing reports of product 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.

S.#	Observations communicated	Response by the firm
1.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.	The firm has submitted that API lot used in stability studies procured from Rajasthan Antibiotics while provided DMF was from Metrochem. We are submitting DMF from Rajasthan antibiotics and COAs accordingly.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required.	Revised pharmaceutical equivalence report has been submitted.
3.	Data of commercial batches with different batch	We do not perform process validation on all

	numbers was given in process validation reports, batch analysis of finished product and stability studies.	manufactured batches. We performed stability study and process validation on different batches however we are submitting revised batch analysis of stability batches.
4.	Pharmaceutical equivalence of the applied drug shall be established with the innovator 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 product should be submitted and discussed as per requirements of section 3.2.P.2.	The firm has submitted we used market leader product (Risek 40mg Injection) of GETZ pharma which was approved by DRAP.
5.	Justification is required for using UV spectrophotometric method in place of HPLC method for assay testing of Delka 40mg Injection IV.	The firm has submitted that since product is of in-house specifications and in-house validated method is applied for testing which is UV-visible spectrophotometer. Validation of analytical method is provided in module 3.
6.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Response not submitted against this point.
7.	Evidence of procurement of drug substance with approval from DRAP is required.	Response not submitted against this point.

Decision: Deferred for following submissions:

- **Scientific justification of manufacturing of applied formulation by way of lyophilization using pre-lyophilized omeprazole sodium from M/s Rajasthan Antibiotics, India.**
- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Approval of API/ DML/GMP certificate of API manufacturer (Rajasthan antibiotics) issued by concerned regulatory authority of country of origin.**
- **Evidence of procurement of drug substance with approval from DRAP.**

124.	Name, address of Applicant / Marketing Authorization Holder	M/s Novartana Pharmaceuticals Pvt Ltd. Plot No. 87-B, Sundar Industrial Estate, Lahore
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot # 145 Industrial Triangles, kahuta Road, Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver) The firm has submitted copy of agreement between M/s Islam Pharmaceuticals and M/s Bio-Labs (Pvt.) Ltd, Islamabad made on 21-01-2020.
	GMP status of the firm	**M/s Novartana Pharmaceuticals:** The firm is granted GMP certificate **M/s Bio-Labs Pvt Ltd:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	The manufacturer has provided 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. 13166: 18-05-2021

	Details of fee submitted	PKR 50,000/-: 07-04-2021
	proposed proprietary name / brand name	Novarzole 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole…….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specification	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s Sandoza Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 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, 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. 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:	The 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)	The firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of API as per Zone-IV 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 and 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	The firm has performed pharmaceutical equivalence of their developed formulation Delka 40mg IV Injection (B # L 289) with comparator product Risek 40mg Injection IV (B # 788P06)

		of M/s GETZ Pharma, Karachi. Quality tests of both products including description, identification, pH, assay, Sterility and bacterial endotoxins were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Rajasthan Antibiotics Ltd., Plot no A-619 & 630, Rico Industrial Area Bhiwadi-301019 Rajesthan, India
API Lot No.	AOSS19032
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)

Delka 40mg IV Injection

Batch No.	L-140	L-163	L-197
Batch Size	25000 vials	20,000 vials	15,000 vials
Manufacturing Date	03-2018	06-2018	11-2018
Date of Initiation	10-03-2018	15-06-2018	13-12-2018
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 (if any)	The firm has submitted reference of already conducted inspection dated……for registration application of ……..approved in 291st meeting of DRB.
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 of M/s Metrochem API (Pvt) Ltd, India issued by Food & Drugs administration, Maharashtra state, India. The certificate is valid till 13 April, 2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Omeprazole sodium.
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 on testing reports of product 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.

S.#	Observations communicated	Response by the firm

1.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacturer.	The firm has submitted that API lot used in stability studies procured from Rajasthan Antibiotics while provided DMF was from Metrochem. We are submitting DMF from Rajasthan antibiotics and COAs accordingly.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required.	Revised pharmaceutical equivalence report has been submitted.
3.	Data of commercial batches with different batch numbers was given in process validation reports, batch analysis of finished product and stability studies.	We do not perform process validation on all manufactured batches. We performed stability study and process validation on different batches however we are submitting revised batch analysis of stability batches.
4.	Pharmaceutical equivalence of the applied drug shall be established with the innovator 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 product should be submitted and discussed as per requirements of section 3.2.P.2.	The firm has submitted we used market leader product (Risek 40mg Injection) of GETZ pharma which was approved by DRAP.
5.	Justification is required for using UV spectrophotometric method in place of HPLC method for assay testing of Delka 40mg Injection IV.	The firm has submitted that since product is of in-house specifications and in-house validated method is applied for testing which is UV-visible spectrophotometer. Validation of analytical method is provided in module 3.
6.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Response not submitted against this point.
7.	Evidence of procurement of drug substance with approval from DRAP is required.	Response not submitted against this point.

Decision: Deferred for following submissions:

- **Scientific justification of manufacturing of applied formulation by way of lyophilization using pre-lyophilized omeprazole sodium from M/s Rajasthan Antibiotics, India.**
- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Approval of API/ DML/GMP certificate of API manufacturer (Rajasthan antibiotics) issued by concerned regulatory authority of country of origin.**
- **Evidence of procurement of drug substance with approval from DRAP.**

125.	Name, address of Applicant / Marketing Authorization Holder	M/s Genix Pharma (Pvt) Ltd, 44-45-B, Korangi Creek Road, Karachi
	Name, address of Manufacturing site.	M/s Genix Pharma (Pvt) Ltd, 44-45-B, Korangi Creek Road, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm is inspected on 02-07-2020 wherein the firm was found to be operating at good level of GMP compliance.
	Evidence of approval of manufacturing facility	The firm has provided Sachet (General) section from confirmed from approved layout plan from licensing division.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale

		☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7173: 04-03-2021
	Details of fee submitted	PKR 50,000/-: 04-06-2021
	proposed proprietary name / brand name	Movcol Jar 578g
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose contains: Polyethylene glycol 3350……17g
	Pharmaceutical form of applied drug	White to off white color powder filled in HDPE bottle.
	Pharmacotherapeutic Group of (API)	Osmotic laxative
	Reference to Finished product specification	Manufacturer's specifications
	Proposed Pack size	1's
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	Miralax for oral solution of M/s Bayer Healthcare LLC (USFDA Approved, over the counter)
	For generic drugs (me-too status)	Not available
	Name and address of API manufacturer.	M/s Avesta Pharma Pvt Ltd., Shivam chambers, 106/108, First Floor, S.V. Road, Goregaon west, Mumbai–400 062 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, solubilities, physical form, manufacturers, 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. 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:	The 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 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 and 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	The firm has performed pharmaceutical equivalence and comparative dissolution profile of Movcol 578g Jar (B#19SB-149-01) and Miralax 578g Jar (B # TN00RM) of M/s Bayer. Quality tests of both products including description, identification, filled weight, moisture content and assay were compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Avesta Pharma Pvt Ltd., Shivam chambers, 106/108, First Floor, S.V. Road, Goregaon west, Mumbai – 400 062 Maharashtra India.		
API Lot No.	AP0919009		
Description of Pack (Container closure system)	HDPE 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)		
Movcol Jar 578g			
Batch No.	19SB-149-01	19SB-150-02	19SB-151-03
Batch Size	50 Bottles	50 Bottles	50 Bottles
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	09-09-2019	09-09-2019	09-09-2019
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 (if any)	NA
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 of M/s. Avesta Pharma Pvt. Ltd, Maharashtra state, India issued by Food and Drug Administration, Maharashtra state, India. It is valid upto 15-09-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of polyethylene glycol-3350 (5000Kg, Batch # AP0919009) attested by AD (I & E) DRAP, Karachi dated 18-04-2019.
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 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	The firm has submitted compliance record of HPLC software from Waters Corporation.

	testing.	Audit trail of testing of product has not 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 data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

S#	Observations communicated	Response by the firm
1.	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.	The firm has submitted analytical method verification report for Assay by GPC (HPLC). The parameters include specificity and system suitability, linearity, precision and accuracy parameters from drug substance manufacturer. Analytical method verification was also performed by drug product manufacturer.
2.	Evidence of approval of formulation in applied pack size i.e., 578g shall be required since bottle of three pack sizes mentioned in chemistry and biopharmaceutics review are 119g, 238g and 527g and unit dose foil pouch of 17g.	The firm has submitted evidence of approval of formulation in applied pack size. Unit dose compliance is achieved via measuring cap of the jar, which is engraved with the unit dose of 17g from inside.
3.	Scientific justification is required for not performing assay testing by HPLC method till 6-month time point in all batches and adopting HPLC method from 6 month onward.	Initially, we had performed stability studies at interval of 1,2,3,4 in spectrophotometric method. After purchasing RI Detector and column L 25 (Waters, Ultrahydrogel 120, 7.8 × 300 mm part No. WaT011520 Lot 002D190651). We had validated the method in HPLC. So 6th month interval and onward testing were conducted in HPLC.
4.	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.	The firm has submitted copy of batch manufacturing records for all the batches.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted compliance record of HPLC software from Waters Corporation.
6.	Documents for the procurement of drug substance with approval from DRAP is required.	The firm has submitted copy of invoice for the import of polyethylene glycol-3350 (5000Kg, Batch # AP0919009) attested by AD (I & E) DRAP, Karachi dated 18-04-2019.

Decision: Registration Board discussed in detail and deferred the case for following:

- **Scientific justification of using Jar container closure system instead of using foil pouch as per reference product i.e., Miralax of M/s Bayer for achieving unit dose dispensing of applied product.**
- **Evidence of availability of drug product in applied container closure system in reference regulatory authorities.**

126.	Name, address of Applicant / Marketing Authorization Holder	M/s Genix Pharma (Pvt) Ltd, 44-45-B, Korangi Creek Road, Karachi
	Name, address of Manufacturing site.	M/s Genix Pharma (Pvt) Ltd, 44-45-B, Korangi Creek Road, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm is inspected on 02-07-2020 wherein the firm was found to be operating at good level of GMP compliance.
	Evidence of approval of manufacturing facility	The firm has provided Sachet (General) section from confirmed from approved layout plan from licensing division.

	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7172: 04-03-2021
	Details of fee submitted	PKR 50,000/-: 25-01-2021
	The proposed proprietary name / brand name	Movcol Jar 238g
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose contains: Polyethylene glycol 3350…….17g
	Pharmaceutical form of applied drug	White to off white color powder filled in HDPE bottle.
	Pharmacotherapeutic Group of (API)	Osmotic laxative
	Reference to Finished product specifications	Manufacturer's specifications
	Proposed Pack size	1's
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	Miralax for oral solution of M/s Bayer Healthcare LLC (USFDA Approved, over the counter)
	For generic drugs (me-too status)	Not available
	Name and address of API manufacturer.	M/s Avesta Pharma Pvt Ltd., Shivam chambers, 106/108, First Floor, S.V. Road, Goregaon west, Mumbai – 400 062 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, solubilities, physical form, manufacturers, 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. 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:	The 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 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 and 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	The firm has performed pharmaceutical equivalence of Movcol 238g Jar (B#19SB-143-01) of M/s Genix pharma with Miralax 238g Jar (B # 0C20PU) of M/s Bayer. Quality tests of both products including description, identification, filled weight, moisture content and assay were compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Avesta Pharma Pvt Ltd., Shivam chambers, 106/108, First Floor, S.V. Road, Goregaon west, Mumbai – 400 062 Maharashtra India.		
API Lot No.	AP0919009		
Description of Pack (Container closure system)	HDPE 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)		
Movcol Jar 238g			
Batch No.	19SB-143-01	19SB-144-02	19SB-145-03
Batch Size	50 Bottles	50 Bottles	50 Bottles
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	09-09-2019	09-09-2019	09-09-2019
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 (if any)	NA
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 of M/s. Avesta Pharma PVT LTD, Maharashtra state, India issued by Food and Drug Administration, Maharashtra state, India. It is valid upto 15-09-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of polyethylene glycol-3350 (5000Kg, Batch # AP0919009) attested by AD (I & E) DRAP, Karachi dated 18-04-2019.
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 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.	The firm has submitted compliance record of HPLC software from Waters Corporation. Audit trail of testing of product has not 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 data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Sr. No.	Observations communicated	Response by the firm
1.	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.	The firm has submitted analytical method verification report for Assay by GPC (HPLC). The parameters include specificity and system suitability, linearity, precision and accuracy parameters from drug substance manufacturer. Analytical method verification was also performed by drug product manufacturer.
2.	Evidence of approval of formulation in applied pack size i.e., 578g shall be required since bottle of three pack sizes mentioned in chemistry and biopharmaceutics review are 119g, 238g and 527g and unit dose foil pouch of 17g.	The firm has submitted evidence of approval of formulation in applied pack size. Unit dose compliance is achieved via measuring cap of the jar, which is engraved with the unit dose of 17g from inside.
3.	Scientific justification is required for not performing assay testing by HPLC method till 6-month time point in all batches and adopting HPLC method from 6 month onward.	Initially, we had performed stability studies at interval of 1,2,3,4 in spectrophotometric method. After purchasing RI Detector and column L 25. (Waters, Ultrahydrogel 120, 7.8 × 300 mm part No. WaT011520 Lot 002D190651). We had validated the method in HPLC. So 6th month interval and onward testing were conducted in HPLC.
4.	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.	The firm has submitted copy of batch manufacturing records for all the batches.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted compliance record of HPLC software from Waters Corporation.
6.	Documents for the procurement of drug substance with approval from DRAP is required.	The firm has submitted copy of invoice for the import of polyethylene glycol-3350 (5000Kg, Batch # AP0919009) attested by AD (I & E) DRAP, Karachi dated 18-04-2019.

Decision: Registration Board discussed in detail and deferred the case for following:

- **Scientific justification of using Jar container closure system instead of using foil pouch as per reference product i.e., Miralax of M/s Bayer for achieving unit dose dispensing of applied product.**
- **Evidence of availability of drug product in applied container closure system in reference regulatory authorities.**

127.	Name, address of Applicant / Marketing Authorization Holder	M/s Standpharm Pakistan Pvt. Ltd., 20-km, Ferozepur Road, Lahore
	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)
	GMP status of the firm	**M/s Standpharm Pakistan:** Panel inspection conducted on 18-02-2020 wherein the panel recommended the renewal of DML.

		M/s Vision Pharmaceuticals: The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	**M/s Vision Pharmaceuticals:** The firm has provided sterile Dry powder injection vials (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. 11788: 20-04-2021
	Details of fee submitted	PKR 50,000/-: 09-03-2021
	proposed proprietary name / brand name	CISEC 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole (as lyophilized powder) ……40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specification	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole 40mg powder for solution for infusion of M/s Sandoz Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML #000806).Plot#22-23,Industrial Triangle Kahuta Road, Islamabad
	Module-II (Quality Overall Summary)	Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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. 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:	The 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	Firm has submitted stability study data of 3 batches of drug

	(Conditions & duration of Stability studies)	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 and 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	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and comparator product Risek Injection 40mg (B # 789P06) of M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.		
API Lot No.	1702901 1702902 1702903		
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)	
Rapid 40mg I.V Injection			
Batch No.	1803707	1803708	1803709
Batch Size	10,000 vials	10,000 vials	10,000 vials
Manufacturing Date	03-2018	03-2018	03-2018
Date of Initiation	03-2018	03-2018	03-2018
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 (if any)	NA
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	The firm has procured material from their semi basic manufacturing facility.

	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 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.	The firm has submitted audit trail on testing reports of 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.

S.#	Observations communicated	Response by the firm
1.	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.	The firm has submitted analytical method verification report from M/s Vision Pharmaceuticals Pvt, Ltd. Islamabad.
2.	Certificate of analysis of both drug substance manufacturer and drug product manufacturer are required.	The firm has submitted COAs of 3 batches of omeprazole lyophilized powder. The firm stated that we have a combined QC of both Formulation (000517) and Semi-Basic (000806) facility having same equipment and analysts for both facilities.
3.	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and Risek 40mg Injection (B # 789P06) manufactured by M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
4.	Scientific justification is required for performing assay testing by UV method instead of HPLC method.	As the stability studies of the Bulk lyophilized material is performed by the Bulk manufacturer in the same QC lab with the same instrument (on HPLC) so just for verification purpose we performed the stability of the said product by UV. The firm has not submitted stability study data performed by HPLC alongwith raw data sheets, chromatograms and summary data sheets.
5.	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.	The firm has submitted copy of batch manufacturing record of 3 batches for which stability studies were carried out.
6.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Stability testing is performed by UV spectrometry therefore audit trail is not required.
7.	Documents for the procurement of drug substance with approval from DRAP is required.	We have procured omeprazole sodium lyophilized ready to fill powder our own Semi-basic facility.
8.	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.	The firm has not submitted the details of reconstitution diluents with which dilution was carried.
9.	Compatibility studies for the dry powder for	Compatibility studies were not provided with

	injections and dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product.	required diluents.

Decision: Deferred for following:

- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Submission of results of in-use stability studies of the drug product to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life.**
- **Submission of compatibility studies for the dry powder for injections to be performed as per the instructions provided in individual label of the drug product.**
- **Capacity assessment of manufacturing and testing facility of M/s Vision Pharmaceuticals Pvt. Ltd.**

128.	Name, address of Applicant / Marketing Authorization Holder	M/s Carer Pharmaceutical Industries. Plot No. 27 Main Road, Rawat Industrial Estate, Rawat, 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)
	GMP status of the firm	**M/s Carer pharmaceutical Industries:** The firm is granted new license on 18/03/2021. **M/s Vision Pharmaceuticals:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	**M/s Vision Pharmaceuticals:** The firm has provided sterile Dry powder injection vials (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. 13450: 19-05-2021
	Details of fee submitted	PKR 50,000/-: 12-02-2021
	proposed proprietary name / brand name	Desan 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole (as lyophilized powder) ……40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specification	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole 40mg powder for solution for infusion of M/s Sandoz Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.

	Module-II (Quality Overall Summary)	Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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. 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:	The 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 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 and 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	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and Risek 40mg Injection (B # 789P06) manufactured by M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.
API Lot No.	1702901 1702902 1702903
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)		
Rapid 40mg I.V Injection			
Batch No.	1803707	1803708	1803709
Batch Size	10,000 vials	10,000 vials	10,000 vials
Manufacturing Date	03-2018	03-2018	03-2018
Date of Initiation	03-2018	03-2018	03-2018
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 (if any)	NA
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).	The firm has procured material from their semi basic manufacturing facility.
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.	The firm has submitted audit trail on testing reports of 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.

S.#	Observations communicated	Response by the firm
1.	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.	The firm has submitted analytical method verification report from M/s Vision Pharmaceuticals Pvt, Ltd. Islamabad.
2.	Certificate of analysis of both drug substance manufacturer and drug product manufacturer are required.	The firm has submitted COAs of 3 batches of omeprazole lyophilized powder. The firm stated that we have a combined QC of both Formulation (000517) and Semi-Basic (000806) facility having same equipment and analysts for both facilities.
3.	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and Risek 40mg Injection (B # 789P06) manufactured by M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water

		content, pH and assay were compared.
4.	Scientific justification is required for performing assay testing by UV method instead of HPLC method.	As the stability studies of the Bulk lyophilized material is performed by the Bulk manufacturer in the same QC lab with the same instrument (on HPLC) so just for verification purpose we performed the stability of the said product by UV. The firm has not submitted stability study data performed by HPLC alongwith raw data sheets, chromatograms and summary data sheets.
5.	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.	The firm has submitted copy of batch manufacturing record of 3 batches for which stability studies were carried out.
6.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Stability testing is performed by UV spectrometry therefore audit trail is not required.
7.	Documents for the procurement of drug substance with approval from DRAP is required.	We have procured omeprazole sodium lyophilized ready to fill powder our own Semi-basic facility.
8.	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.	The firm has not submitted the details of reconstitution diluents with which dilution was carried.
9.	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.	Compatibility studies were not provided with required diluents.

Decision: Deferred for following:

- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Submission of results of in-use stability studies of the drug product to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life.**
- **Submission of compatibility studies for the dry powder for injections to be performed as per the instructions provided in individual label of the drug product.**
- **Capacity assessment of manufacturing and testing facility of M/s Vision Pharmaceuticals Pvt. Ltd.**

129.	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 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)
	GMP status of the firm	**M/s Nagarsons Pharmaceuticals:** The firm is inspected on 23-05-2019 which concluded that overall GMP compliance could be graded as Good for visited sections as of today. The firm has provided 8 sections. **M/s Vision Pharmaceuticals:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	**M/s Vision Pharmaceuticals:** The firm has provided sterile Dry powder injection vials (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. 8314: 15-03-2021
	Details of fee submitted	PKR 50,000/-: 07-01-2021
	The proposed proprietary name / brand name	Nagzole 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole (as lyophilized powder) …….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole 40mg powder for solution for infusion of M/s Sandoz Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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. 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:	The 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 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 and 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	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and comparator product (B # 789P06) of M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.		
API Lot No.	1702901 1702902 1702903		
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)		
Rapid 40mg I.V Injection			
Batch No.	1803707	1803708	1803709
Batch Size	10,000 vials	10,000 vials	10,000 vials
Manufacturing Date	03-2018	03-2018	03-2018
Date of Initiation	03-2018	03-2018	03-2018
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 (if any)	NA
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).	The firm has procured material from their semi basic manufacturing facility.
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	The firm has submitted audit trail on testing reports of product.

	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 data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

S.#	Observations communicated	Response by the firm
1.	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.	The firm has submitted analytical method verification report from M/s Vision Pharmaceuticals Pvt, Ltd. Islamabad.
2.	Certificate of analysis of both drug substance manufacturer and drug product manufacturer are required.	The firm has submitted COAs of 3 batches of omeprazole lyophilized powder. The firm stated that we have a combined QC of both Formulation (000517) and Semi-Basic (000806) facility having same equipment and analysts for both facilities.
3.	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and Risek 40mg Injection (B # 789P06) manufactured by M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
4.	Scientific justification is required for performing assay testing by UV method instead of HPLC method.	As the stability studies of the Bulk lyophilized material is performed by the Bulk manufacturer in the same QC lab with the same instrument (on HPLC) so just for verification purpose we performed the stability of the said product by UV. The firm has not submitted stability study data performed by HPLC alongwith raw data sheets, chromatograms and summary data sheets.
5.	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.	The firm has submitted copy of batch manufacturing record of 3 batches for which stability studies were carried out.
6.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Stability testing is performed by UV spectrometry therefore audit trail is not required.
7.	Documents for the procurement of drug substance with approval from DRAP is required.	We have procured omeprazole sodium lyophilized ready to fill powder our own Semi-basic facility.
8.	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.	The firm has not submitted the details of reconstitution diluents with which dilution was carried.
9.	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.	Compatibility studies were not provided with required diluents.

Decision: Deferred for following:

- **Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.**
- **Submission of results of in-use stability studies of the drug product to be reconstituted before use, along**

with proposed in-use storage statement and in-use shelf-life. • **Submission of compatibility studies for the dry powder for injections to be performed as per the instructions provided in individual label of the drug product.** • **Capacity assessment of manufacturing and testing facility of M/s Vision Pharmaceuticals Pvt. Ltd.**		
130.	Name, address of Applicant / Marketing Authorization Holder	M/s Pharmedic laboratories., 15-16 Km, Multan Road Lahore.
	Name, address of Manufacturing site.	M/s English Pharmaceuticals. Indus Link Kattar Band Road, Thokar Niaz Baig, Multan Road, Lahore
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	**M/s Pharmedic Laboratories:** GMP inspection report dated 04-02-2020 in which the panel concludes satisfactory level of cGMP compliance. The panel further reported that since the firm had upgraded the layout of anti-cancer section, therefore the firm was advised to get the anticancer section regularized and approved by DRAP, Islamabad after fulfilment of all codal formalities. **M/s English Pharmaceuticals:** Certificate of GMP Issued to English Pharmaceuticals on 16-01-2018.
	Evidence of approval of manufacturing facility	**M/s English Pharmaceuticals:** The firm has provided Dry powder injection vials (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. 4848: 12-02-2021
	Details of fee submitted	PKR 50,000/-: 06-02-2020,
	The proposed proprietary name / brand name	EPSOL 40mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Esomeprazole as sodium (lyophilized)…….40mg
	Pharmaceutical form of applied drug	Powder for solution for injection and infusion
	Pharmacotherapeutic Group of (API)	Proton pump inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per policy
	The status in reference regulatory authorities	Nexium IV Injection of M/s Astrazeneca (USFDA approved)
	For generic drugs (me-too status)	Es-Loprot Injection 40mg of M/s Nabiqasim industries (Pvt) ltd
	Name and address of API manufacturer.	M/s Sterile India Pvt. Ltd Plot No.100, 118-G, Sector-56, Phase-IV, HSIIDC, 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, 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. 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:	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 6 months accelerated and 36 months real time data of 3 batches of API.
	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	The Firm has performed pharmaceutical equivalence of their developed formulation Esopep 40mg Injection (B # 2004710) with Nexum 40mg injection (B # 134p07) of M/s GETZ Pharma. Quality tests of both products including description, identification, pH, assay, bacterial endotoxin and sterility were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Sterile India Pvt. Ltd Plot No.100, 118-G, Sector-56, Phase-IV, HSIIDC, Kundli District Sonepat, Haryana, India
API Lot No.	SI/EPZ/00040819
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)

ESOPEP 40mg Injection			
Batch No.	ZOI-064	ZOI-065	ZOI-066
Batch Size	6947 vials	10300 vials	17175 vials
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	02-04-2020	02-04-2020	19-04-2020
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 (if any)	N/A
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 Sterile India Pvt Ltd., India issued by Food and Drug administration Haryana, India. The certificate is valid till 12-07-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Esomeprazole lyophilized powder (10kg) attested by Assistant Director (I&E), DRAP, Lahore dated 11-10-2019.
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 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.	21 CFR status and audit trail reports on testing of product were 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.

The firm has submitted copy of contract agreement between M/s Pharmedic Laboratories, and M/s English Pharmaceuticals.

S#	Observations communicated	Response by the firm
1.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required to be submitted.	Details of the reference and applicant product have been submitted as under: Applicant product: B # ZOI-064 Reference product: B # 134p07
2.	Copy of purchase invoice for the procurement of API shall be submitted.	The firm has submitted copy of invoice for the import of Esomeprazole lyophilized powder (10kg) attested by Assistant Director (I&E), DRAP, Lahore dated 11-10-2019.
3.	The submitted copy of GMP certificate is expired you are required to submit updated copy of GMP certificate.	Firm has submitted copy of GMP certificate (No. 12/80-2Drug1-2019/5941 issued by Food and Drugs Administration Haryana dated 25-07-2019. The certificate is valid till 12-07-2022.
4.	Brand name of applied formulation needs to be clarified since it is mentioned NILCID injection in the fee challan while EPSOL is mentioned on Form-5F.	The fee challan were exchanged between applications of NILCID & EPSOL injection. The correct challan has been placed in relevant dossiers now.
5.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The firm has submitted record of data logger for temperature and humidity monitoring of stability chambers.
6.	GMP status of M/s Pharmedic laboratories	**M/s Pharmedic Laboratories:** GMP inspection report dated

	as well as M/s English pharmaceuticals shall be submitted.	04-02-2020 in which the panel concludes satisfactory level of cGMP compliance. The panel further reported that since the firm had upgraded the layout of anti-cancer section, therefore the firm was advised to get the anticancer section regularized and approved by DRAP, Islamabad after fulfilment of all codal formalities. **M/s English Pharmaceuticals:** Certificate of GMP Issued to English Pharmaceuticals on 16-01-2018.

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.**

131.	Name, address of Applicant / Marketing Authorization Holder	M/s Pharmedic laboratories., 15-16 Km, Multan Road Lahore.
	Name, address of Manufacturing site.	M/s English Pharmaceuticals. Indus Link Kattar Band Road, Thokar Niaz Baig, Multan Road, Lahore
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	**M/s Pharmedic Laboratories:** GMP inspection report dated 04-02-2020 in which the panel concludes satisfactory level of cGMP compliance. The panel further reported that since the firm had upgraded the layout of anti-cancer section, therefore the firm was advised to get the anticancer section regularized and approved by DRAP, Islamabad after fulfilment of all codal formalities. **M/s English Pharmaceuticals:** Certificate of GMP Issued to English Pharmaceuticals on 16-01-2018.
	Evidence of approval of manufacturing facility	**M/s English Pharmaceuticals:** The firm has provided Dry powder injection vials (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. 4847: 12-02-2021
	Details of fee submitted	PKR 50,000/-: 06-02-2020,
	The proposed proprietary name / brand name	NILCID 40mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole as sodium (lyophilized)……40mg
	Pharmaceutical form of applied drug	Powder for solution for injection and infusion
	Pharmacotherapeutic Group of (API)	Proton pump inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per policy
	The status in reference regulatory authorities	Omeprazole powder for solution for infusion of M/s

		Sandoza Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No.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, 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. 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:	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 6 months accelerated and 24 months real time data of 3 batches of Omeprazole sodium lyophilized powder.
	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	The Firm has performed pharmaceutical equivalence of their developed formulation Zolat 40mg injection (B # 2004710) with comparator product Risek 40mg Injection (B # 134p07) of M/s GETZ Pharma. Quality tests of both products including description, identification, pH, assay, bacterial endotoxin and sterility were performed and compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Vision Pharmaceuticals (Pvt) Ltd. Plot No.22-23, Industrial Triangle, Kahuta Road, Islamabad, Pakistan.
API Lot No.	2002905

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)

ZOLAT 40MG INJECTION

Batch No.	ZOI064	ZOI065	ZOI066
Batch Size	6947 vials	10300 vials	17175 vials
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	02-04-2020	02-04-2020	19-04-2020
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 (if any)	N/A
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 Pharmaceuticals, Islamabad 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).	The firm has submitted copy of invoice for the purchase of Omeprazole lyophilized powder (3Kg) from M/s Vision Pharmaceuticals 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.	21 CFR status and audit trail reports on testing of product were 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.

The firm has submitted copy of contract agreement between M/s Pharmedic Laboratories, and M/s English Pharmaceuticals.

S.#	Observations communicated	Response by the firm
1.	Clarification is required regarding stability studies of API conducted at 30°C ± 2°C / 65% ± 5% RH while storage conditions of the API mentioned in USP are 2-8°C (cold place).	The USP recommended storage condition is for the pure API, since we have procured pre-lyophilized powder the temperature stability increases so we conduct the stability of our product at 30°C ± 2°C / 65% ± 5% RH.
2.	Details of applicant batch number and comparator product batch number used for pharmaceutical equivalence studies are required to be submitted.	Details of the reference and applicant product have been submitted as under: Applicant product: B # ZOI-064 Reference product: B # 134p07
3.	Copy of purchase invoice for the procurement of API (Omeprazole sodium) shall be submitted.	The firm has submitted copy of invoice for the purchase of Omeprazole lyophilized powder (3Kg) from M/s Vision Pharmaceuticals dated 05-08-2020.
4.	Approval of API/ DML/GMP certificate of	The firm has submitted copy of GMP certificate for M/s

	API manufacturer issued by concerned regulatory authority of country of origin.	Vision Pharmaceuticals, Islamabad issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
5.	Brand name of applied formulation needs to be clarified since it is mentioned NILCID injection in the fee challan while EPSOL is mentioned on Form-5F.	The fee challan were exchanged between applications of NILCID & EPSOL injection. The correct challan has been placed in relevant dossiers now.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The firm has submitted record of data logger for temperature and humidity monitoring of stability chambers.
7.	GMP status of M/s Pharmedic laboratories as well as M/s English pharmaceuticals shall be submitted.	**M/s Pharmedic Laboratories:** GMP inspection report dated 04-02-2020 in which the panel concludes satisfactory level of cGMP compliance. The panel further reported that since the firm had upgraded the layout of anti-cancer section, therefore the firm was advised to get the anticancer section regularized and approved by DRAP, Islamabad after fulfilment of all codal formalities. **M/s English Pharmaceuticals:** Certificate of GMP Issued to English Pharmaceuticals on 16-01-2018.

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.**

Case No.07: Registration applications of local manufacturing of human drugs submitted on Form5F format

a. Deferred Cases

132.	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	ERLIN 5MG TABLET
	Composition	Each Film Coated Tablet Contains: 6.48mg Ertugliflozin L-Pyroglutamic Acid eq to Ertugliflozin……...5mg
	Diary No. Date of R& I & fee	Dy. No. 10086 dated 04-03-2019, Rs.50,000/- 04-03-2019
	Pharmacological Group	SGLT2 inhibitors
	Type of Form	Form-5D
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	As per PRC
	Approval status of product in Reference Regulatory Authorities	Steglatro 5mg Tablet of Merck Sharp Dhome (USFDA Approved)
	Me-too status	N/A
	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	
133.	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	ERLIN 15MG TABLET
	Composition	Each Film Coated Tablet Contains: 19.43mg Ertugliflozin L-Pyroglutamic Acid eq to Ertugliflozin ……..15mg
	Diary No. Date of R& I & fee	Dy. No. 10087 dated 04-03-2019 Rs.50,000/- 04-03-2019

	Pharmacological Group	SGLT2 inhibitors
	Type of Form	Form-5D
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	As per PRC
	Approval status of product in Reference Regulatory Authorities	Steglatro 15mg Tablet of Merck Sharp Dhome (USFDA Approved)
	Me-too status	N/A
	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	

STABILITY STUDY DATA			
Name of Manufacturer	M/s Pharmevo Private Limited., Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi		
Manufacturer of API	M/s Shangai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd., Daixi Street, Louyang Town, Wujin District, Changzhou, Jiangsu 213105, China		
API Lot No.	ETG20190101		
Description of Pack (Container closure system)	Alu Alu Blister pack 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		
ERLIN 5MG TABLET			
Batch No.	19PD-2717-01-T	19PD-2718-02-T	19PD-2719-03-T
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	04-2019	04-2019	04-2019
Date of Initiation	25-05-2019	25-05-2019	25-05-2019
No. of Batches	03		
Date of Submission	10-04-2020 (Dy. No. 6745)		
ERLIN 15MG TABLET			
Batch No.	19PD-2714-09-T	19PD-2715-10-T	19PD-2716-11-T
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	04-2019	04-2019	04-2019
Date of Initiation	25-05-2019	25-05-2019	25-05-2019
No. of Batches	03		
Date of Submission	10-04-2020 (Dy. No. 6746)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT	
Documents To Be Provided	**Status**
Certificate of analysis of API.	Yes
Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Shanghai Pharma Group Changzhou Kony pharmaceutical Co., Ltd. China issued by China Food and Drug Administration, China. It is valid upto 26-11-2023.
Protocols followed for conduction of stability	Yes

study and details of tests.	
Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc.	Yes
Documents confirming import of API etc.	The firm has submitted copy of invoice for the purchase of Ertugliflozin L-pyroglutamic acid (1.2Kg), attested by Assistant Director (I & E) DRAP, Karachi dated 01-2-2019. The invoice also mentions: Ertugliflozin impurities A (20mg) Ertugliflozin impurities B (100mg) Ertugliflozin L-pyroglutamic acid WS (400mg)
All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Yes
Commitment to continue real time stability study till assigned shelf life of the product.	Yes
Commitment to follow Drug Specification Rules, 1978.	Yes

REMARKS OF EVALUATOR

- The firm has submitted 06 months Accelerated and 06 months Real Time Stability Data for 03 Batches.

Report on Investigation of Authenticity / Genuineness of data submitted for registration of Erlin (Ertugliflozin) 5mg and 15mg Tablets by M/s PharmEvo (Pvt.) Limited, A-29, North Western Industrial Zone, Port Qasim, Karachi.

Reference No: F.1-2/2020-PEC dated 29th December, 2020.
Investigation Date and Time: 04 February, 2021.
Investigation Site: M/s PharmEvo (Pvt.) Limited, A-29, North Western Industrial Zone, Port Qasim, Karachi.
Background:
Chairman Registration Board considered the applications of M/s PharmEvo (Pvt.) Limited, A-29, North Western Industrial Zone, Port Qasim, Karachi for registration of Erlin (Ertugliflozin) 5mg and 15mg Tablets and constituted a two members panel to investigate the authenticity / genuineness of data (import of raw material and stability data). Panel was advised to conduct inspection of the firm and to submit report for further consideration.

Composition of Panel:

1. Mr. Muhammad Shoaib Ansari, Chief Drug Inspector Sindh, Karachi.
2. Dr. Affan Ali Qureshi, Assistant Director, CDL, DRAP, Karachi.

Scope of investigation:
Investigation of the authenticity / genuineness of data (import of raw material and stability data), manufacturing of stability batches and stability studies on these batches.
Tools for Investigation:
The investigation was conducted by using a structured questionnaire of DRAP. For objective evidence physical inspection of the facilities for manufacturing and quality control, material used and retained, personnel involved, ongoing studies, printed data and integrity and security of data in respective databases were also audited. The details of investigation may be summarized as under:
Details of Investigation:
Erlin (Ertugliflozin) 5mg and 15mg Tablets

Q.#	Question	Observation by panel
1.	Do you have documents confirming the import of Ertugliflozin API including approval from DRAP?	The firm has imported Ertugliflozin 1.2Kg vide Invoice No. PSPW-190116-1 dated 16/01/2019 from M/s Shangai Pansopharm Technology Co. Ltd. Manufactured by M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co. Ltd. The firm has approval for the import of the API from DRAP, Karachi dated 01-02-2019.

2.	What was the rationale behind selecting the particular manufacturer of API?	The rationale behind selecting the particular source of API is the laid down criteria of the firm in their Vendor Evaluation procedure which include the GMP status of the firm, DMF source and capability to provide API reference standard and impurity standard.
3.	Do you have documents confirming the import of Ertugliflozin, reference standard and impurity standards?	Firm has documents confirming the import of Ertugliflozin. They have working standard & impurity standard which were imported with the API.
4.	Do you have certificate of Analysis of the API, reference standards and impurity standards?	The firm has certificates of analysis for API, Working standards of the API and impurities standards.
5.	Do you have GMP certificate of API Manufacturer issued by regulatory Authority of country of origin?	Firm has GMP certificate issued by the China Food and Drug Administration.
6.	Do you use API manufacturer method of testing for testing API?	The firm has used API manufacturer method for testing the API.
7.	Do you have stability studies reports on API?	The firm have stability studies reports on API.
8.	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	The stability testing has been performed as per SIM method and however no degradation products are reported by the manufacturer. However process related impurities have been quantified during stability studies.
9.	Do you have method for quantifying the impurities in the API?	The firm has API manufacturer method for quantifying the impurities in the API.
10.	Do you have some remaining quantities of the API, its reference standard and impurities standards?	Firm has 379g of API and 20mg of working standard, however, they have consumed all the impurity standards.
11.	Have you used pharmaceutical grade excipients?	The firm has used pharmaceutical grade excipients and include: Microcrystalline cellulose-102, Lactose Monohydrate, Sodium Starch Glycolate, Magnesium Stearate. The firm has used & FC4W-E-White & Iron Oxide Black and FC4W-E-White & Iron Oxide Red for Ertugliflozin 5 mg and Ertugliflozin 15 mg respectively.
12.	Do you have documents confirming the import of the used excipients?	The firm has necessary documents confirming the import of the used excipients.
13.	Do you have test reports and other records on the excipients used?	The firm has test reports and other records on the excipients used.
14.	Do you have written and authorized protocols for the development of Ertugliflozin 5mg & 15mg Tablets?	Firm has written and authorized protocols for the development of ERTUGLIFLOZIN 5mg&15mg Tablets.
15.	Have you performed Drug-excipient compatibility studies?	Firm has not performed Drug-excipient compatibility studies as the composition of their tablets is similar to the innovator product (STEGLATRO TABLETS).
16.	Have you performed comparative dissolution studies?	As per literature of the innovator available with the firm, the product falls in BCS Class I. The same has been demonstrated by the firm on their product i.e. the product dissolves more than 85% in all 3 media. Therefore, f2 calculations is not necessary.
17.	Do you have product development (R&D) section?	The firm has dedicated R&D section with reasonable facilities of equipment, human resource and utilities.

18.	Do you have necessary equipment available in product development section for development of Ertugliflozin 5mg & 15mg Tablets?	The firm has all necessary equipment related to manufacturing available in R&D section for manufacturing of Ertugliflozin 5mg & 15mg tablet. The quality control related to development work has been done in the routine quality control laboratory; however, there are dedicated HPLCs and Human Resource for this purpose.
19.	Are the equipment in product development section qualified?	All the equipment used in product development are qualified.
20.	Do you have proper maintenance/ calibration / re-qualification program for the equipment used in PD section?	The firm has proper maintenance/ calibration / re-qualification program for the equipment used in PD section.
21.	Do you have qualified staff in product development section with proper knowledge and training in product development?	The firm has 06 pharmacists and 01 chemist in manufacturing section of product development section currently with suitable knowledge and training in product development. 02 QC Analysts are dedicated for new products testing.
22.	Have you manufactured three stability batches for the stability studies of Ertugliflozin 5mg & 15mg Tablets as required?	The firm has manufactured three stability batches for the stability studies of: **Ertugliflozin 5mg Tablets with Batch Numbers:** 19PD-2717-01-T, 19PD-2718-02-T & 19PD-2719-03-T **Ertugliflozin 15mg Tablets with Batch Numbers:** 19PD-2714-09-T, 19PD-2715-10-T & 19PD-2716-11-T
23.	Do you have any criteria for fixing the batch size of stability batches?	The criteria for fixing batch size is according to requirement of stability studies.
24.	Do you have complete record of production of stability batches?	The firm has complete record of production of stability batches.
25.	Do you have protocols for stability testing of stability batches?	The firm has detailed protocols for stability testing of stability batches.
26.	Do you have developed and validated the method for testing of stability batches?	The firm has developed its own method based on API manufacture method of testing for their finished product with validation supported by forced degradation.
27.	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Method transfer studies is not applicable since the firm has developed and validated its own method based on API manufacturer's method of testing.
28.	Do you have documents confirming the qualification of equipment's / instruments being used in the test and analysis of Ertugliflozin and the finished drug?	The firm has documents confirming the installation and operational qualification of the equipment's / instruments being used in the test and analysis of Ertugliflozin and the finished drug.
29.	Do your method of analysis stability indicating?	The firm's method of testing is stability indicating as supported by forced degradation studies.
30.	Do your HPLC software 21CFR Compliant?	The testing has been done on HPLC Shimadzu Prominence i LC-2030. HPLC software i.e. Lab Solution DB is 21CFR Compliant as per record available with the firm.
31.	Can you show Audit trail reports on Ertugliflozin testing?	Audit trail on the testing reports is available.
32.	Do you have some remaining quantities of degradation products and stability batches?	The firm has remaining quantities of the stability batches kept in stability chambers.
33.	Do you have stability batches kept on stability testing?	The firm has kept all the three batches on real time and accelerated stability testing. Currently, 18 months studies have been completed with satisfactory results.
34.	Do you have valid calibration status for the Equipment used in Ertugliflozin 5mg & 15mg Tablets production and analysis?	The firm has valid calibration status for the equipment used in Ertugliflozin tablets production and analysis.

35.	Do proper and continuous monitoring and control are available for stability chamber?	The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All the chambers are properly qualified. All the chambers are provided with continuous power supply and data loggers for continuous monitoring.
36.	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	The firm has manufacturing area provided with necessary qualified equipment and utilities. The manufacturing personnel are suitable in number and qualification to run the manufacturing processes as per GMP requirements. The environmental conditions and their controls are also proper. The overall GMP conditions can be rated as compliant.

Conclusions:

1. On the basis of risk-based approach the genuineness / authenticity of stability data submitted by the firm for registration of Ertugliflozin 5mg & 15mg Tablets is verifiable to satisfactory level.
2. The related manufacturing area, equipment, personnel and utilities are GMP compliant and well suited for the manufacturing of Ertugliflozin 5mg & 15mg Tablets.

Recommendations:

1. The firm may kindly be granted necessary registration of Ertugliflozin 5mg & 15mg Tablets.

Previous Decision: Registration Board decided to defer the applications of Erlin (Ertugliflozin) 5mg and 15mg Tablets for submission of Comparative dissolution studies of each strength against the innovator product (M-308).

Evaluation by PEC: The firm has submitted comparative dissolution profile of Erlin 15mg Tablet and innovator product. The details are as follows:

Product detail	**PharmEvo (Pvt) Ltd**	**Pfizer Manufacturing Deutschland Germany**
Product name	Ertugliflozin 15mg Tablet	Steglatro 15mg Tablet
Batch No	19PD-2714-09-T	U019768
Manufacturing date	April-19	Feb-21

The firm has submitted comparative dissolution profile of Erlin 5mg Tablet and innovator product. The details are as follows:

Product detail	**PharmEvo (Pvt) Ltd**	**Pfizer Manufacturing Deutschland Germany**
Product name	Ertugliflozin 5mg Tablet	Steglatro 5mg Tablet
Batch No	19PD-2717-01-T	U017971
Manufacturing date	April-19	Feb-21

Decision: Registration Board approved the registrations of Erlin 5mg and 15mg 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.**
- **Registration letter shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

134.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals Pvt Ltd, Plot # 204-205, Industrial Triangle, Kahuta Road, 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)
	GMP status of the firm	The firm has submitted copy of panel inspection dated 24-12-2018 wherein renewal of DML was granted.
	Evidence of approval of manufacturing facility	The firm has provided Capsule (General) Section as confirmed from GMP certificate.
	Status of application	☒ New Drug Product (NDP)

		☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29489: 05-11-2020
	Details of fee submitted	PKR 50,000/-: 05-11-2020,
	The proposed proprietary name / brand name	RAPIDFLO 4MG CAPSULE
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule Contains: Silodosin……4mg
	Pharmaceutical form of applied drug	Hard Gelatin Capsule
	Pharmacotherapeutic Group of (API)	Alpha-adrenoreceptor antagonists
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	RAPAFLO Capsule (**USFDA** Approved)
	For generic drugs (me-too status)	N/A
	Name and address of API manufacturer.	M/s Anhui Haikang pharmaceuticals Co., Ltd. Address: No. 21, Huancheng West Road, Daguan District, Anqing, Anhui, 246000, 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, 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.
	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 6 months accelerated and 24 months real time data of 3 batches of API.
	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 and comparative dissolution profile of their developed formulation Rapidflo 4mg capsule (B # ST19E018) with innovator product Rapaflo 4mg capsule (B # K61031) of M/s Allergan pharma in 0.1 N HCl, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of similarity factor f_2 showed that dissolution profile of both products is comparable.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA			
Manufacturer of API	M/s AnHui HaiKang Pharmaceutical Co., Ltd. Address: No. 21, Huancheng West Road, Daguan District, Anqing, Anhui, 246000, China		
API Lot No.	20181101		
Description of Pack (Container closure system)	HDPE Bottle containing 30 capsule		
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, 9, 12 (Months)		
RAPIDFLO 4MG CAPSULE			
Batch No.	ST19E018	ST19E019	ST19E020
Batch Size	7500 Capsules	7500 Capsules	7500 Capsules
Manufacturing Date	05-2019	05-2019	05-2019
Date of Initiation	14-06-2019	14-06-2019	14-06-2019
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 (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 265th meeting decided to approve registration of D-Lanz 30mg capsule and D-Lanz 60mg capsule. **Inspection date:** 26th December, 2019. As per the report, the HPLC software was not 21 CFR compliant. Continuous monitoring and control was available for stability chambers.
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 Anhui Haikang Pharmaceutical Co., Ltd. China issued by Anqing Biomedical Industry Association, China. It is valid till 07-07-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Silodosin (500g) attested by Assistant Director (I&E), DRAP, Islamabad dated 07-03-2019.

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 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 on testing reports of product 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.

S.#	Observations communicated	Response by the firm
1.	The summary of results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 shall be submitted and discussed in QOS as well as in module 3 .	The Firm has submitted summarized results of comparative dissolution profile of their developed formulation Rapidflo 4mg capsule (B # ST19E018) with innovator product Rapaflo 4mg capsule (B # K61031) of M/s Allergan pharma in 0.1 N HCl, acetate buffer pH 4.5 and phosphate buffer pH 6.8.
2.	GMP certificates of API manufacturer is expired. Submission of valid copy of GMP certificate is required.	The firm has submitted copy of GMP certificate for M/s Anhui Haikang Pharmaceutical Co., Ltd. China issued by Anqing Biomedical Industry Association, China. It is valid till 07-07-2025.
3.	Justify the acceptance criteria of dissolution test i.e. NLT 80% of the labeled amount of Silodosin dissolved in 20 minutes, since the Clinical Pharmacology & Biopharmaceutics Review of innovator specifies that the acceptance criteria for dissolution test is not less than 85% in 15 minutes.	We adopted the dissolution limit of NLT 80% in 20 minutes, which is within the criteria mentioned in the above guideline. But our formulation is comparable in all three mediums with innovators i.e., showing >85% dissolution in 15 min. However, our product has ability to qualify that criteria too.
4.	Silodosin is a light sensitive material therefore the whole analytical procedures should avoid exposure to light using brown volumetric flask and sampler vials. Justify the performance of analytical procedures in volumetric flasks and other glasswares without taking this precaution.	While analysis of silodosin precautions of using brown volumetric flask and sampler vials was taken but this precaution was not incorporated in SAP of raw material and finished product. Now SAP has been revised accordingly.
5.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Submitted.

Previous Decision: Registration Board deferred the case for submission of real time and accelerated stability study data of two batches till 1 month with revised dissolution specifications (i.e. NLT Q in 15 minutes) as per decision of 293rd meeting of Registration Board (M-307).

Evaluation by PEC: The firm has submitted stability study data of 1 month with revised dissolution specifications NLT 80% in 15 min. The details of batches are as follows:

Batch No.	PT21G013	PT21G014
Batch Size	1000 Capsules	1000 Capsules
Manufacturing Date	07-2021	07-2021
Date of Initiation	12-07-2021	12-07-2021

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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		
135.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals Pvt Ltd, Plot # 204-205, Industrial Triangle, Kahuta Road, 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)
	GMP status of the firm	The firm has submitted copy panel inspection dated 24-12-2018 wherein renewal of DML was granted.
	Evidence of approval of manufacturing facility	The firm has provided Capsule (General) Section as confirmed from GMP certificate.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29098: 03-11-2020
	Details of fee submitted	PKR 50,000/-: 03-11-2020,
	The proposed proprietary name / brand name	RAPIDFLO 8MG CAPSULE
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule Contains: Silodosin……8mg
	Pharmaceutical form of applied drug	Hard Gelatin Capsule
	Pharmacotherapeutic Group of (API)	Alpha-adrenoreceptor antagonists
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	RAPAFLO Capsule (**USFDA** Approved)
	For generic drugs (me-too status)	N/A
	Name and address of API manufacturer.	M/s Anhui Haikang pharmaceuticals Co., Ltd. Address: No. 21, Huancheng West Road, Daguan District, Anqing, Anhui, 246000, 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, 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.
	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 6 months accelerated and 60 months real time data of 3 batches of API.
	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 and comparative dissolution profile of their developed formulation Rapidflo 8mg capsule (B # ST19H018) with innovator product Rapaflo 8mg capsule (B # K61031) of M/s Allergan pharma in 0.1 N HCl, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of similarity factor f_2 showed that dissolution profile of both products is comparable.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA			
Manufacturer of API	M/s Anhui Haikang pharmaceuticals Co., Ltd. Address: No. 21, Huancheng West Road, Daguan District, Anqing, Anhui, 246000, China		
API Lot No.	20181101		
Description of Pack (Container closure system)	HDPE Bottle containing 30 capsule		
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)		
RAPIDFLO 8MG CAPSULE			
Batch No.	ST19E021	ST19E022	ST19E023
Batch Size	7500 Capsules	7500 Capsules	7500 Capsules
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	14-06-2019	14-06-2019	14-06-2019
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 (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 265th meeting decided to approve registration of D-Lanz 30mg capsule and D-Lanz 60mg capsule. **Inspection date:** 26th December, 2019. As per the report, the HPLC software was not 21 CFR compliant. Continuous monitoring and control was available for stability chambers.
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 Anhui Haikang Pharmaceutical Co., Ltd. China issued by Anhui Anqing Daguan Economic development Area management Committee Environmental Protection Agency, China. It is valid till 07-11-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Silodosin (500g) attested by Assistant Director (I&E), DRAP, Islamabad dated 07-03-2019.
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 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 on testing reports of product 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.

Sr.#	Observations communicated	Response by the firm
1	The summary of results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 shall be submitted and discussed in QOS as well as in module 3 .	The firm has submitted summarized results of comparative dissolution profile of their developed formulation Rapidflo 8mg capsule (B # ST19E021) with innovator product Rapaflo 8mg capsule (B # K61031) of M/s Allergan pharma in 0.1 N HCl, acetate buffer pH 4.5 and phosphate buffer pH 6.8.
2.	GMP certificates of API manufacturer is expired. Submission of valid copy of GMP certificate is required.	The firm has submitted copy of GMP certificate for M/s Anhui Haikang Pharmaceutical Co., Ltd. China issued by Anqing Biomedical Industry Association, China. It is valid till 07-07-2025.
3.	Justify the acceptance criteria of dissolution test i.e. NLT 80% of the labeled amount of Silodosin dissolved in 20 minutes, since the Clinical Pharmacology & Biopharmaceutics Review of innovator specifies that the acceptance criteria for dissolution test is not less than 85% in 15 minutes.	We adopted the dissolution limit of NLT 80% in 20 minutes, which is within the criteria mentioned in the above guideline. But our formulation is comparable in all three mediums with innovators i.e., showing >85% dissolution in 15 min. However, our product has ability to qualify that criteria too.
4.	Silodosin is a light sensitive material therefore the whole analytical procedures should avoid exposure to light using brown volumetric flask and sampler vials. Justify the performance of analytical procedures in volumetric flasks and other glasswares without taking this precaution.	While analysis of silodosin precautions of using brown volumetric flask and sampler vials was taken but this precaution was not incorporated in SAP of raw material and finished product. Now SAP has been revised accordingly.
5.	Record of Digital data logger for	Submitted.

	temperature and humidity monitoring of stability chambers (real time & accelerated).	

Previous Decision: Registration Board deferred the case for submission of real time and accelerated stability study data of two batches till 1 month with revised dissolution specifications (i.e. NLT Q in 15 minutes) as per decision of 293rd meeting of Registration Board (M-307).

Evaluation by PEC: The firm has submitted stability study data of 1 month with revised dissolution specifications NLT 80% in 15 min. The details of batches are as follows:

Batch No.	PT21G016	PT21G017
Batch Size	1000 Capsules	1000 Capsules
Manufacturing Date	07-2021	07-2021
Date of Initiation	12-07-2021	12-07-2021

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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

136.	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)
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 24-10-2018 and it is valid till 23-10-2021.
	Evidence of approval of manufacturing facility	The firm has provided Tablet general section as confirmed from GMP certificate.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1849: 14-01-2021
	Details of fee submitted	PKR 20,000/-: 22-12-2020,
	proposed proprietary name / brand name	Soglu 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Empagliflozin……10mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	SGLT2 Inhibitors
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	As per SRO
	Proposed unit price	14's
	The status in reference regulatory	Jardiance 10 mg film-coated tablets of Boehringer Ingelheim

	authorities	Pharma GmbH (USFDA Approved)
	For generic drugs (me-too status)	Emsyn 10mg tablets of M/s The Searle Company
	Name and address of API manufacturer.	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city, Lianing province -123000, 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, 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.
	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)	The firm has submitted stability study data of 6 months accelerated and 24 months real time data of 3 batches of API. The storage conditions of real time stability data are not as per Zone-IVA.
	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 and comparative dissolution profile of their developed formulation Soglu 10mg Tablet (B # ST20D014) with innovator product Jardiance 10mg Tablet (B # 805966) of M/s Boehinger Ingelheim 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. Since both formulations released more than 85% in 15min therefore there is no need to calculate f2 factor.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.
STABILITY STUDY DATA		
Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city, Lianing province -123000, China	

API Lot No.	E-20190920-D02-E06-01		
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)	
Soglu 10mg Tablet			
Batch No.	ST20D014	ST20D015	ST20D016
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	04-2020	04-2020	04-2020
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 (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 265th meeting decided to approve registration of D-Lanz 30mg capsule and D-Lanz 60mg capsule. **Inspection date:** 26th December, 2019. As per the report, the HPLC software was not 21 CFR compliant. Continuous monitoring and control was available for stability chambers.
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 Fuxin Long Rui Pharmaceutical Co, Ltd., China issued by Fuxin Food & Drug Administration, China. Certificate is valid till 27-9-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Empagliflozin (1.5 kg) attested by Assistant Director (I&E), DRAP, Islamabad dated 10-01-2020.
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 on testing reports of product 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.

The firm has submitted 6 months accelerated and 6 months real time stability study data for applied product.

Sr.#	Observations communicated	Response by the firm
1.	Justify dissolution limits i.e., NLT 80% in 30 min since innovator product (Jardiance) specifies NLT Q in 15 min. Clarification is required.	We have FDA specifications for dissolution limits which is revised as "Dissolution testing and acceptance criteria for immediate release solid oral dosage form drug products containing high solublity drug substances." These references provides dissolution limits NLT 80% in 30 min.
2.	The submitted copy GMP certificates of API manufacture is expired, you are	The firm has submitted copy of GMP certificate for M/s Fuxin long Rui Pharmaceutical Co., Ltd, Fluoride industrial

	required to submit updated copies of GMP certificates.	park, Fuxin city, Lianong province – 123000, china.

Previous Decision: Registration Board deferred the case for submission of stability study data of two batches with revised dissolution specifications as per decision of 293rd meeting of Registration Board (M-307).

Evaluation by PEC: The firm has submitted stability study data of 1 month with revised dissolution specifications NLT 80% in 15 min. The details of batches are as follows:

Batch No.	PT21G019	PT21G020
Batch Size	1500 Tablets	1500 Tablets
Manufacturing Date	07-2021	07-2021
Date of Initiation	14-07-2021	14-07-2021

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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

137.	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)
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 24-10-2018 and it is valid till 23-10-2021.
	Evidence of approval of manufacturing facility	The firm has provided Tablet general section as confirmed from GMP certificate.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 3929: 03-02-2021
	Details of fee submitted	PKR 20,000/-: 24-12-2020
	proposed proprietary name / brand name	Deglu 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Dapagliflozin as propanediol ……..10mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	SGLT2 Inhibitors
	Reference to Finished product specification	Innovator's specifications
	Proposed Pack size	As per SRO
	Proposed unit price	14's
	The status in reference regulatory authorities	Farxiga 10mg Tablets of AstraZeneca Pharmaceuticals Lp, Mount Vernon Indiana, USA (USFDA approved)

	For generic drugs (me-too status)	Xiga 10mg tablets by CCL Pharmaceuticals (Reg#090505)
	Name and address of API manufacturer.	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city, Lianing province -123000, 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, 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.
	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)	The firm has submitted stability study data of 6 months accelerated and 24 months real time data of 3 batches of API.
	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 and comparative dissolution profile of their developed formulation Deglu 10mg Tablet (B # ST20D023) with innovator product Forxiga 10mg Tablet (B # RB194) of M/s Astrazeneca Pharmaceuticals 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. Since both formulations released more than 85% in 15min therefore there is no need to calculate f2 factor.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA

Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city, Lianing province -123000, China.
API Lot No.	DG-20190327-D01-DG06-05
Description of Pack	Alu Alu Blister

(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)		
Deglu 10mg Tablet			
Batch No.	ST20D023	ST20D024	ST20D025
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	22-04-2020	22-04-2020	22-04-2020
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 (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 265th meeting decided to approve registration of D-Lanz 30mg capsule and D-Lanz 60mg capsule. **Inspection date:** 26th December, 2019. As per the report, the HPLC software was not 21 CFR compliant. Continuous monitoring and control was available for stability chambers.
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 Fuxin Long Rui Pharmaceutical Co, Ltd., China issued by Fuxin Food and Drug Administration, China. The certificate is valid till 23-08-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Dapagliflozin (1.5 kg) attested by Assistant Director (I&E), DRAP, Islamabad dated 10-01-2020.
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 on testing reports of product 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.

The firm has submitted 6 months accelerated and 6 months real time stability study data for applied product.

Sr.#	Observations communicated	Response by the firm
1.	Justify dissolution limits i.e., NLT 80% in 30 min since innovator product (Farxiga) specifies NLT Q in 15 min. Clarification is required.	The firm has not submitted stability study data as per 293rd meeting.
2.	The submitted copy GMP certificates of API manufacture is expired, you are required to submit updated copies of GMP certificates.	The firm has submitted copy of GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co, Ltd., China issued by Fuxin Food and Drug Administration, China. The certificate is valid till 23-08-2023.

3.	The storage conditions under which stability studies conducted were not as per Zone IV-A conditions.	The firm has submitted stability study data of drug substance with storage conditions as per Zone IV-A.

Previous Decision: Registration Board deferred the case for submission of stability study data of two batches with revised dissolution specifications as per decision of 293rd meeting of Registration Board (M-312).

Evaluation by PEC: The firm has submitted stability study data of 1 month with revised dissolution specifications NLT 80% in 15 min. The details of batches are as follows:

Batch No.	PT21G029	PT21G030
Batch Size	1500 Tablets	1500 Tablets
Manufacturing Date	07-2021	07-2021
Date of Initiation	11-08-2021	11-08-2021

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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

138.	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)
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 24-10-2018 and it is valid till 23-10-2021.
	Evidence of approval of manufacturing facility	The firm has provided Tablet general section as confirmed from GMP certificate.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5913: 23-02-2021
	Details of fee submitted	PKR 20,000/-: 24-12-2020
	proposed proprietary name / brand name	Deglu 5mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Dapagliflozin as propanediol……..5mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	SGLT2 Inhibitors
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	As per SRO
	Proposed unit price	14's
	The status in reference regulatory	Farxiga 5mg Tablets of AstraZeneca Pharmaceuticals Lp, Mount

	authorities	Vernon Indiana, USA (USFDA approved)
	For generic drugs (me-too status)	Xiga 5mg tablets by CCL Pharmaceuticals (Reg#090504)
	Name and address of API manufacturer.	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city, Lianing province -123000, 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, 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.
	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)	The firm has submitted stability study data of 6 months accelerated and 24 months real time data of 3 batches of API. The storage conditions of real time stability data are not as per Zone-IVA.
	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 and comparative dissolution profile of their developed formulation Deglu 5mg Tablet (B # ST20D020) with innovator product Forxiga 10mg Tablet (B # RE 415) of M/s Astrazeneca Pharmaceuticals 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. Since both formulations released more than 85% in 15min therefore there is no need to calculate f2 factor.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.
STABILITY STUDY DATA		
Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city,	

	Lianing province -123000, China		
API Lot No.	DG-20190327-D01-DG06-05		
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)9**		
Deglu 5mg Tablet			
Batch No.	ST20D020	ST20D021	ST20D022
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	22-04-2020	22-04-2020	22-04-2020
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 (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 265th meeting decided to approve registration of D-Lanz 30mg capsule and D-Lanz 60mg capsule. **Inspection date:** 26th December, 2019. As per the report, the HPLC software was not 21 CFR compliant. Continuous monitoring and control was available for stability chambers.
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 Fuxin Long Rui Pharmaceutical Co, Ltd., China issued by Fuxin Food and Drug Administration, China. The certificate is valid till 27-09-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Dapagliflozin (1.5 kg) attested by Assistant Director (I&E), DRAP, Islamabad dated 10-01-2020.
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 on testing reports of product 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.

The firm has submitted 6 months accelerated and 6 months real time stability study data for applied product.

Sr.#	Observations communicated	Response by the firm
1.	Justify dissolution limits i.e., NLT 80% in 30 min since innovator product (Farxiga) specifies NLT Q in 15 min. Clarification is required.	The firm has not submitted stability study data as per 293rd meeting.
2.	The submitted copy GMP certificates of API manufacture is expired, you are required to	The firm has submitted copy of GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co, Ltd., China

	submit updated copies of GMP certificates.	issued by Fuxin Food and Drug Administration, China. The certificate is valid till 23-08-2023.
3.	The storage conditions under which stability studies conducted were not as per Zone IV-A conditions.	The firm has submitted stability study data of drug substance with storage conditions as per Zone IV-A.

Previous Decision: Registration Board deferred the case for submission of stability study data of two batches with revised dissolution specifications as per decision of 293rd meeting of Registration Board (M-312).

Evaluation by PEC: The firm has submitted stability study data of 1 month with revised dissolution specifications NLT 80% in 15 min. The details of batches are as follows:

Batch No.	PT21G031	PT21G032
Batch Size	1500 Tablets	1500 Tablets
Manufacturing Date	07-2021	07-2021
Date of Initiation	11-08-2021	11-08-2021

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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

139.	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)
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 24-10-2018 and it is valid till 23-10-2021.
	Evidence of approval of manufacturing facility	The firm has provided Tablet general section as confirmed from GMP certificate.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 3928: 03-02-2021
	Details of fee submitted	PKR 20,000/-: 22-12-2020,
	proposed proprietary name / brand name	Soglu 25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Empagliflozin……25mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	SGLT2 Inhibitors
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	As per SRO

	Proposed unit price	14's
	The status in reference regulatory authorities	Jardiance 25 mg film-coated tablets of Boehringer Ingelheim Pharma GmbH (USFDA Approved)
	For generic drugs (me-too status)	Emsyn 25mg tablets of M/s The Searle Company
	Name and address of API manufacturer.	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city, Lianing province -123000, 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, 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.
	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)	The firm has submitted stability study data of 6 months accelerated and 24 months real time data of 3 batches of API.
	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 and comparative dissolution profile of their developed formulation Soglu 25mg Tablet (B # ST20D017) with innovator product Jardiance 25mg Tablet (B # 806902) of M/s Boehinger Ingelheim 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. Since both formulations released more than 85% in 15min therefore there is no need to calculate f2 factor.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.
STABILITY STUDY DATA		
Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical co. Ltd., Fluoride industrial park, Fuxin city,	

	Lianing province -123000, China		
API Lot No.	E-20190920-D02-E06-01		
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)		
Soglu 25mg Tablet			
Batch No.	ST20D017	ST20D018	ST20D019
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	04-2020	04-2020	04-2020
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 (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 265th meeting decided to approve registration of D-Lanz 30mg capsule and D-Lanz 60mg capsule. **Inspection date:** 26th December, 2019. As per the report, the HPLC software was not 21 CFR compliant. Continuous monitoring and control was available for stability chambers.
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 Fuxin Long Rui Pharmaceutical Co, Ltd., China issued by Fuxin Food and Drug Administration, China. The certificate is valid till 27-09-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the import of Empagliflozin (1.5 kg) attested by Assistant Director (I&E), DRAP, Islamabad dated 10-01-2020.
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 on testing reports of product 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.

The firm has submitted 6 months accelerated and 6 months real time stability study data for applied product.

Sr.#	Observations communicated	Response by the firm
1.	Justify dissolution limits i.e., NLT 80% in 30 min since innovator product (Jardiance) specifies NLT Q in 15 min. Clarification is	The firm has not submitted stability study data as per 293rd meeting.

	required.	
2.	The submitted copy GMP certificates of API manufacture is expired, you are required to submit updated copies of GMP certificates.	The firm has submitted copy of GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co, Ltd., China issued by Fuxin Food and Drug Administration, China. The certificate is valid till 27-09-2023.

Previous Decision: Registration Board deferred the case for submission of stability study data of two batches with revised dissolution specifications as per decision of 293rd meeting of Registration Board (M-312).

Evaluation by PEC: The firm has submitted stability study data of 1 month with revised dissolution specifications NLT 80% in 15 min. The details of batches are as follows:

Batch No.	PT21G027	PT21G028
Batch Size	1500 Tablets	1500 Tablets
Manufacturing Date	07-2021	07-2021
Date of Initiation	10-08-2021	11-08-2021

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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

140.	Name, address of Applicant / Marketing Authorization Holder	M/s Bosch Pharmaceuticals (Pvt.) Ltd., Bosch House 221, Sector 23, Korangi Industrial area, Karachi
	Name, address of Manufacturing site.	M/s Bosch Pharmaceuticals (Pvt.) Ltd., Bosch House 221, Sector 23, Korangi Industrial area, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted GMP certificate based on the inspection conducted dated 07-06-2018.
	Evidence of approval of manufacturing facility	The firm has provided Tablet (General) section confirmed from submitted copy of renewal of DML issued by licensing vide letter No. F. 2-4/91-Lic (Vol-V).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22157 : 28-10-2019
	Details of fee submitted	PKR 20,000/-: 28-10-2019
	proposed proprietary name / brand name	BALIQUIS 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	Immediate release Film coated tablet
	Pharmacotherapeutic Group of (API)	Anticoagulant (B01AF02)
	Reference to Finished product specification	Innovators specifications

	Proposed Pack size	3 x10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ELIQUIS 5mg film coated tablets by Bristol Meyers Squibb **(USFDA** Approved)
	For generic drugs (me-too status)	APIXA Tablet 5mg of M/s CCL Pharma
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi 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. 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:	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 25^{o}C/60%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 results of comparative dissolution profile of their Batch No. TR-BAL-02 with the innovator product i.e. Eliquis Tablet 5mg (Batch # AJ9214) of M/s Bristol Myers Squibb. Firm has performed CDP in 0.1 N HCl, acetate buffer and phosphate buffer. The results of drug release were greater than 85% in 15 minutes in all medium therefore the firm did not calculate similarity factor f_2 values.
	Analytical method validation/verification of product	Firm has submitted protocols and reports of validation studies of analytical method.
STABILITY STUDY DATA		
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province, China	

API Lot No.	YF20190409		
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)		
Products applied	Batch No.	Batch size	Manufacturing date
BALIQUIS 5MG TABLET	TR-BAL-02 TR-BAL-03 TR-BAL-04	2000 Tablets	08-2019

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

#	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.	The firm has submitted copy of GMP Certificate (Certificate#JX20150013) for M/s Jiangxi Synergy Pharmaceutical Co., Ltd., China issued by Jiangxi Food and Drug Administration, China. It is valid till 17-09-2020.
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.	Firm has submitted copy of invoice specifying import of 0.10Kg of APIXABAN. The invoice is attested by AD (I&E) DRAP Karachi office dated 15-07-2019.
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

REMARKS OF EVALUATOR-XIV

Dissolution conditions of innovator as per Biopharmaceutics Review:
Apparatus: USP II
Spindle rotation: 75 rpm
Medium volume: 900ml
Temperature: 37ºC
Medium: pH 6.8 phosphate buffer, 0.05% SLS
Acceptance criteria: NLT Q at 30 min

Sr.#	Observations communicated	Response by the firm
1.	Quality Overall Summary (QOS) needs to be submitted as per WHO QOS-PD template by filling the template without any modification.	The firm has provided QOS as per WHO QOS-PD template.
2.	Evidence of import of API including copy of commercial invoice cleared by DRAP field office.	Firm has submitted copy of invoice specifying import of 0.10Kg of APIXABAN. The invoice is attested by AD (I&E) DRAP Karachi office

		dated 15-07-2019.
3.	Provide certificate of analysis of each batch of API used in the stability studies of the three submitted batches.	Submitted
4.	Summary of batch analyses release results of the drug product manufacturer for relevant batch needs to be submitted as per 2.3.S.4.4 (b).	Submitted.
5.	Provide data of pharmaceutical equivalence against innovator product including data of comparative dissolution profile to justify your formulation development as per the requirement of section 3.2.P.2.2.1.	The firm has provided data of CDP for Baliquis 5mg Tablet only however pharmaceutical equivalence is required to be conducted for both strengths.
6.	Justify the dissolution specification NLT 80% (Q) after 45 minutes, since the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT (Q) in 30 minutes.	The firm has revised the dissolution specifications and submitted commitment to perform dissolution test as per innovator in commercial batches.

Previous Decision: Deferred for submission of pharmaceutical equivalence data of the applied product with innovator / reference / comparator product (M-297).
Evaluation by PEC: The firm has submitted pharmaceutical equivalence data with the innovator product Eliquis 5mg Tablet (Batch # AJ9214) of M/s Bristol Myers Squibb.

Decision: Approved with innovator 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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

141.	Name, address of Applicant / Marketing Authorization Holder	M/s Bosch Pharmaceuticals (Pvt.) Ltd., Bosch House 221, Sector 23, Korangi Industrial area, Karachi
	Name, address of Manufacturing site.	M/s Bosch Pharmaceuticals (Pvt.) Ltd., Bosch House 221, Sector 23, Korangi Industrial area, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	Firm has submitted GMP certificate based on the inspection conducted dated 07-06-2018.
	Evidence of approval of manufacturing facility	The firm has provided Tablet (General) section confirmed from submitted copy of renewal of DML issued by licensing vide letter No. F. 2-4/91-Lic (Vol-V).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.22156: 28-10-2019
	Details of fee submitted	PKR 20,000/-: 28-10-2019
	proposed proprietary name / brand name	BALIQUIS 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	Immediate release Film coated tablet
	Pharmacotherapeutic Group of (API)	Anticoagulant (B01AF02)
	Reference to Finished product specification	Innovators specifications
	Proposed Pack size	3 x10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ELIQUIS 2.5mg film coated tablets by Bristol Meyers Squibb **(USFDA** Approved)
	For generic drugs (me-too status)	APIXA Tablet 2.5mg of M/s CCL Pharma
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi 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. 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:	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 25ºC/60%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 results of comparative dissolution profile of their Batch No. TR-BAL-02 with the innovator product i.e. Eliquis Tablet 5mg (AJ9214). Firm has performed CDP in 0.1 N HCl, acetate buffer and phosphate buffer. The results of drug release were greater than 85% in 15 minutes in all medium therefore the firm did not calculate similarity factor *f*2 values.
	Analytical method validation/verification of product	Firm has submitted protocols and reports of validation studies of analytical method.

STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province, China		
API Lot No.	YF20190409		
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)		
Product applied	Batch No.	Batch size	Manufacturing date
BALIQUIS 2.5MG TABLET	TR-BAL-05 TR-BAL-06 TR-BAL-07	4000 Tablets	08-2019

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

#	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.	The firm has submitted copy of GMP Certificate (Certificate#JX20150013) for M/s Jiangxi Synergy Pharmaceutical Co., Ltd., China issued by Jiangxi Food and Drug Administration, China. It is valid till 17-09-2020.
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.	Firm has submitted copy of invoice specifying import of 0.10Kg of APIXABAN. The invoice is attested by AD (I&E) DRAP Karachi office dated 15-07-2019.
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

REMARKS OF EVALUATOR

Dissolution conditions of innovator as per Biopharmaceutics Review:
Apparatus: USP II
Spindle rotation: 75 rpm
Medium volume: 900ml
Temperature: 37ºC
Medium: pH 6.8 phosphate buffer, 0.05% SLS
Acceptance criteria: NLT Q at 30 min

Sr.#	Observations communicated	Response by the firm

1.	Quality Overall Summary (QOS) needs to be submitted as per WHO QOS-PD template by filling the template without any modification.	The firm has provided QOS as per WHO QOS-PD template.
2.	Evidence of import of API including copy of commercial invoice cleared by DRAP field office.	Firm has submitted copy of invoice specifying import of 0.10Kg of APIXABAN. The invoice is attested by AD (I&E) DRAP Karachi office dated 15-07-2019.
3.	Provide certificate of analysis of each batch of API used in the stability studies of the three submitted batches.	Submitted
4.	Summary of batch analyses release results of the drug product manufacturer for relevant batch needs to be submitted as per 2.3.S.4.4 (b).	Submitted.
5.	Provide data of pharmaceutical equivalence against innovator product including data of comparative dissolution profile to justify your formulation development as per the requirement of section 3.2.P.2.2.1.	The firm has provided data of CDP for Baliquis 5mg Tablet only however pharmaceutical equivalence is required to be conducted for both strengths.
6.	Justify the dissolution specification NLT 80% (Q) after 45 minutes, since the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT (Q) in 30 minutes.	The firm has revised the dissolution specifications and submitted commitment to perform dissolution test as per innovator in commercial batches.

Previous Decision: Deferred for following submissions (M-297):

- Pharmaceutical equivalence data of the applied product with innovator / reference / comparator product
- Comparative Dissolution Profile (CDP) data of the applied product along innovator / reference / comparator product.

Evaluation by PEC: The firm has submitted pharmaceutical equivalence and comparative dissolution data of Baliquis 2.5mg Tablet (Batch # TR-BAL-05) with innovator product Eliquis 2.5mg Tablet (Batch # AJ9209) of M/s Bristol Myers Squib, UK.

Decision: Approved with innovator 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 shall be issued after submission of applicable fee for revision of specifications in Form-5F as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

Case No. 08 Registration applications of import human drugs submitted on CTD format

a. Deferred Cases

142.	Name, address of Applicant / Importer	M/s AJM Pharma (Pvt) Ltd., 1st floor, shafi court, Merewether road, Civil lines, Karachi.
	Details of Drug Sale License of importer	License No: 1015 Address: 1st floor, shafi court, Merewether road, Civil lines, Karachi. Validity: 18-06-2021 Status: License to sell drugs by way wholesale
	Name and address of marketing authorization holder (abroad)	M/s Samyang Biopharmaceuticals Corporation, 79 Sinildong-ro, Daedeok-gu, Daejeon, Republic of Korea.
	Name, address of manufacturer(s)	M/s Samyang Biopharmaceuticals Corporation, 79 Sinildong-ro, Daedeok-gu, Daejeon, Republic of Korea.

	Name of exporting country	Republic of Korea
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**COPP:** The firm has submitted legalized copy of COPP for Protezomib Injection issued on 29-10-2019 by Ministry of Food and Drug safety, Daejeon regional office of Food and drug safety, 166, Cheongsa-ro, Seo-gu, Daejeon, Korea which confirms free sale status of applied formulation in exporting country. **GMP certificate:** The firm has submitted original, legalized GMP certificate (No. 2019-G1-2029) dated 29-10-2019 issued by Ministry of Food and Drug safety, Daejeon regional office of Food and drug safety, 166, Cheongsa-ro, Seo-gu, Daejeon, Korea.
	Details of letter of authorization / sole agency agreement	Firm has submitted notarized copy of letter of authorization from Samyang Biopharmaceuticals corporation, 79 Sinildong-ro, Daedeok-gu, Daejeon, Republic of Korea. The letter specifies that Samyang Biopharmaceuticals corporation authorize M/s AJM Pharma (pvt) Ltd, Karachi for Bortezomib Inj. 3.5mg as their local agents to be responsible for importation and distribution in the territory of Pakistan. The authorization letter was issued on 27 December 2019 and is valid for 5 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 ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 15178: 29-06-2020
	Details of fee submitted	PKR 100,000/-: 16-04-2020
	proposed proprietary name / brand name	PROTEZOMIB Injection 3.5mg /vial
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Bortezomib trimer 3.3mg (as Bortezomib 3.5mg)
	Pharmaceutical form of applied drug	Lyophilized powder for solution for injection (Subcutaneous, Intravenous)
	Pharmacotherapeutic Group of (API)	Other antineoplastic agents (L01XX32**)**
	Finished product specifications	In-house specifications
	Proposed Pack size	1 vial, Type 1 clear glass vial
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	VELCADE for injection 3.5mg per vial of Millenium pharms (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. 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 Samyang Biopharmaceuticals Corporation, 79 Sinildong-ro, Daedeok-gu, Daejeon, 306-230, Korea
	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 long term storage conditions (-20ºC) and stability data of 1 batch of API at short term storage conditions (5±3ºC) for 6 months. The stability study of long-term 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	Firm has submitted pharmaceutical equivalence of test formulation (BZ1V1401) with comparator product (DLB0000) summarizing results of all quality tests of both formulations. However, details of comparator product are 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	PROTEZOMIB solution for injection will be filled into Type I glass vials. The vials are closed with rubber stoppers and capped with aluminium
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches at following conditions: • 40ºC ±2ºC / 75%± 5% RH for 6 months • 25ºC ±2ºC / 60% ± 5% RH for 36 months • 30ºC ±2ºC / 75% ± 5% RH for 6 months

Remarks of Evaluator

Sr.#	Shortcomings	Response by the Firm
1.	Submit data in section 3.2.P.2.6 as per the decision of 293rd meeting of Registration Board which states that "Compatibility studies for the dry powder for injections and dry powder for suspension should be performed as per the instructions provided in individual label of the drug product."	The firm has submitted report for in use stability test of Bortezomib inj. 3.5mg. In this study, Protezomib injection samples were reconstituted to prepare 1mg / ml for intravenous administration and 2.5 mg / ml for subcutaneous administration and such sample solutions were stored at 25 ºC and tested for appearance, assay and related compounds.
2.	Submit details of comparator product (including manufacturer name, reference	VELCADE (Bortezomib) is co-developed by Takeda and Janssen Pharmaceutical companies. The

	country in which product is approved) with which pharmaceutical equivalence has been conducted.	manufacturer is Janssen Korea. Reference countries where product approved is US, EU and South korea.
3.	Justify acceptance criteria of 95%-105% for the accuracy parameter in analytical method validation of assay test under section 3.2.P.5.3.5.	The firm has submitted that this parameter is assessed by adding known amount of bortezomib into placebo and determining the recovery rate. 80~120% of bortezomib (based on the amount of bortezomib contained in the drug product) is added and recovery rates are determined.
4.	Justify submission of stability study data of long-term storage conditions for 6 months only. It is important to submit stability data as per claimed shelf life.	Now the firm has submitted stability data of 24 months as per Zone IVb i.e., 30ºC ± 2ºC, 75% ± 5%RH.

Previous Decision: Registration Board deferred the case for justification of acceptance criteria for the accuracy parameter in analytical method validation since ICH guidelines recommend acceptance criteria of ± 2% **(M-297).**
Evaluation by PEC: The firm has submitted that our test method validation acceptance criteria have been properly established based in accordance with AOAC guidelines. It is based on the concentration used in the corresponding analysis. In our test method validation, the concentration of the sample solution used for precision and accuracy is 1,000 ppm = 0.1 %, which is the default concentration for precision and accuracy in AOAC guideline. AOAC set the limit as ≤ 3.7% RSD and 95 -105% recovery, respectively, corresponding to 0.1% sample concentration.

Discussion: Registration Board deliberated on the matter and discussed that the AOAC guidelines referred by the firm are for dietary supplements and botanicals and therefore the recommendations of these guidelines cannot be applied on the pharmaceutical products.

Previous Decision: Deferred for justification in the light of ICH guidelines which recommend acceptance criteria of RSD ± 2% for accuracy parameter of analytical method validation (M-307).
Evaluation by PEC: The firm has submitted that we, Samyang Biopharmaceuticals Corporation, do hereby declare that the limit 95% to 105% pertains to assay value which is not related with % RSD. Our RSD value for accuracy parameter was ± 2% which is as per ICH guidelines. Our results of RSD of accuracy parameter are also within the range.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

Agenda of Evaluator PEC-IV

Case no. 01 Registration applications for local manufacturing of (Human) drugs

a. New cases(Form- 5F)

143.	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. 7854 dated 10/03/2021
	Details of fee submitted	PKR 20,000/-: dated 26/02/2021
	proposed proprietary name / brand name	BEGRON ER 25mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended release film coated tablet contains: Mirabegron MS…25mg Innovator's Specs
	Pharmaceutical form of applied drug	Brown colour, round shaped, film coated tablet, plain from both sides
	Pharmacotherapeutic Group of (API)	Urinary frequency and incontinence
	Reference to Finished product specification	Innovator's Specifications
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Betmiga 25 mg prolonged-release tablets Mfr. by M/s. Astellas Pharma Ltd EMA approved
	For generic drugs (me-too status)	MIBEGA Mfr. By Getz (Reg # 089375)
	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.	Jinagxi Synergy Pharmaceutical Co., Ltd Jiangxi Fengxin Industrial Park, Jiangxi Province,330700,China
	Module-II (Quality Overall Summary)	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. 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.
	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 substances.
	Stability studies	Firm has submitted 6 months accelerated and 36 months real time stability data of 3 batches of API as per Zone IV b
	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 have been established against the brand leader that is Betmiga 25mg Tablets by M/s. Astellas Pharma Ltd by performing quality tests CDP has been performed against the same brand that is Betmiga 25mg Tablets by M/s. Astellas Pharma Ltd., in Acid media (pH 1.2), Phosphate Buffer (pH 6.8) & acetate buffer (pH 4.5). 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, robustness, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Jinagxi Synergy Pharmaceutical Co., Ltd Jiangxi Fengxin Industrial Park, Jiangxi Province,330700,China		
API Lot No.	20190101V		
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, 1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	04-2020	04-2020	04-2020
Date of Initiation	07-05-2020	07-05-2020	07-05-2020
No. of Batches	03		
Administrative Portion			

7.	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 "EMPOLI (Empagliflozin) 10mg & 25mg Tablets" which was presented in 290th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 13th June, 2019. 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
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by Jiangxi Fengxin Market and Quality Supervision Administration , valid till 23/08/2022
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying import of 2kg of Mirabegron (Batch # 20190101V). (invoice # JXS190438) attested by AD (I&E), Karachi dated 29-05-2019
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 complete record of testing of all 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	Firm has submitted audit trail record of product testing of HPLC for all test intervals.
12.	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.	1.5.15 – 1.5.20	Commitments are not signed	Signed commitments submitted
2.	1.6.5	Name of API Paracetamol, is mentioned . Clarification is required	It was a typographical mistake. Revised document attached
3.	3.2.P.2.1	Compatibility studies of the Drug Substance(s) with excipients shall be provided if the qualitative composition of the formulation is not similar to innovator / reference product as Sentry Polyox WSR N60K-LEO NF Grade and Silicon Dioxide are not included in Innovator product	Development of Mirabegron ER 25mg tablet was done as per reference listed drug (RLD) i.e. Betmiga 25mg PR tablet. Literature data of RLD product is enclosed for ready reference (Anex I, Page No. 14). The literate data of RLD shows that it contains polyethylene oxide in its formulation as release modifier. Polyethylene oxide is generic name and the brand name available for commercial use is Sentry Polyox WSR N60K-LEO NF of M/S. DOW/Colorcon Limited UK. We have used the same brand in our formulation. As far as the use of silicon dioxide in our formulation is concerned, the MSDS and COA of Sentry Polyox WSR N60K-LEO NF shows that it contains silicon dioxide as an ingredient (MSDS and COA of the manufacture is enclosed – Anex-II). As silicon dioxide is an ingredient used in Sentry Polyox WSR N60K-LEO NF, therefore compatibility of this formulation was not performed. Moreover the initial and six months stability results shows that the formulation is stable and the raw materials are found compatible

4.	3.2.P.2.1.2	• Firm claimed that excipients were selected for the development of Begron ER as used by innovator product, but excipients are different. Clarify . • Describe the Role of Sentry Polyox WSR N60K-LEO NF Grade	• Development of Mirabegron ER 25mg tablet was done as per reference listed drug (RLD) i.e. Betmiga 25mg PR tablet. Literature data of RLD product is enclosed for ready reference (Anex I, Page No. 14). The literate data of RLD shows that it contains polyethylene oxide in its formulation as release modifier. Polyethylene oxide is generic name and there are different commercial brand with different grades available for polyethylene oxide, however, based on available information of the RLD product, we have used Sentry Polyox WSR N60K-LEO NF grade of M/S. DOW/Colorcon Limited UK. As far as the use of silicon dioxide in our formulation is concerned, the MSDS and COA of Sentry Polyox WSR N60K-LEO NF shows that it contains silicon dioxide as an ingredient (MSDS and COA of the manufacture is enclosed – Anex - II). As silicon dioxide is an ingredient used in Sentry Polyox WSR N60K-LEO NF, therefore we have also used silicon dioxide in our formulation to improve flowability of our granules as the same is also part of Sentry Polyox WSR N60K-LEO NF. • Sentry Polyox WSR N60K-LEO NF Grade is a non-ionic, water-soluble polymer composed of Silicon Dioxide and Polyethylene oxide. It has a molecular weight of 2,000,000. Sentry Polyox WSR N60K-LEO NF is used as dissolution modifier. Polyethylene oxide (PEO) has been extensively studied as a matrix-forming polymer. POLYOX Water-Soluble Resins NF have a long history of successful applications in pharmaceutical products, in uses such as controlled release solid dose matrix systems, tablet binding, transdermal drug delivery systems, and mucosal bio-adhesives. POLYOX Water-Soluble Resins NF are very versatile polymers for controlled release applications. Upon exposure to water or gastric juices, they hydrate and swell rapidly to form hydrogels with properties ideally suited for controlled drug-delivery vehicles. Because POLYOX Water-Soluble Resins NF are nonionic, no interaction between drug and polymers is to be expected
5.	3.2.P.2.2.1	• As per relevant guidelines & structure of Form 5F, Pharmaceutical equivalence has to be performed at the time of formulation development, while according to your submitted data, Pharmaceutical equivalence have been performed after commencing stability studies. Justification shall be submitted. • In Pharmaceutical equivalence in innovator Pfizer is	1. We developed our product on the basis of parameters mentioned in FDA Chemistry review. After complying with these parameters, we kept the batches on stability studies and simultaneously performed the pharmaceutical equivalence with innovator. 2. Pharmaceutical equivalence is performed against Betmiga Tablet of Astellas Pharma. Pfizer was mistakenly written due to typographical error. Revised report after correction is attached. 3. Comparative Dissolution Profile is

		mentioned while claimed Innovator is Astellas Pharma • Justify time points for Comparative dissolution in reference to relevant guidelines.	performed according to the timelines mentioned in FDA Chemistry review. However this is our routine practice to perform the dissolution profile at different time points at development stage. However, at your suggestion, we have also performed the CDP at variable time points against DRAP approved product and found similar. Data attached
6.	3.2.P.5.3	As per relevant guidelines & structure of Form 5F Analytical test method validation has to be performed at the time of formulation development, while according to your submitted data, Analytical test method verification has been performed after commencement of stability studies 11-05-2020 while stability studies started on 07-05-2020. Justification shall be submitted in this regard.	This is our routine practice that after method development, we perform Pre-AMV studies in which accuracy at 100% concentration is checked (Pre-AMV report is attached). However, complete method validation studies were performed on 15-05-2020, before the testing of first month stability time point and analytical method qualified all parameters

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 letter will be issued after submission of applicable fee**

144.	Name, address of Applicant / Marketing Authorization Holder	M/s Indus Pharma (Pvt.) Ltd Plot No. 26-27 & 63/67, Sector 27, Korangi Industrial Area, Karachi-74900.
	Name, address of Manufacturing site.	M/s Indus Pharma (Pvt.) Ltd Plot No. 26-27 & 63/67, Sector 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.12551 dated 28/04/2021
	Details of fee submitted	PKR 20,000/-: dated 28/4/2021
	proposed proprietary name / brand name	Symol Plus Tablets 37.5mg + 325mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tramadol HCl……37.5mg Paracetamol……325mg
	Pharmaceutical form of applied drug	Blue color, oval shaped, biconvex, film coated tablet, one side is plain and bisect line on other side.
	Pharmacotherapeutic Group of (API)	Opioid Analgesic with combination of Aniline Analgesic
	Reference to Finished product specifications	USP

	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ULTRACET Tablets 37.5mg + 325mg by JANSSEN PHARMACEUTICALS INC, USFDA Approved.
	For generic drugs (me-too status)	Tonoflex-P Tablets 37.5mg + 325mg by SAMI Pharmaceuticals (Pvt.) Ltd., Reg. No. 067163
	GMP status of the Finished product manufacturer	Certificate of cGMP of dated: 18-12-2020 on the basis of evaluation conducted on 28-11-2019
	Name and address of API manufacturer.	**Tramadol HCl:** SUPRIYA LIFESCIENCE LTD. Address: A -5/ 2, LOTE PARSHURAM INDUSTRAIL AREA, MIDC, KHED - 415722 , Dist – RATNAGIRI. **Paracetamol:** PHARMAGEN LIMITED. Address: KOT NABI BUKSHWALA, 34-KM, FEROZEPUR ROAD, LAHORE – PAKISTAN.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template
	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: **Tramadol HCl:** Real time: 30˚C ± 2˚C / 75% ± 5%RH for 60 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months **Paracetamol:** 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):	Firm has submitted relevant information against the Module III, including, "Process validation protocol, Finished product analytical method validation report & stability studies data
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Comparator product Tonoflex-P Tablets 37.5mg + 325mg by SAMI Pharmaceuticals (Pvt.) Ltd. by performing quality tests. CDP has been performed against the same brand that is Tonoflex-P Tablets 37.5mg + 325mg by SAMI Pharmaceuticals (Pvt.) Ltd. in HCl Buffer (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	**Tramadol HCl:** SUPRIYA LIFESCIENCE LTD. **Paracetamol:** PHARMAGEN LIMITED.
API Lot No.	**Tramadol HCl:** SLL/TDM/0619018 **Paracetamol:** 00510911/103/2019
Description of Pack (Container closure system)	Alu. Alu. Blister strips of 2x5 Tablets packed in a final printed 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.	TR-1/ SYML TAB	TR-2/ SYML TAB	TR-3/ SYML TAB
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	12-2019	12-2019	12-2019
Date of Initiation	26-12-2019	26-12-2019	26-12-2019
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 previous inspection report of "Canazin tablets (Canagliflozin)", which was presented in 289th meeting of Registration Board. Registration Board approved the application of Canazin tablets and wherein HPLC system was declared as 21 CFR compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Tramadol HCl:** Firm has submitted copy of GMP certificate (Certificate# NEW-WHO-GMP/CERT/KD/67649/2018/11/25185) in the name of M/s SUPRIYA LIFESCIENCE LTD, India, valid up to 04/10/2021 issued by FDA Maharashtra, India. **Paracetamol:** Firm has submitted copy of GMP certificate (Certificate# 06/2019-DRAP (AD/607409-530) in the name of M/s PHARMAGEB LIMITED, Pakistan, valid up to 08/01/2022 issued by DRAP.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Tramadol HCl:** Firm has submitted copy of invoice (Invoice# SLL/E/19-20/416), in the name of M/s Indus Pharma (Pvt.) Ltd. specifying the quantity of 25Kg of Tramadol HCl from M/s SUPRIYA LIFESCIENCE LTD, India. attested by AD(Karachi) dated ; 24-07-2019 **Paracetamol:** Firm has submitted copy of FOC invoice (Invoice# 2058), in the name of M/s Indus Pharma (Pvt.) Ltd. specifying the quantity of 03 Kg of Paracetamol M/s PHARMAGEB LIMITED, Pakistan.
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.	Module II	Drug Product part of QOS not submitted.	Submitted

2.	3.2.P.4.3	Analytical Method Verification studies performed by the Drug Product manufacturer of drug substance(s)after commencement of stability studies. Justification shall be submitted.	Kindly note that the finished product specifications of our applied product is pharmacopeial (present in USP). Therefore, the specification of the product was developed based on the USP monograph and the Analytical Method Verification was commenced afterwards.
3.	3.2.P.2.2.1	As per relevant guidelines & structure of Form 5F, Pharmaceutical equivalence has to be performed at the time of formulation development, while according to your submitted data, Pharmaceutical equivalence have been performed after commencing stability studies. Justification shall be submitted.	Kindly note that the testing results are included in the Product Development Report and as the product is in development phase until the satisfactory accelerated results achieved, hence Pharmaceutical Equivalence was conducted after satisfactory studies
4.	3.2.P.4.5	Excipients of Human or Animal Origin shall be addressed for the use of "Magnesium stearate" in the applied formulation	Magnesium stearate is of vegetable source and free from BSE/TSE.

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.**

145.	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
	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 specification	USP
	Proposed Pack size	1's (5ml)
	Proposed unit price	As per SRO

	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, 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: 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 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)	Firm has referred to their previous inspection report of "Sofonil 400mg Tablet (Sofosbuvir)", which was presented in 268th meeting of Registration Board. Registration Board approved the application of Sofonil 400mg Tablet and wherein HPLC system was declared as 21 CFR compliant.		
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.	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 (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 /	Owing to the prevailed condition of covid throughout the world We had performed PE after formulation development due to

		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.	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: 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.**

146.	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. 7448 dated 08/03/2021
	Details of fee submitted	PKR 50,000/-: dated 01/02/2021
	proposed proprietary name / brand name	TEDIZ 200mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tedizolid Phosphate MS …….200mg Innovator's Specs.
	Pharmaceutical form of applied drug	Yellow color, capsular shaped, film coated tablet, with SAMI engraved on one side and plain on the other side
	Pharmacotherapeutic Group of (API)	Antibacterial for systemic use, other antibacterial
	Reference to Finished product specification	Innovator's Specifications
	Proposed Pack size	6's, 10's, 12's & 20's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	SIVEXTRO 200mg film-coated tablets Mfr. By M/s Merck Sharp & Dohme B.V
	For generic drugs (me-too status)	NA
	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.	Chongqing Kangle Pharmaceutical Co., Ltd. Address: No. 4 Huazhong Road, Chongqing (Changshou) Chemical Industries Park, Chongqing, China 401221
	Module-II (Quality Overall Summary)	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. 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.
	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 substances.
	Stability studies	Firm has submitted 6 months accelerated and 24 months real time stability data of 3 batches of API as per Zone IVA
	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 not performed Pharmaceutical equivalence and comparative dissolution profile.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision, robustness, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Chongqing Kangle Pharmaceutical Co., Ltd. Address: No. 4 Huazhong Road, Chongqing (Changshou) Chemical Industries Park, Chongqing, China 401221
API Lot No.	ASC003-OR-191201
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, 1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	1000 Tablets	1000 Tablets	1000 Tablets
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	28-03-2020	28-03-2020	28-03-2020
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 "EMPOLI (Empagliflozin) 10mg & 25mg Tablets" which was presented in 290th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 13th June, 2019. 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. CQ20190054 issued by China food and Drugs Administration valid till 25/11/2024
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying import of 1000gm of Tedizolid Phospahte (Batch # ASC003-OR-191201). (invoice # ASC-SAMI19121101) attested by AD (I&E), Karachi dated 20-01-2020
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:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.15 – 1.5.20	Commitments are not signed	Signed commitments attached
2.	3.2.S.4	In COA's residual solvents test limits of Acetone is greater of Drug product manufacturer than Drug substance manufacturer. Clarification is required.	The limit of Acetone is same in both COA's of API provided by DP manufacturer and DS manufacturer (NMT 0.5%).
3.	3.2.P.2.2.1	Pharmaceutical equivalence is not performed	Pharmaceutical Equivalence against the innovator product cannot be performed due to its unavailability in Pakistan. Although, we have considered and ensured the following parameters which gives the confidence that in-

			vitro parameter of our product is comparable with the innovator; 1) Formulation of our product is qualitatively similar to that of innovator. 2) Dissolution method adopted as per FDA review of innovator product and also set the tighter acceptance criteria of NLT 80% (Q) in 20 minutes.
Decision: Deferred for Performance of Pharmaceutical Equivalence and CDP by Drug product manufacturer.			

b. Deferred cases

147.	Name and address of manufacturer / Applicant	M/s Welwink Pharmaceuticals. Factory G.T. Road, Industrial Estate, Gujranwala Cantt.
	Brand Name +Dosage Form + Strength	Antrosit 60mg Injection
	Composition	Each Vial Contains: Artesunate……60mg
	Diary No. Date of R& I & fee	Dy.No. 33692 dated 10-10-2018 Rs.20,000/- Dated 10-10-2018
	Pharmacological Group	Antimalarial
	Type of Form	Form- 5
	Finished product Specification	IP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	WHO recommended formulation
	Me-too status	Misonate 60mg Injection by M/s Tabros Pharma (Reg#057719)
	GMP status	Keeping in view the panel inspection of your firm dated 25-02-2020 and clarification mentioned above, It is advised to not to resume production activities in Liquid Injectable Section till submission of compliance report, verification by panel and subsequent approval from competent authority as panel did not recommend the Liquid Injectable Section
	Remarks of the Evaluator	• Firm applied as USP specifications but monograph not available in USP monograph. • Firm revise master formulation without overage
	Previous decision(s) **(M-312)**	**Deferred for following reasons:** Registration board deferred the case for updated GMP status of firm.
	Evaluation by PEC	Firm submitted cGMP certificate on the basis of evaluation conducted on 25-02-2020
	Decision: Registration board deferred the case for updated GMP status of firm for injectable section	
148.	Name and address of manufacturer / Applicant	M/s Welwink Pharmaceuticals. Factory G.T. Road, Industrial Estate, Gujranwala Cantt.
	Brand Name +Dosage Form + Strength	Antrosit 120mg Injection
	Composition	Each Vial Contains: Artesunate…….120mg
	Diary No. Date of R& I & fee	Dy.No. 33693 dated 10-10-2018 Rs.20,000/- Dated 10-10-2018
	Pharmacological Group	Antimalarial
	Type of Form	Form- 5
	Finished product Specification	IP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	WHO recommended formulation
	Me-too status	Gen-M Injection of M/s Genix Pharma
	GMP status	Keeping in view the panel inspection of your firm dated 25-02-2020 and clarification mentioned above, It is advised to not to resume production activities in Liquid Injectable Section till

		submission of compliance report, verification by panel and subsequent approval from competent authority as panel did not recommend the Liquid Injectable Section
	Remarks of the Evaluator	• Firm applied as USP specifications but monograph not available in USP monograph. • Firm revise master formulation without overage
	Previous decision(s)	**Deferred for following reasons:** Registration board deferred the case for updated GMP status of firm.**(M-312)**
	Evaluation by PEC	Firm submitted cGMP certificate on the basis of evaluation conducted on 25-02-2020
	Decision: Registration board deferred the case for updated GMP status of firm for injectable section	
149.	Name and address of manufacturer / Applicant	M/s. Wenovo Pharmaceuticals, Rawalpindi
	Brand Name +Dosage Form + Strength	Pantowen 40mg capsule
	Composition	Each capsule contains: Panntoprazole enteric coated pellets eq. to Pantoprazole…..40mg
	Diary No. Date of R& I & fee	DY.No 220, 17-1-2014, Rs 20,000/-
	Pharmacological Group	Proton Pump Inhibitor
	Type of Form	Form- 5
	Finished product Specification	Mfg
	Pack size & Demanded Price	2*7‘s Alu Alu blister pack, As per MOH
	Approval status of product in Reference Regulatory Authorities	A-Pan , India
	Me-too status	Pantozole by Valour Pharma
	GMP status	Last Inspection Report 11-1-2017, the firm is complying GMP as of today.
	Remarks of the Evaluator	Pellets are obtained from Vision Pharma, Isb □□GMP of Vision Pharma is valid upto 21-2-2018 □□Stability studies of pellets are provided. □□International availability cannot be confirmed □□Rs 20,000 fee challan is not in original. □□Firm has claimed Mfg Specifications and the product is not present in available pharmacopoeia (USP39, BP2016)) while following documents have not been provided as per decision of Registration Board taken by it in its 267th meeting; 1. Product and formulation development data 2. Manufacturing method development and process validation 3. Analytical method development and validation Minutes for 270th Registration Board Meeting 65 (accuracy, precision, specificity, linearity, ruggedness and robustness) against analytical method and innovator‘s product 4. Comparative pharmaceutical equivalence against innovator‘s product including comparative dissolution profiling and preferably bio-equivalence 5. Stability study data of the product for accelerated and real time period against innovator‘s product as a reference
	Previous decision(s)	**Deferred for following reasons:** Deferred for evidence of approval in Reference Regulatory Authorities and verification of fee challans Rs.20,000/-(**M-270)**
	Evaluation by PEC Firm now change formulation from capsule to tablet without submission of fee.	
	Brand Name +Dosage Form + Strength	Pentop 40mg Tablet
	Composition	Each Enteric Coated Tablet contains:

		Pantoprazole sodium Sesquihydrate eq. to Pantoprazole…..40mg
	Diary No. Date of R& I & fee	DY.No 28424, 15-10-2021,
	Pharmacological Group	Proton Pump Inhibitor
	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	PROTONIX tablet of USFDA approved
	Me-too status	Amipro Tablets by Pharmatec
	GMP status	Last Inspection Report of 30-09-2018 & 29-10-2018, and the report concludes that the firm is compliant to GMP.
	Decision: Approved with innovator's specification as following **Each Enteric Coated Tablet contains:** **Pantoprazole sodium Sesquihydrate eq. to Pantoprazole…..40mg** **Registration letter will be issued after submission of applicable fee.**	

Case no. 02 Registration applications of import cases

a. New Cases (Human)

150.	Name, address of Applicant / Importer	M/s Merixil Pharma, Office 28, 2nd floor rose plaza, I-8 Markaz, Islamabad Pakistan
	Name and address of marketing authorization holder (abroad)	M/s Seacross Pharmaceuticals Co., Ltd., Stanmore Bussiness & Innovation Centre, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK.
	Name, address of manufacturer(s)	M/s Sichuan Huiyu Pharmaceutical Ltd. No. 5 Road Chengxi economic area, Neijiang, Sichuan-641000, China.
	Name of exporting country	UK
	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. 14639 dated 08-08-2019
	Details of fee submitted	PKR 100,000/-: 02-07-2019
	proposed proprietary name / brand name	Azacitidine Seacross 100mg powder for suspension for injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Azacitidine……..100mg
	Pharmaceutical form of applied drug	Powder for suspension for injection
	Pharmacotherapeutic Group of (API)	Antineoplastic agent
	Reference to Finished product specifications	USP

	Firm response: 1) We applied for registration of above mention product on 08th August 2019. 2) During evaluation it was noted that Ahsan pharma Karachi has also applied for registration of same product from same manufacturer & marketing authorization holder. 3) This matter was discussed in 292nd meeting of Registration board it was decided to write email to marketing Authorization holder M/s Sea cross Pharmaceuticals Limited (UK) 4) Their reply was discussed in 295th meeting of Registration board in which they clarified that for this product Authorized agent for Pakistan is Ahsan Pharma Karachi & Merixil Pharma is authorized agent for Bendamustine & honorable Registration board approve this. According to this decision of Honorable Registration board we hereby withdraw our application for registration of Injection Azacitidine Seacross 100mg	
	Decision: Registration Board aceeded the firm's request and decided to reject Azacitidine Seacross 100mg powder for suspension for injection.	
151.	Name, address of Applicant / Importer	M/s Ahsan Pharma Room no.2 Delhi Muslim Building Aram Bagh Road, Karachi.
	Name and address of marketing authorization holder (abroad)	M/s Seacross Pharmaceuticals Co., Ltd., Stanmore Bussiness & Innovation Centre, Stanmore Place Howard Road, Stanmore London HA7 1BT, UK.
	Name, address of manufacturer(s)	M/s Sichuan Huiyu Pharmaceutical Ltd. No. 5 Road Chengxi economic area, Neijiang, Sichuan-641000, China.
	Name of exporting country	UK
	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. 14639 dated 06-09-2019
	Details of fee submitted	PKR 100,000/-: 06-09-2019
	The proposed proprietary name / brand name	Bendamustine Hydrochloride 100mg powder for concentrate for Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Bendamustine HCl (as bendamustine hydrochloride monohydrate) ……..100mg
	Pharmaceutical form of applied drug	Powder for suspension for injection
	Pharmacotherapeutic Group of (API)	Antineoplastic, alkylating agent
	Reference to Finished product specifications	Manufacturer specification
	Remarks of Evaluator: 1) Ahsan Pharmaceuticals applied for registration of above mention product on 06th September 2019. 2) During evaluation it was noted that Merixil pharma has also applied for registration of same product from same manufacturer & marketing authorization holder. 3) This matter was discussed in 292nd meeting of Registration board it was decided to write email to	

	marketing Authorization holder M/s Sea cross Pharmaceuticals Limited (UK) 4) Their reply was discussed in 295th meeting of Registration board in which they clarified that for this product Authorized agent for Pakistan is Merixil Pharma & Ahsan Pharma Karachi is authorized agent for Azacitidine Seacross 100mg & honorable Registration board approve this. According to this decision of Honorable Registration board withdraw application for registration of Injection Bendamustine Hydrochloride 100mg powder for concentrate for Infusion
	Decision: Registration Board decided to reject Bendamustine Hydrochloride 100mg powder for concentrate for Infusion

c. Deferred cases

i. Human

152.	Name, address of Applicant / Importer	M/s AJM Pharma (Pvt) Ltd 1st Floor, Shafi Court, Merewether Road, Civil Lines, Karachi
	Details of Drug Sale License of importer	DSL No.: 1016 Address: AJM Pharma (Pvt) Ltd 1st Floor, Shafi Court, Merewether Road, Civil Lines, Karachi. Validity: 18/06/2021 Status: By way of Wholesale
	Name and address of marketing authorization holder (abroad)	M/s Jiangsu Hansoh Pharmaceutical Group Co., Ltd. No. 5 Dongjin Road Economical and Technical Development Zone, Lianyungang, Jiangsu Province, China.
	Name, address of manufacturer(s)	M/s Jiangsu Hansoh Pharmaceutical Group Co., Ltd. No. 5 Dongjin Road Economical and Technical Development Zone, Lianyungang, Jiangsu Province, China.
	Exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP issued by Guangdong province Food and Drug Administration, China issued on 11/12/2020. The applied product is present in the market of exporting country for free sale. The facilities and operations conform to WHO-GMP. **Certificate No**: JS20200404 **Issuing authority:** Jiangsu Drug Administration **Date of issue:** 11/12/2020 **Validity:**05-09-2021 **MAH and Manufacturer:** M/s Jiangsu Hansoh Pharmaceutical Group Co., Ltd. No. 5 Dongjin Road Economical and Technical Development Zone, Lianyungang, Jiangsu Province, China.. • Copy of GMP certificate No : JS20180777 Valid till 22-02-2023 is submitted issued by China food and drug adminstration	
	Details of letter of authorization / sole agency agreement Original/notarized Sole Agency Agreement is submitted whereby M/s AJM Pharma (Pvt) Ltd is the sole and exclusive exporting subjected products of representative of M/s Jiangsu Hansoh Pharmaceutical Group Co., Ltd,. for the applied product. PEMOSH 100mg/Vial	
	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 4843 Dated 12/02/2021
	Details of fee submitted	Rs. 100,000/- Dated 11/01/2021
	proposed proprietary name / brand name	Pemosh 100mg/Vial for Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Pemetrexed disodium hemipentahydrate Eq to Pemetrexed……..…100mg
	Pharmaceutical form of applied drug	Lyophilized Powder for Injection
	Pharmacotherapeutic Group of (API)	Folate analog metabolic inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	10ml glass vial
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Almita 100mg /Vial of,USFDA approved.
	For generic drugs (me-too status)	Almita 100mg /Vial of Eli Lilly ,
	Module-II (Quality Overall Summary)	Submitted.
	Name, address of drug substance manufacturer	M/s Jiangsu Hansoh Pharmaceutical Group Co., Ltd. Addrress: Kaiitai Road, Dapu Industrial Park, Economical and Technical Development Zone, Lianyungang, Jiangsu Province, China.
	Module-III Drug Substance:	Submitted
	Stability Studies of Drug Substance: (Conditions & duration of Stability studies)	• 36 months real time stability data at -20˚C ± 5˚Cof 03 batches. • 06 month accelerated stability data 5˚C ± 3˚C of 03 batches.
	Module-III Drug Product:	Submitted.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is established against Alimta 100mg/ml *by M/s Eli Lilly.*
	Analytical method validation/verification of product	The firm has submitted all the relevant data including analytical method verification studies.
	Container closure system of the drug product	• 10ml TypeI clear Glass vial, Sealed with20- D2 Lyophilization bromobutyl rubber stopper for injection and secured with aluminium flip –off seal
	Stability study data of drug product, shelf life and storage conditions	• 36 months real time stability data at 30˚C ± 2˚C / 75% ± 5%RH of 03 batches (151101, 51102, 51103) • 06 month accelerated stability data 40˚C ± 2˚C / 75% ± 5%RH of 03 batches (20140601, 20140602, 20140603) • In -use 25mg/ml at 2-8˚C (20140601, 20140602, 20140603) • In -use 1mg/ml at (20140601, 20140602, 20140603)

Evaluation by PEC-IV

S.No	Section	Shortcomings Communicated	Reply
1.	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	Submitted.
2.	3.2.S.7	Reference product manufacturer conducted	Based on the patent, the pemetrexed

		Drug Substance stability studies at 25 °C / 60% RH Long term and 40 °C / 75% RH Accelerated stability studies while Drug substance manufacturer is conducting stability at -20°C ± 5°C Long term and 5°C ± 3°C Accelerated stability studies. Clarification is required in this regard.	Disodium Heptahydrate is more stable than the Pemetrexed Disodium Hemipentahydrtae. In this patent, stability study was performed at 25°C ± 2°C RH 60% ± 5% in 6 months with Pemetrexed Disodium Heptahydrate and Pemetrexed Disodium Hemipentahydrate, and the results shows that the degradation of the related substances for Pemetrexed Disodium Hemipentahydrate is more obvious than the pemetrexed Disodium heptahydrate. We Acknowledge that controlled room temperature is specified on the storage condition for Pemetrexed Disodium Heptahydrate in both USP and EP monograph. But considering the special attributes of the Hemipentahydrate, Hansoh prefer to use storage condition of -20°C ± 5°C for our Pemetrexed Disodium Hemipentahydrate. Results from accelerated stability study conducted under 5± 3°C and long-term stability study under -20°C ± 5°C support the proposed shelf life under the current storage condition and packages configuration. The quality index of our drug substance Pemetrexed Dsodium Hemipentahydrate can be well maintained at storage condition of -20°C ± 5°C

Previous Decision (M-312): Deferred for clarification whether applied product contains same Active Pharmaceuticals Ingredient as that of Reference product or otherwise.

Firm submitted reply:

"Drug product Pemetrexed for injection 100mg/Vial and the RLD (Almita, 100mg/vial) owned by Eli Lilly and company is supplied as single-use vial as sterile, lyophilized powder and administered as parenteral solutions after reconstitution, contain the same active ingredient and the same formulation"

Evaluation: FDA product contain Pemetrexed disodium heptahydrate while applied formulation contains Pemetrexed disodium hemipentahydrate**.**

Evaluation by PEC : FDA product Almita contains Pemetrexed disodium Heptahydrate however firm applied Pemetrexed disodium hemipentahydrate**.** EMA approved produc**t** Pemetrexed Krka contains same active ingredient that is Pemetrexed disodium hemipentahydrate**.**

Decision: Since the product approved by EMA contains same hydrate form of drug substance as that in the applied product. Therefore, the Board decided to defer the case for submission of Pharmaceutical Equivalence against the product containing the same hydrate form of drug substance.

Case no. 03 Registration applications of drugs for which stability study data is submitted

a. New cases

153.	Name and address of manufacturer / Applicant	M/s Neutro pharma (Pvt) Ltd., 9.5Km, Seikhupura Road, Lahore
	Brand Name +Dosage Form + Strength	Velamer-C 0.8g Sachet
	Composition	Each Sachet contains: Sevelamer Carbonate…….0.8g
	Diary No. Date of R& I & fee	Dy.No 8626 dated 08-03-2018 Rs.50,000/- 07-03-2018

	Pharmacological Group	Phosphate removing agent
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	15's, 60's, 90's,: As per SRO
	Approval status of product in Reference Regulator Authorities	Renvela Approved by US FDA
	Me-too status	
	GMP status	

STABILITY STUDY DATA

Drug	Velamer-C 0.8g Sachet		
Name of Manufacturer	M/s Neutro pharma (Pvt) Ltd., 9.5Km, Seikhupura Road, Lahore		
Manufacturer of API	M/S Century Pharmaceuticals Ltd, India		
API Lot No.	08528001-SLC		
Description of Pack (Container closure system)	Sachet		
Stability Storage Condition	Real time : 30˚C ± 2˚C / 75% ± 5% RH Accelerated: 40˚C ± 2˚C / 65% ± 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.	Vel-SH-0.8-001-19	Vel-SH-0.8-002-19	Vel-SH-0.8-003-19
Batch Size	360gm	360gm	360gm
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	07-10-2019	07-10-2019	07-10-2019
No. of Batches	03		
Date of Submission	29-08-2020 (21597)		

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	• Not submitted
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copy of COA of Sevelamer Carbonate (Batch#08528001-SLC) from M/S Century Pharmaceuticals Ltd, India is submitted Copy of COA of Sevelamer Carbonate (Batch#08528001-SLC)) from M/S Neutro Pharma is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Yes
4.	Stability study data of API from API manufacturer	The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 48 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.	Copy of GMP certificate (Certificate No# 20011803) for M/s Century Pharmaceuticals Limited, 103-106, GDC Halol-389350, Dist- Panchmahal issued Food and Drug

		Control Adminstration Gandhinagar, Gujrat stat, India is submitted, valid upto 08-01-2023
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Commercial Invoice No: CPLEXp1800043 Dated: 30-06-2018 from M/S Century Pharmaceuticals Limited, is submitted attested by AD(Lahore) dated ; 04-07-2018 for Sevelamer Carbonate quantity 4Kg Batch no # 08528001-SLC
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes
9.	Drug-excipients compatibility studies (where applicable)	NA
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted copy of Trial batch manufacturing record. Details are as under: Velamer-C 0.8mg Sachet **Batch No.** / **Bach size** / **Mfg. Started** Vel-SH-0.8-001-19 / 360g / 02-10-2019 Vel-SH-0.8-002-19 / 360g / 03-10-2019 Vel-SH-0.8-003-19 / 360g / 03-10-2019
11.	Record of comparative dissolution data (where applicable)	Not submitted
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	NA
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

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S.#	Shortcomings communicated	Reply
1.	Certificate of Analysis of API from API Manufacturer Provided of different batch than batch No mentioned in commercial invoice. Clarify.	COA of API from API manufacturer of relevant batch No submitted.
2.	Submit Certificate of Analysis of API from Finished Product manufacturer.	COA from finished product manufacturer submitted
3.	Submit Valid Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin as submitted GMP certificate is invalid.	Valid GMP certificate submitted. Valid until 08-01-2023
4.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer.	Submitted but test for Sevelamer carbonate Assay is titratable amines by potentiometric titration in reference product which is not performed by both API manufacturer and drug product manufacturer. Phosphate binding capacity (by UV) and carbonate content is performed by both API manufacturer and drug product manufacturer
5.	Stability study data of API from API	Submitted but in 48 months of stability studies Phosphate

	manufacturer.	binding capacity and carbonate content
6.	Complete batch manufacturing record of three stability batches.	Submitted
7.	Provide reference finished pharmaceuticals specifications including Phosphate Binding Capacity and assay of Sevelamer carbonate.	Not submitted.

Decision: Deferred for Scientific justification for not performing test of Titratable amines as required by reference product (i.e Renvela 0.8g & 2.4g powder for oral suspension) approved by US FDA, EMA and TGA Australia.

154.	Name and address of manufacturer / Applicant	M/s Neutro pharma (Pvt) Ltd., 9.5Km, Seikhupura Road, Lahore
	Brand Name +Dosage Form + Strength	Velamer-C 2.4g Sachet
	Composition	Each Sachet contains: Sevelamer Carbonate…….2.4g
	Diary No. Date of R& I & fee	Dy.No 8627 dated 08-03-2018 Rs.50,000/- 07-03-2018
	Pharmacological Group	Phosphate removing agent
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	15's, 60's, 90's,: As per SRO
	Approval status of product in Reference Regulator Authorities	Renvela Approved by US FDA
	Me-too status	
	GMP status	

STABILITY STUDY DATA

Drug	Velamer-C 2.4g Sachet		
Name of Manufacturer	M/s Neutro pharma (Pvt) Ltd., 9.5Km, Seikhupura Road, Lahore		
Manufacturer of API	M/S Century Pharmaceuticals Ltd, India		
API Lot No.	08528001-SLC		
Description of Pack (Container closure system)	Sachet		
Stability Storage Condition	Real time : 30˚C ± 2˚ C / 75% ± 5% RH Accelerated: 40˚C ± 2˚C / 65% ± 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.	Vel-SH-2.4-001-19	Vel-SH-2.4-002-19	Vel-SH-2.4-003-19
Batch Size	300 g	300 g	300 g
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	07-10-2019	07-10-2019	07-10-2019
No. of Batches	03		
Date of Submission	29-08-2020 (21598)		

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	• Not submitted

<table>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Copy of COA of Sevelamer Carbonate (Batch#08528001-SLC) from M/S Century Pharmaceuticals Ltd, India is submitted

Copy of COA of Sevelamer Carbonate (Batch#08528001-SLC)) from M/S Neutro Pharma is submitted</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Yes</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 48 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>Copy of GMP certificate (Certificate No# S-GMP/1803664) for M/s Century Pharmaceuticals Limited, 103-106, GDC Halol-389350, Dist- Panchmahal issued Food and Drug Control Adminstration Gandhinagar, Gujrat stat, India is submitted, valid upto 04-03-2020</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Commercial Invoice No: CPLEXp1800043 Dated: 30-06-2018 from M/S Century Pharmaceuticals Limited, is submitted attested by AD(Lahore) dated ; 04-07-2018 for Sevelamer Carbonate quantity 4Kg Batch no # 08528001-SLC</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA</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><td colspan="3">Velamer-C 2.4mg Sachet</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr>
<tr><td>Vel-SH-2.4-001-19</td><td>360gm</td><td>02-10-2019</td></tr>
<tr><td>Vel-SH-2.4-002-19</td><td>360gm</td><td>04-10-2019</td></tr>
<tr><td>Vel-SH-2.4-003-19</td><td>360gm</td><td>04-10-2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>NA</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>Yes</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Not submitted</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>Not submitted</td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td>S.#</td><td>Shortcomings communicated</td><td>Reply</td></tr>
<tr><td>1.</td><td>Certificate of Analysis of API from API Manufacturer Provided of different batch than</td><td>COA of API from API manufacturer of relevant batch No submitted.</td></tr>
</table>

	batch No mentioned in commercial invoice. Clarify.	
2.	Submit Certificate of Analysis of API from Finished Product manufacturer.	COA from finished product manufacturer submitted
3.	Submit Valid Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin as submitted GMP certificate is invalid.	Valid GMP certificate submitted. Valid until 08-01-2023
4.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer.	Submitted but test for Sevelamer carbonate Assay is titratable amines by potentiometric titration in reference product which is not performed by both API manufacturer and drug product manufacturer. Phosphate binding capacity (by UV) and carbonate content is performed by both API manufacturer and drug product manufacturer
5.	Stability study data of API from API manufacturer.	Submitted but in 48 months of stability studies Phosphate binding capacity and carbonate content
6.	Complete batch manufacturing record of three stability batches.	Submitted
7.	Provide reference finished pharmaceuticals specifications including Phosphate Binding Capacity and assay of Sevelamer carbonate.	Not submitted.
8.	Batch size mentioned is 300 gm and fill weight of sachet 5 gm, while sample size in stability sheets mentioned is 110 sachet. Clarify.	Actual quantity of batch is 360gm and fill weight is 2.70gm. so calculated no of sachet is 133. As mentioned in Trial cards and BMR.
Decision: Deferred for Scientific justification for not performing test of Titratable amines as required by reference product (i.e Renvela 0.8g & 2.4g powder for oral suspension) approved by US FDA, EMA and TGA Australia.		

Item No. I: Agenda of Evaluator PEC-VI

Case no. 01 Registration applications for local manufacturing of (Human) drugs/ Form 5 F

a. New cases

155.	Name, address of Applicant / Marketing Authorization Holder	M/s Searle Company Limited 32km , Multan road Lahore
	Name, address of Manufacturing site.	M/s Searle IV Solutions Pvt. Ltd. 1.5 km, Manga 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. 12584 dated 28/04/2021
	Details of fee submitted	PKR 50,000/-: dated 20/11/2020
	proposed proprietary name / brand name	Nuberol P Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API)	Each 100ml contains: Paracetamol…….1000mg

	per unit	
	Pharmaceutical form of applied drug	Clear, transparent liquid, free from any visible particles. Strength Label Claim: Paracetamol 1gm
	Pharmacotherapeutic Group of (API)	Analgesic & Antipyretic
	Reference to Finished product specifications	In House
	Proposed Pack size	100ml (Glass Vial)
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Acetaminophen of (USFDA approved)
	For generic drugs (me-too status)	Panam 1g/100ml Infusion M/s English Pharmaceutical Industries
	GMP status of the Finished product manufacturer	Last GMP inspection conducted on 19-10-2020, and the report concludes that the current compliance level of firm is rated as satisfactory, and DML renewal inspection conducted on 02.03.2021 and renewed the DML up to 2025. The firm has Large volume parenteral and liquid injectable vial section.
	Name and address of API manufacturer.	M/s Anqiu Lu'an Pharmaceutical Co., ltd. No. 35, Weixu North Road, Anqiu City, Shandong Province, 262100 China Tel: 86-536-4386559 Fax: 86-536-4390696
	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 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/ 75%RH± 5% for 3 months to 2 years Accelerated: 40˚C ± 2˚C/ 75%RH ± 5% for 6 months Batches: (18H015, 18H016, 18H017)
	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 of Nuberol-P 1gm Infusion have been established against the brand leader that is Provas Infusion by (Sami Pharmaceuticals) & Bofalgan Infusion by

		(Bosch Pharmaceuticals) by performing quality tests (Identification, Assay, bacterial endotoxin of dosage form). (pH 4.0-7.0). The 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		M/s Anqiu Lu'an Pharmaceutical Co., ltd. No. 35, Weixu North Road, Anqiu City, Shandong Province, 262100 China.		
API Lot No.		1711017Z		
Description of Pack (Container closure system)		100ml Glass Vial (1's)		
Stability Storage Condition		Real time: 30˚C ± 2˚C/ 65%RH± 5% Accelerated: 40˚C ± 2˚C/ 75%RH ± 5%		
Time Period		Real time: 3 months to 2 Years Accelerated: 6 months		
Frequency		Accelerated: initial, 1,2,3,6 (Months) Real Time: initial, 3,6,9,12,18,24 (Months)		
Batch No.		18H015	18H016	18H017
Batch Size		10000 Vials	10000 Vials	10000 Vials
Manufacturing Date		08-2018	08-2018	08-2018
Date of Initiation		23-08-2018	28-08-2018	24-08-2018
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 not submitted any 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. SD20170560 issued by CFDA valid till 01/02/2022.		
15.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of Import Invoice DRAP Ref. No. 2796/2020/DRAP dated 21/02/2020 is submitted wherein the permission to import of APIs (Paracetamol) for the purpose of test/analysis and stability studies is granted.		
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	Not Submitted		
18.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted **Climatic Chamber Detail** 1. 400L Galvano Scientific Lahore Pakistan 2. 750L Instruments Lahore Pakistan 3. 750L Instruments Lahore Pakistan		
Sr no.	**Short coming**	**Replies**		

a)	3.2.S.4 Control of Drug Substance (Validation of analytical procedures) 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.	The firm has submitted protocol and reports on analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer
b)	Submit raw data sheets to support the calculation of results of assay throughout the stability studies	The firm has submitted raw data sheets to support the calculation of results of assay throughout the stability studies
c)	Paracetamol exists in 3 polymorphic form, how will you differentiate between these.	**API Manufacturer:** In the literature, it is reported that Paracetamol has three polymorphic forms, a monoclinic (form I), an orthorhombic (form II), and an unstable phase (form III). We, Anqiu Lu'an Pharmaceutical Co., Ltd., hereby confirm that we started to perform the study of polymorphic form since year 2009, we ever selected three batches of Paracetamol (one batch manufactured in year 2004 and two batches manufactured in year 2009) and studied the polymorphic form in year 2009. After the analysis of three batches by the DSC, IR adoption and X-Ray diffraction, we found that our Paracetamol hold the same polymorphic form, which belong to Form I. **Drug Product manufacturer:** As mentioned in the statement of the manufacturer that they are manufacturing Paracetamol Form I (Monoclinic)which we are using in our production. We are performing complete test analysis of Paracetamol using British Pharmacopeia monograph, in which melting point (168 -L72"Cl testing showing that the polymorphs form we are using in our product is Form I (Monoclinic). The attached literature showing that Paracetamol Form I melting point is 767 - L69"C whereas Form ll(orthorhombic) has melting point 156"C, which has proven that paracetamol we are using, is Form l(Monoclinic).
Remarks OF Evaluator:		
Decision: Approved with innovators specifications. 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 **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**		
156.	Name, address of Applicant / Marketing Authorization Holder	M/s Rogen Pharmaceuticals Plot # 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/-: dated 21/02/2020 (#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 Pharma: GMP certificate issued on 24-12-2018 on the basis of inspection conducted on 24-10-2018. Global pharma has carbapenem dry powder section
	Name and address of API manufacturer.	Shandong Anxin Pharmaceutical Co., Ltd, No. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, 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)	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: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (HF7001D1, HF7002D2 & HF7003D3)

	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	Shandong Anxin Pharmaceutical Co., Ltd, No. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China		
API Lot No.	HF8047D8		
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: 12 months Accelerated: 24 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	17D123	17D124	17D125
Batch Size	3883 Vial	10,000 Vial	10,000 Vial
Manufacturing Date	04-2017	04-2017	04-2017
Date of Initiation	02-05-2017	03-05-2017	05-05-2017
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 No.2018001 issued by CFDA valid till 24/07/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Commercial Invoice No: THLH181009-X dated: 11-01-2018 duly endorsed by AD (1&E) DATED: 13-11-2018
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 the Evaluator:		
157.	Name, address of Applicant / Marketing Authorization Holder	M/s Rogen Pharmaceuticals Plot # 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 7864 dated 10-03-2021
	Details of fee submitted	PKR 50,000/-: dated 21/02/2020 (2005274)
	The proposed proprietary name / brand name	P-Becten Injection IV 2.5gm
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Glass vial contains: Piperacillin Sodium eq. to Piperacillin…….2gm 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 2 g/0.25 g powder for solution for infusion MHRA Approved
	For generic drugs (me-too status)	Zoycin Injection 2.25gm By M/S Global Pharmaceuticals (Pvt) Ltd Reg No: 066340
	GMP status of the Finished product manufacturer	Global Pharma: GMP certificate issued on 24-12-2018 on the basis of inspection conducted on 24-10-2018. Global pharma has carbapenem dry powder section
	Name and address of API manufacturer.	Shandong Anxin Pharmaceutical Co., Ltd No. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, 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)	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 & its verification, batch analysis & 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: (HF7001D1, HF7002D2 & HF7003D3)
	Module-III (Drug Product):	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 2.25gm 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	Shandong Anxin Pharmaceutical Co., Ltd, No. 10678 Wenliang Road, Dongjia Town, Licheng District, Jinan, Shandong, China		
API Lot No.	HF8047D8		
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: 12 months Accelerated: 24 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	18K344	18L320	18L344
Batch Size	4120 Vial	4120 Vial	4120 Vial
Manufacturing Date	10-2018	11-2018	11-2018
Date of Initiation	31-10-2018	19-12-2018	05-05-2018
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 No.2018001 issued by CFDA valid till 24/07/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Commercial Invoice No: THLH181009-X dated: 11-01-2018 duly endorsed by AD (1&E) DATED: 13-11-2018
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

S.#	Section	Shortcoming	Reply
1.	1.5.5	Submitted pharmacological group is not correct.	Pharmacological group has been corrected. **Annexure I**
2.	3.2.S.4.1	Assay limits declared in the Drug substance specification by the M/s Global pharma are different form that declared by the Drug substance manufacturer.	**Global Limit calculation for Piperacillin & Tazobactam for injection:-** Molecular weight of Piperacillin sodium = 539.54 Molecular weight of Piperacillin = 516.54 %age of Piperacillin in Piperacillin sodium = (516.54/535.54)*100 = **95.74%** Water = 1% Limit of Piperacillin sodium as USP = 95.0% ~ 102.0%, --- **Theoretical factor = (535.54/516.54) = 1.037** --- Molecular weight of Tazobactam sodium = 323.3 Molecular weight of Tazobactam = 300.3 %age of Tazobactam in Tazobactam Sodium = (300.3/323.3)*100 = **92.88%** Water = 0.6% --- **Theoretical factor = (323.3/300.3) = 1.077** --- **With the theoretical ratio of Piperacillin and Tazobactam being 8:1, or 80:10** As per USP Piperacillin and Tazobactam must be 90 to 110% of label claim:- **<u>The ratio of Piperacillin is: - 8 or 80mg as per 100mg label claim</u>** Piperacillin sodium contains water = 1% So on anhydrous basis Piperacillin will be 80 + 1% = 80.75%---------- which is the lower limit The upper limit 80.75 + 10% = 88.83% And **<u>The ratio of Tazobactam is: - 1 or 10mg as per 100mg label claim</u>** Tazobactam sodium contains water = 0.6% So on anhydrous basis Piperacillin will be 10 + 0.6% = 10.06%---------- which is the lower limit The upper limit 10.06 + 10% = 11.06% Please note that the supplier is providing the material with 7% addition in upper limit, whereas Global is calculating with 10% limit as per USP. **Annexure II**
3.	3.2.S.4.2	i. Details of mobile phase & chromatographic condition mentioned in the assay test of Analytical method of drug substance manufacturer are different from the recommended in USP monograph of "Piperacillin & Tazobactam for injection"	The drug substance follows the old version of USP monograph while Global Pharmaceuticals is using updated version of USP. Drug substance manufacturer and Drug product manufacturer both follows USP specifications. But difference of mobile phase & chromatographic condition are due to adaption of difference versions of USP monographs. **Annexure III**

		ii. Details of mobile phase & chromatograph condition mentioned in the assay test of Analytical method of drug product manufacturer are different form that mentioned in Analytical method of drug substance manufacturer.	The drug substance follows the old version of USP monograph while Global Pharmaceuticals is using updated version of USP. Drug substance manufacturer and Drug product manufacturer both follows USP specifications. But difference of mobile phase & chromatographic condition are due to adaption of difference versions of USP monographs. **Annexure IV**
4.	3.2.S.4.4	i. Acceptance criteria for pH test are different between the COA form drug substance manufacturer & drug product manufacturer.	Acceptance criteria for pH test are different between different COA of drug substance because we were following pH range of 5.5 – 6.8, but later on it was revised as per USP specification and updated to 5.0 – 7.0. Moreover results obtained are also well within the limits. Therefore, there is no impact on the quality of product. **Annexure V**
		ii. Acceptance criteria for Assay test are different between the COA form drug substance manufacturer & drug product manufacturer.	**Global Limit calculation for Piperacillin & Tazobactam for injection:-** Molecular weight of Piperacillin sodium = 539.54 Molecular weight of Piperacillin = 516.54 %age of Piperacillin in Piperacillin sodium = (516.54/535.54)*100 = **95.74%** Water = 1% Limit of Piperacillin sodium as USP = 95.0% ~ 102.0%, --- **Theoretical factor = (535.54/516.54) = 1.037** --- Molecular weight of Tazobactam sodium = 323.3 Molecular weight of Tazobactam = 300.3 %age of Tazobactam in Tazobactam Sodium = (300.3/323.3)*100 = **92.88%** Water = 0.6% --- **Theoretical factor = (323.3/300.3) = 1.077** --- **With the theoretical ratio of Piperacillin and Tazobactam being 8:1, or 80:10** As per USP Piperacillin and Tazobactam must be 90 to 110% of label claim:- **<u>The ratio of Piperacillin is: - 8 or 80mg as per 100mg label claim</u>** Piperacillin sodium contains water = 1% So on anhydrous basis Piperacillin will be 80 + 1% = 80.75%---------- which is the lower limit The upper limit 80.75 + 10% = 88.83% And **<u>The ratio of Tazobactam is: - 1 or 10mg as per 100mg label claim</u>** Tazobactam sodium contains water = 0.6% So on anhydrous basis Piperacillin will be 10 + 0.6% = 10.06%---------- which is the lower limit The upper limit 10.06 + 10% = 11.06% Please note that the supplier is providing the material with 7% addition in upper limit, whereas Global is calculating with 10% limit as per USP. **Annexure VI**

<table>
<tr><td></td><td></td><td>iii. Submitted chromatograms by M/s Global pharma reflect run time of 20 minutes for Assay analysis, whereas the Analytical method from drug substance manufacturer declared run time of 70 minutes.</td><td>Run time fixation is not recommended, applicant can set run up to the emergence of peak. In this all peaks emerge within 20 minutes and no peak appears after 20 minutes therefore run time of 20 has been set. Moreover while studying chromatograms by drug substance manufacturer it is evident that no peak appears after 20 minutes even up 70 minutes.
Attached are;
• Chromatograms by drug substance manufacturer
• Chromatograms by drug product manufacturer
Annexure VII</td></tr>
<tr><td></td><td></td><td>iv. Evidence of availability of HPLC with refrigerated auto sampler (with temperature range of 5 ± 3°) shall be submitted.</td><td>Evidence of availability of HPLC with refrigerated auto sampler is enclosed.
Annexure VIII</td></tr>
<tr><td>5.</td><td>3.2.S.7</td><td>Stability summary and conclusion section declares the long term stability condition as 25 ± 2°C 65 ± 5% , whereas the stability summary sheets mention the long-term stability condition 30 ± 2°C 65 ± 5%</td><td>This is a typographic mistake; correction has been made in stability summary and conclusion as well.
Annexure IX</td></tr>
<tr><td>6.</td><td>3.2.P.1</td><td>Justify the quantity of Piperacillin & Tazobactam in gm/vial. With reference to equivalency factors.</td><td>Justification for the quantities of Piperacillin & Tazobactam is attached.
Annexure X</td></tr>
<tr><td>7.</td><td>3.2.P.2.2 .1</td><td>i. Details of batch # of the product of M/s Global pharma used for pharmaceuticals equivalence studies shall be submitted.</td><td>Details of Product Name, Batch Number, Manufacturing Date and Expiry Date are mentioned below:-
Pharmaceutical Equivalence
<table>
<tr><th colspan="3">Reference Product details</th></tr>
<tr><th>S.No.</th><th>Parameter</th><th>Details</th></tr>
<tr><td>1.</td><td>Product Name</td><td>Zoycin 4.5gm Injection</td></tr>
<tr><td>2.</td><td>Batch Number</td><td>18L334</td></tr>
<tr><td>3.</td><td>Manufacturing Date</td><td>11-2018</td></tr>
<tr><td>4.</td><td>Expiry Date</td><td>10-2020</td></tr>
</table>
Annexure XI</td></tr>
<tr><td></td><td></td><td>ii. Results for Assay of Piperacillin & Tazobactam shall be identified separately in pharmaceutical equivalence studies.</td><td>We have understanding that as Piperacillin comes first while pronunciation and then comes Tazobactam; therefore results of Piperacillin are displayed first and then Tazobactam.
Moreover as per your advice we have separately identified results for assay of Piperacillin and Tazobactam
Report attached.
Annexure XII</td></tr>
<tr><td></td><td></td><td>iii. Tests of sterility, water determination & particulate matter have not been performed in pharmaceutical equivalence studies.</td><td>Tests of sterility, water determination & particulate matter were not performed during pharmaceutical equivalence due to limited quantity of innovator sample. Therefore, only all included major test while performed pharmaceutical equivalence.
Annexure XIII</td></tr>
<tr><td>8.</td><td>3.2.P.3</td><td>Compatibility studies with the diluents recommended in label of the drug product shall be performed.</td><td>Compatibility studies are attached.
Annexure XIV</td></tr>
</table>

<table>
<tr><td>9.</td><td>3.2.P.3.2</td><td>Batch formula shall declare the contents of Piperacillin & Tazobactam individually.</td><td>Theoretical content of Piperacillin and Tazobactam has been individually declared as:-
<table>
<tr><th rowspan="2">S. No</th><th rowspan="2">Materials</th><th colspan="2">Quantity per vial</th></tr>
<tr><th>Quantity</th><th>Unit</th></tr>
<tr><td>1.</td><td>Piperacillin</td><td>2.0</td><td>gm</td></tr>
<tr><td>2.</td><td>Tazobactam</td><td>0.25</td><td>gm</td></tr>
</table>
<table>
<tr><th rowspan="2">S. No</th><th rowspan="2">Materials</th><th colspan="2">Quantity per vial</th></tr>
<tr><th>Quantity</th><th>Unit</th></tr>
<tr><td>1.</td><td>Piperacillin</td><td>4.0</td><td>gm</td></tr>
<tr><td>2.</td><td>Tazobactam</td><td>0.5</td><td>gm</td></tr>
</table>
Annexure XV</td></tr>
<tr><td>10.</td><td>3.2.P.3.3</td><td>Description of manufacturer process mentions use of Ampoules instead of vials.</td><td>Due to typographic error word of “ampoule” has been mentioned instead of “vial”.
Correct description is manufacturing process is attached.
Annexure XVI</td></tr>
<tr><td>11.</td><td>3.2.P.3.4</td><td>Specification for test of Water are not as per the USP monograph of “Piperacillin & Tazobactam for Injection”</td><td>It was due to typographic error, correction has been made in specifications.
Annexure XVII</td></tr>
<tr><td rowspan="2">12.</td><td rowspan="2">3.2.P.5.1</td><td>i. Limits of pH & loss on drying are different from the USP monograph of “Piperacillin & Tazobactam for Injection”</td><td>It was due to typographic error, correction has been made in specifications.
Annexure XVIII</td></tr>
<tr><td>ii. Submitted specification does not include test of particulate matter.</td><td>We have purchase Liquid particle counter in March 2020, that why this test was not performed during manufacturing of stability batches. Currently we use Liquid particle counter to perform this test.
Attached are documents for your review;
• Service report of IQ, OQ and PQ of Liquid Particle counter is enclosed for your review.
• Report including test of particulate matter is attached.
Annexure XIX</td></tr>
<tr><td rowspan="3">13.</td><td rowspan="3">3.2.P.5.2</td><td>i. Limits of fill weight mentioned in analytical method is different from that declared in section 3.2.P.5.1.</td><td>Initially in 2017 fill weight of Zoycin 4.5gm was calculated with overage i.e. 5.15gm/vial. But after accelerated stability completion of excess in fill weight was removed and later on in 2018 product fill weight was revised to 4.854gm/vial. Same was revised in test method of product. While submission of stability data old batches with fill weight of 5.15gm/vial were submitted with revised test method.
Annexure XX</td></tr>
<tr><td>ii. Chromatographic condition do not declare the Auto sampler temperature</td><td>Auto sampler temperature was typographically missed in testing method, now method has been revised.
Copy of revised method is attached.
Annexure XXI</td></tr>
<tr><td>iii. Evidence of availability of HPLC with refrigerated auto sampler (with temperature range of 5 ± 3°.) shall be submitted.</td><td>Evidence of refrigerated auto sampler (with temperature range of 5 ±3°C) is attached.
Annexure XXII</td></tr>
</table>

14.	3.2.P.5.4	As per submitted COAs following tests. As required by the USP monograph of "Piperacillin & Tazobactam for Injection" have not been performed: i. Water determination ii. Particulate matter.	Test of water determination was included in the specification of drug product but could not be included in provided test report. We have purchase Liquid particle counter in March 2020, that why this test was not performed during manufacturing of stability batches. Currently we use Liquid particle counter to perform this test. Attached are documents for your review; • Service report of IQ, OQ and PQ of Liquid Particle counter is enclosed for your review. • Report including test of particulate matter is attached. **Annexure XXIII**
15.	3.2.P.6	COA of primary / secondary reference standard including source and lot number shall be provided.	Certificate of analysis of primary reference standard including source and lot number are attached. **Annexure XXIV**
16.	3.2.P.8.3	i. Submitted stability data sheet of batch# 17D125 reflect the significant change in the assay results of Tazobactam.	Assay results of initial time point of 17D125 batch are significantly high than all remaining samples tested during whole stability. This is because of high fill weight vial of finished product tested at zero time point. As for as results of all other time points are concerned there is a little difference between assays results i.e. hardly two to three percent. Therefore, speculation regarding significant change in results of Tazobactam is completely ruled out as no such trend has been seen in other stability batches. **Annexure XXV**
		ii. Submitted stability data reflects that following tests, as required by the USP monograph of "Piperacillin & Tazobactam for Injection" have not been performed. i. Water determination ii. Particulate matter.	Test of water determination was included in the specification of drug product but could not be included in provided test report. We have purchase Liquid particle counter in March 2020, that why this test was not performed during manufacturing of stability batches. Currently we use Liquid particle counter to perform this test. Attached are documents for your review; • Service report of IQ, OQ and PQ of Liquid Particle counter is enclosed for your review. • Report including test of particulate matter is attached. **Annexure XXVI**
		iii. Batch sizes mentioned on the analytical reports is different from that mentioned in stability data sheets.	This is typographic error and correction has been made. **Annexure XXVII**
		iv. The raw data sheets shall be elaborated in term of the weight of standard, sample dilution & potency of standards used.	As per your advice elaboration in term of weight of standard, sample dilution and potency of standard will be incorporated in raw data sheets. **Annexure XXVIII**
		v. Reports of microbial testing shall be submitted for test of bacterial endotoxin & sterility performed during stability studies.	Microbial endotoxin and sterility test was not performed during stability studies at that time period due to shortage of stability chambers as if stability sample includes sample for microbial endotoxin and sterility test, sample size increases significantly. But now as we have enough stability chambers so microbial endotoxin and sterility test have been made part of stability studies. **Annexure XXIX**

		vi. Documents confirming import of API, attested by relevant DRAP I & E office shall be submitted.	Import documents, attested by relevant DRAP I & E office are attached. **Annexure XXX**
17.	With reference to submitted BMRs, justify following. I. Fill weight of 5.15gm / vial. II. Quantity of drug substance dispensed, with reference to the actual potency of Piperacillin & Tazobactam determined in Drug substance batch analysis performed by the M/s Global Pharma. III. Batch size mentioned is different form that declares in the analytical data sheets.		I. By adding 6% overages in API fill weight of Zoycin 4.5gm Injection reaches to 5.15gm/vial. This overage is assed to overcome machine variation and weight variation issues and also to ensure the efficacy of the product till shelf life. Molecular weight of Piperacillin sodium= 540 Molecular weight of Piperacillin = 516 --- For 2000mg Piperacillin = (540/516)*4000 = 4186mg --- Molecular weight of Tazobactum sodium= 323 Molecular weight of Tazobactum = 300 --- 250mg Tazobactum = (323/300)*250 = 538mg --- Total Weight on dried basis = (4186mg +538mg) = 4724mg/vial --- Water contents = 2.5% Total Weight on hydrous basis = (4724)*100/ (100 – 2.5) = 4845mg/vial --- 4845mg/vial = 4.845grams/vial --- 4.845 + 6 % = 5.15 gm/Vila II. Already 6% overage is incorporated in filled weight of the Zoycin 4.5gm Injection so Potency adjustment was not done during dispensing of these Stability batches. III. Actual batch size is 3883 Vials which calculated based on below mentioned Calculation. 20 Kg x 1000 = 3883 Vials 5.15 Batch size mentioned on analytical data sheets was mistakenly written wrong. **Annexure XXXI**
Decision: Deferred for scientific justification for the points at Sr no 2 section 3.2.S.4.1, 4 section 3.2.S.4.4 (iii) , 7 section 3.2.P.2.2.1(iii), 16 section 3.2.P.8.3(i), 17 (i,ii).			

b. Deferred cases

Ref :- Letter No.F.1-6/2019-PR-I (EFD) dated 18th March 2021, M/s Horizon Healthcare Pvt Limited Taxila have achieved the benchmark of USD50,000/- However application received from the firm is of M/s Horizon healthcare Pvt Ltd plot no 33. Sundar Industrial Estate Lahore. The application was deferred in 308th meeting for consideration on its turn.

M/s Horizon Healthcare Pvt Limited Taxila 01 molecule/ 2 products

158.	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 7328, 05-03-2021
	Details of fee submitted	PKR 50,000/-: 26-02-2021
	Proposed proprietary name/brand name	Vonz Tablet 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	Tablet (film coated)
	Pharmacotherapeutic Group of (API)	First-in-class potassium-competitive acid blocker (A02BC08)
	Reference to Finished product specifications	As Per Innovator's Specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	PMDA JAPAN
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	GMP certificate based on evaluation conducted on 18-6-2020.
	Name and address of API manufacturer.	Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China
	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, Pharmaceutical equivalence through comparative dissolution profile against the reference product "Vocinti 10mg" tablet, Process validation protocol, Finished product analytical method validation report & stability studies data.

STABILITY STUDY DATA

Manufacturer of API	Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development, Zone,Guangdong Province, China	
API Lot No.	TAK09R20040	
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, 6,12,18,24 (Months)
Batch No.	VL-001	VL-002
Batch Size	5000 tablets	5000 tablets
Manufacturing Date	08-2020	07-2022

No. of Batches	02	
Details of Documents submitted		
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 products of 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. Following points were reported in the report: i. The HPLC software is 21 CFR compliant. ii. Audit trail on the testing reports was available
2	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	M/s Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development, Zone,Guangdong Province, China has drug establishment current registration site (USFDA) and is valid upto 12/2021
3	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice (Invoice#. JF20200220-1) attested by AD DRAP I&E LAHORE, dated 29-04-2020, in the name of M/s Horizon Healthcare (Pvt) Ltd.specifying the quantity of12Kg of Vonoprazan Fumarate (Batch# TAK09R200401) from Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development, Zone,Guangdong 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	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)
Decision of 308th : Deferred for consideration on its turn.		
Remarks of the Evaluator	Firm requested to kindly consider our dossier Vonz 10mg Tablet	

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**

159.	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 7329, 05-03-2021	
Details of fee submitted	PKR 50,000/-: 26-02-2021	
Proposed proprietary name / brand name	Vonz 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	Tablet (Film Coated)	
Pharmacotherapeutic Group of (API)	First-in-class potassium-competitive acid blocker (A02BC08)	
Reference to Finished product specifications	As per Innovator's Specification	
Proposed Pack size	As per SRO	
Proposed unit price	As per SRO	
Status in reference regulatory authorities	PMDA JAPAN	
For generic drugs (me-too status)	N/A	
GMP status of the Finished product manufacturer	Manufacturer has received the GMP certificate after successful inspection of DRAP.	
Name and address of API manufacturer.	M/s Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China	
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, Pharmaceutical equivalence through comparative dissolution profile against the reference product "Vocinti 20mg" tablet, Process validation protocol, Finished product analytical method validation report & stability studies data.	
Remarks:		
STABILITY STUDY DATA		
Manufacturer of API	Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development, Zone,Guangdong Province, China	
API Lot No.	TAK09R200401	
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, 6,9,12,18,24 (Months)	
Batch No.	VH-001	VH-002
Batch Size	5000 tablets	5000 tablets
Manufacturing Date	08.2020	07-2022

	No. of Batches	02
	Details of Documents submitted	
	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.	Firm has submitted US FDA Drug Establishments Current Registration Site status for M/s Enantiotech Corporation Limited which is valid upto 31/12/2021 and verifiable form following web link: https://www.accessdata.fda.gov/scripts/cder/drls/getdrls.cfm
	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice (Invoice#. JF20200220-1) attested by AD DRAP I&E LAHORE, dated 29-04-2020, in the name of M/s Horizon Healthcare (Pvt) Ltd.specifying the quantity of12Kg of VonoprazanFumarate (Batch# TAK09R200401) from Enantiotech Corporation Limited. No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development, Zone,Guangdong Province, China.
	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.
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail reports on product testing.
	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)
Decision of 308th: Deferred for consideration on its turn.		
Remarks of the Evaluator	Firm requested to kindly consider our dossier Vonz 20mg Tablet	

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**

Case no. 02 Registration applications for local manufacturing of (Human) drugs/ Form 5

a) Deferred cases

160.	Name and address of manufacturer / Applicant	M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.
	Diary No. Date of R& I & fee	Form-5 Dy.No 16930 dated 07-03-2019 Rs.20,000/-
	Brand Name +Dosage Form + Strength	Dysrtone 10mg tablets
	Composition	Each film coated tablet contains Dydrogesterone…..10mg
	Pharmacological Group	Progestogens
	Type of Form	Form-5
	Finished product Specification	BP
	Pack size & Demanded Price	20's, As per SRO
	Approval status of product in Reference Regulatory Authorities	Duphaston by BGP Products (Swissmedic Approved)
	Me-too status	Duphaston by Abbott (Reg. No. 006654)

	GMP status	cGMP inspection dated 11.11.2020 shows good level of cGMP compliance of the firm.
	Decision of 293rd: Steroidal hormone section is not confirmed in 293rd meeting.	
	Remarks of the Evaluator [VI]	Now Firm has submitted section approval letter dated & Inspection report of Steroidal hormone tablet section dated 20th September 2021
	Decision: The Board deliberated the *Trans* form of Dydrogesterone is described by Brithish Pharmacopoeia (B.P.) and the firm has also claimed B. P specifications. Therefore, the Board decided to approve the case and directed the the firm to strickly follow B.P specificationsfor Dydrogesterone to ensure safety, efficacy and quality parameters.	
161.	Name and address of manufacturer / Applicant	M/S Medisave Pharmaceuticals Plot No: 578-579 Sundar Industrial Estate, Sundar Raiwind Road, Lahore – Pakistan.
	Diary No. Date of R& I & fee	Dy No. 337 4-6-2012 Rs. 8000 Rs. 12000 19-11-2014
	Brand Name +Dosage Form + Strength	Dipho Syrup
	Composition	Each 5ml Contains:- Dimemorfan phosphate …..12.5mg
	Pharmacological Group	Antitussive-cough suppressant
	Type of Form	Form 5
	Finished product Specification	Manufacturer specification
	Pack size & Demanded Price	60ml, As per SRO
	Approval status of product in Reference Regulatory Authorities.	PMDA japan approved
	Me-too status	Inventive Syrup, Amson vaccines & Pharma,
	GMP status	Firm was granted GMP certificate based upon inspection conducted on 11-12-2017 & 10-01-2018 and recommended for renewal of DML.
	Remarks of the Evaluator. (VI)	
	Decision 0f 264th : Deferred for Evidence of approval in reference regulatory authorities. Evaluation by PEC: The product is approved in PMDA japan http://www.pmda.go.jp/PmdaSearch/iyakuDetail/GeneralList/2229001	
	Decision: Approved with innovator's Specifications.	

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

a. New DML

b. New/Additional section(s)

CLB in its 275th meeting held on 25th January 2020 has considered and approved the following 3 additional sections

a) Capsule (Cephalosporin)
b) Dry Powder Injectable(Cephalosporin)
c) Oral Dry Powder Suspension (Cephalosporin) 1 molecule/ 2 products

162.	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 27478 Dated 05.10.2021
	Details of fee submitted	Rs.30,000/- dated 24.09.2021 Deposit Slip # 993430923250
	proposed proprietary name / brand name	OnCef 250mg/5mL Dry Powder Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5mL contains Cefadroxil Monohydrate equivalent to Cefadroxil…….250 mg
	Pharmaceutical form of applied drug	Oral Dry Powder Suspension
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibacterial
	Reference to Finished product specification	USP Specification
	Proposed Pack size	30mL , 60mL, 90mL & 120mL
	Proposed unit price	As Per SRO
	status in reference regulatory authorities	Approved by **UK MHRA**
	For generic drugs (me-too status)	Duricef 250mg /5mL Oral Suspension of Glaxo Smith Kline Pakistan Limited., Reg # 010057
	GMP status of the Finished product manufacturer	GMP certificate issued on 12.11.2020
	Name and address of API manufacturer.	**Name:** ACS Dobfar S.p.A. **Address:** Viale Addetta, 4/12, 20067 Tribiano (MI), Italia (I) **Telephone:** +39 – 02 – 906931 Fax: +39 – 02 – 9064566 **E-mail:** reach@acsdobfar.it
	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	**Cefadroxil Monohydrate:** 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 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 **"Duricef 250mg /5mL Oral Suspension of GSK pakistan**".
	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:** ACS Dobfar S.p.A. **Address:** Viale Addetta, 4/12, 20067 Tribiano (MI), Italia (I) **Telephone:** +39 – 02 – 906931 Fax: +39 – 02 – 9064566 **E-mail:** reach@acsdobfar.it		
API Lot No.	550202 0004 0		
Description of Pack (Container closure system)	**API Container:** Linear low density polyethylene. Inner and outer white **Product Container:** Filled 60mL in amber glass bottles sealed with P.P caps with conical plug and packed in card board carton (30ml, 60mL, 90mL & 120mL)		
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	30 Bottles	30 Bottles	30 Bottles
Manufacturing Date	11.2020	11.2020	11.2020
Date of Initiation	03.12.2020	04.12.2020	04.12.2020
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 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# IT-API/51/H/2019) issued by Italian Medicine Agency AIFA valid upto 25.03.2022
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. **Cefadroxil Monohydrate:**

Batch No.	Quantity Imported	Date of approval by DRAP
550202 0004 0	1.50 Kg	27.07.2020

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 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)
Sr no.	**Short coming**	**Replies**
d)	3.2.P.2 Compatibility studies for the dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product	Compatibility studies for the dry powder for suspension has been performed as per the instructions provided in individual label of the drug product herewith. The diluent recommended for reconstitution is cool boiled water. ANNEX 01
e)	Submit raw data sheets to support the calculation of results of assay throughout the stability studies	Manufacturer part of drug substance including analytical procedure & specification is attached herewith. **ANNEX 02**
f)	Provide analytical record including COA at each time point, HPLC chromatograms, raw data sheets using page separators to segregate the data of each time point.	Firm has submitted the data calculation of stability study results is attached herewith. ANNEX 03
g)	Submit reference for the acceptance limits of each test in the drug product and drug substance specifications. Also provide justification in case acceptance limits mentioned in official monograph is not followed	We have followed the USP monograph regarding the substance product specification & data is attached herewith. ANNEX 04
Remarks OF Evaluator:		
Decision: Approved • **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**		
163.	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. 29985 Dated 03.11.2021
	Details of fee submitted	Rs.30,000/- dated 24.10.2021 Deposit Slip # 35711425515

	proposed proprietary name / brand name	OnCef 125mg/5mL Dry Powder Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5mL contains Cefadroxil Monohydrate equivalent to Cefadroxil……125 mg
	Pharmaceutical form of applied drug	Oral Dry Powder Suspension
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	30mL , 60mL, 90mL & 120mL
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved by UK MHRA & ANSM (France)
	For generic drugs (me-too status)	Duricef 125mg /5mL Oral Suspension of Glaxo Smith Kline Pakistan Limited., Reg # 008014
	GMP status of the Finished product manufacturer	GMP certificate issued on 12.11.2020
	Name and address of API manufacturer.	**Name:** ACS Dobfar S.p.A. **Address:** Viale Addetta, 4/12, 20067 Tribiano (MI), Italia (I) **Telephone:** +39 – 02 – 906931 Fax: +39 – 02 – 9064566 **E-mail:** reach@acsdobfar.it
	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 & controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system & stability studies of drug substance.
	Stability studies	**Cefadroxil Monohydrate:** 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 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 *"Duricef 125mg /5mL Oral Suspension of GSK Pakistan".*

	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:** ACS Dobfar S.p.A. **Address:** Viale Addetta, 4/12, 20067 Tribiano (MI), Italia (I) **Telephone:** +39 – 02 – 906931 Fax: +39 – 02 – 9064566 **E-mail:** reach@acsdobfar.it		
API Lot No.	550202 0004 0		
Description of Pack (Container closure system)	**API Container:** Linear low density polyethylene. Inner and outer white **Product Container:** Filled 60mL in amber glass bottles sealed with P.P caps with conical plug and packed in card board carton (30ml, 60mL, 90mL & 120mL)		
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		
Testing Frequency	0,3,6 for Accelerated study 0,3,6,9,12,18,24 long-term stability study		
Batch No.	T-001	T-002	T-003
Batch Size	30 Bottles	30 Bottles	30 Bottles
Manufacturing Date	11.2020	11.2020	11.2020
Date of Initiation	03.12.2020	04.12.2020	04.12.2020
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 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# IT-API/51/H/2019) issued by Italian Medicine Agency AIFA valid upto 25.03.2022
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. **Cefadroxil Monohydrate:** **Batch No.** | **Quantity Imported** | **Date of approval by DRAP** 550202 0004 0 | 1.50 Kg | 27.07.2020
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 and analytical record.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product	Firm has submitted audit trail reports on product testing.

	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)
Sr no.	**Short coming**	**Replies**
a)	3.2.P.2 Compatibility studies for the dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product	Compatibility studies for the dry powder for suspension has been performed as per the instructions provided in individual label of the drug product herewith. ANNEX 01
b)	Submit raw data sheets to support the calculation of results of assay throughout the stability studies	Manufacturer part of drug substance including analytical procedure & specification is attached herewith. **ANNEX 02**
c)	Provide analytical record including COA at each time point, HPLC chromatograms, raw data sheets using page separators to segregate the data of each time point.	Firm has submitted the data calculation of stability study results is attached herewith. ANNEX 03
d)	Submit reference for the acceptance limits of each test in the drug product and drug substance specifications. Also provide justification in case acceptance limits mentioned in official monograph is not followed	We have followed the USP monograph regarding the substance product specification & data is attached herewith. ANNEX 04
Remarks OF Evaluator:		
Decision: Approved. • **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**		
Capsule (Cephalosporin) 1molecule/ 1 capsule		
164.	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. 24701 Dated 07.09.2021
	Details of fee submitted	Rs.30,000/- dated 03.08.2021 Deposit Slip # 82613607220
	proposed proprietary name / brand name	OnCef 500mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains Cefadroxil Monohydrate equivalent to Cefadroxil…….500 mg

	Pharmaceutical form of applied drug	Oral Capsule
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibacterial
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	2x6's & 2x7's
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved by UK MHRA
	For generic drugs (me-too status)	Duricef 500mg Capsule of Glaxo Smith Kline Pakistan Limited., Reg # 008013
	GMP status of the Finished product manufacturer	GMP certificate issued on 12.11.2020 GMP Certificate validity 12.11.2022
	Name and address of API manufacturer.	**Name:** ACS Dobfar S.p.A. **Address:** Viale Addetta, 4/12, 20067 Tribiano (MI), Italia (I) **Telephone:** +39 – 02 – 906931 Fax: +39 – 02 – 9064566 **E-mail:** reach@acsdobfar.it
	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	**Cefadroxil Monohydrate:** 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 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 "Duricef 500mg Capsule of **M/s GSK Pakistan**".
	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:** ACS Dobfar S.p.A.	

<table>
<tr><td colspan="2"></td><td colspan="3">Address: Viale Addetta, 4/12, 20067 Tribiano (MI), Italia (I)
Telephone: +39 – 02 – 906931
Fax: +39 – 02 – 9064566
E-mail: reach@acsdobfar.it</td></tr>
<tr><td colspan="2">API Lot No.</td><td colspan="3">550209 0018 0</td></tr>
<tr><td colspan="2">Description of Pack
(Container closure system)</td><td colspan="3">API Container: Linear low density polyethylene. Inner and outer white
Product Container: Alu-Alu blister packed in unit carton (2x6’s & 2x7’s)</td></tr>
<tr><td colspan="2">Stability Storage Condition</td><td colspan="3">Real time: 30°C ± 2°C / 65% ± 5%RH
Accelerated: 40°C ± 2°C / 75% ± 5%RH</td></tr>
<tr><td colspan="2">Time Period</td><td colspan="3">Real time: 6 months
Accelerated: 6 months</td></tr>
<tr><td colspan="2">Frequency</td><td colspan="3">Accelerated: 0, 3, 6 (Months)
Real Time: 0, 3, 6 (Months)</td></tr>
<tr><td colspan="2">Batch No.</td><td>T-001</td><td>T-002</td><td>T-003</td></tr>
<tr><td colspan="2">Batch Size</td><td>1,000 Capsules</td><td>1,000 Capsules</td><td>1,000 Capsules</td></tr>
<tr><td colspan="2">Manufacturing Date</td><td>11.2020</td><td>11.2020</td><td>11.2020</td></tr>
<tr><td colspan="2">Date of Initiation</td><td>24.11.2020</td><td>30.11.2020</td><td>30.11.2020</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">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.</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">Copy of GMP certificate (Certificate# IT-API/51/H/2019) issued by Italian Medicine Agency AIFA valid upto 25.03.2022</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.
Cefadroxil Monohydrate:
<table>
<tr><th>Batch No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>550209 0018 0</td><td>2Kg</td><td>27.07.2020</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 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 and humidity monitoring of stability chambers (real time & 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>
</table>

Sr no.	Short coming	Replies
a)	Submit raw data sheets to support the calculation of results of assay throughout the stability studies	Manufacturer part of drug substance including analytical procedure & specification is attached herewith. **ANNEX 02**
b)	Provide analytical record including COA at each time point, HPLC chromatograms, raw data sheets using page separators to segregate the data of each time point.	Firm has submitted the data calculation of stability study results is attached herewith. ANNEX 03
c)	Submit reference for the acceptance limits of each test in the drug product and drug substance specifications. Also provide justification in case acceptance limits mentioned in official monograph is not followed	We have followed the USP monograph regarding the substance product specification & data is attached herewith. ANNEX 04

Remarks OF Evaluator:

Decision: Approved.

- **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**

Case no. 07 Registration applications of drugs for which stability study data is submitted

a. New cases
b. Deferred cases
c. Verification of stability study data

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
165.	M/s Horizon Healthcare Pvt. Ltd. Plot No 35-A, small industrial Estate, Taxila-Pakistan	Xetine Tablet 10mg Each film coated tablet contains: Vortioxetine Hydrobromide Eq. to Vortioxetine…10mg Innovator's Specifications.	Form-5 Dy. No: 9987 Dated. 04-03-2019 Rs.20,000/- 14's, 28's As per SRO	USFDA Approved 22-02-2019 & 01-03-2019 The firm was found to be operating at satisfactory level of GMP

STABILITY STUDY DATA

Drug	Xetine Tablet 10mg
Name of Manufacturer	M/s Horizon Healthcare Pvt. Ltd. Plot No 35-A, small industrial Estate, Taxila-Pakistan
Manufacturer of API	M/s Lianyungang Jari Pharmaceuticals Co Ltd,China
API Lot No.	Batch No. 20181101
Description of Pack (Container closure system)	Al-alu
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:6 months

Frequency	Accelerated: 0,1,2,3,4,6 (month) Real Time: 0,3,6, (month)		
Batch No.	V001	V002	V003
Batch Size	2500 tablet	2500 tablet	2500 tablet
Manufacturing Date	6-2019	6-2019	6-2019
Date of Initiation	6-2019	6-2019	6-2019
No. of Batches	03		
Date of Submission	04-03-2019		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr.#	Documents To Be Provided	Status
1.	COA of API	Yes
	Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	GMP certificate is issued by Jiangsu Food and Drug Administration China.
2.	Protocols followed for conduction of stability study and details of tests.	Yes
3.	Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc.	Yes
4.	Documents confirming import of API etc.	Copy of commercial invoice has been submitted it is attested by AD, DRAP. Invoice No. EA190128 Dated: 28/01/2019 Quantity: 130 gram
5.	All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Yes
6.	Commitment to continue real time stability study till assigned shelf life of the product.	Yes
7.	Commitment to follow Drug Specification Rules, 1978.	Yes

REMARKS OF EVALUATOR

Scope of Inspection: Verification of authenticity of stability data of Xetine 10mg Tablet (Vortioxetine as Hydrobromide) in reference to DRAP PEC Letter No. F.1-2/2020-PEC dated 06-07-2020.

Name of Manufacturer	M/s Horizon Healthcare (Pvt) Ltd.
Physical Address	Plot No.35-A, Small industrial Estate, Taxila
Date of Inspection	03-11-2020
Purpose of inspection	Verification of authenticity of stability data of Xetine 10mg Tablet (Vortioxetine as Hydrobromide) in reference to DRAP PEC Letter No. F.1-2/2020-PEC dated 06-07-2020
Name of inspector	Mr. MuzzamilWaheed, Director DTL, Rawalpindi Ms. Mahvish Ansari, Area FID Mr. Hafiz Ahsan, Assistant Director PE&R, DRAP, Islamabad.
Name of firm's Representative(s)	Mr. RahmatHadi, Product Development Manager, Mr. Nasr Ullah Khan, Quality Operation Manager. Mr. Muhammad Pervaiz, General Manager Operations.

Sr.#	Questions	Observations
01.	Whether the firm has documents confirming import of API.	Yes, Firm has imported 130 grams of Vortioxetine Hydrobromide from M/s. Lianyungang Jari Pharmaceutical Co., Ltd, China against Invoice No:

		EA190128 dated 28-01-2019 and has clearance from DRAP Islamabad. Documents including NOC, commercial invoice and License to import drugs were available.
02.	What was the rationale behind selecting the particular manufacturer of API?	The rationale behind selecting the particular manufacturer of API was GMP status, drug master file study and study of API specifications based on documented evidence.
03.	Whether documents confirm the import of API reference standards & Impurity standards.	Firm had imported two impurities (Oxide, 2,6 Impurity) and working standards of Vortioxetine hydrobromide from API manufacturer.
04.	Whether the firm has COAs of API, working standard and Impurities from exporter.	COAs of API, working standard and Impurities from API manufacturer were available. However, COA of working standard contains less testing.
05.	Whether the firm has any approval of API or GMP certificate of API manufacturer issued by regulatory authority of country of origin?	Firm has GMP certificate of API manufacturer issued by Lianyungang Drug Administration, China valid till 11-04-2024.
06.	Whether firm use API manufacturer method of testing?	No. *Firm has developed in-house method for testing of API.*
07.	Whether firm has a stability study report on API?	Yes, Firm has accelerated (6 months) and real time (24 months) stability study reports on API performed by API manufacturer available.
08.	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	Stability testing of API has not been performed by as per SIM method.
09.	Whether firm has method for quantifying the impurities in the API?	*No,method of analysis did not demonstrate the quantification of impurities in the API*.
10.	Whether firm has some remaining quantities of the API, its reference standard and impurities standards?	Yes, firm has 11 grams of API, and no remaining quantity of working standard and 5mg of impurities standards each.
11.	Whether firm has used pharmaceutical grade excipients?	Excipients used are Mannitol, Hydroxypropyl cellulose, Microcrystalline cellulose, Sodium starch glycolate, Magnesium stearate. Excipients used were of pharmaceutical grade.
12.	Whether firm has documents confirming the import of the used excipients.	Yes, Invoices of excipients procured were available.
13.	Whether firm has test reports and other records on the excipients used?	Firm possess COAs of excipients, however log Books record of SAP were not available.
14.	Whether firm has written and authorized protocols for the development of tablet?	The firm has written and authorized protocol for development of applied product. *However,product development protocol to be updated for roles and responsibilities.*
15.	Whether firm has performed Drug-Excipient compatibility studies?	The firm claimed that they have used same excipients as those of innovator product hence drug-excipient compatibility studies not performed.
16.	Whether firm has performed comparative dissolution studies?	Firm has performed comparative dissolution studies of their developed product (Batch # V001) with innovator product i.e., Trintellix 10mg tablet manufactured by H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark in pH 1.2, pH 4.5 and pH 6.8 media.
17.	Whether firm has product development (R&D) section?	Yes, R&D lab for trial batch execution were available.
18.	Whether firm has necessary equipment available in product development (R&D) section for development of finished product?	Yes, firm has necessary equipment available in product development (R&D) section for development of finished product including Balance, sieves, Single punch compression machine, cone mixer, ribbon-Mixer

		and Coating Pan. *However, log book record of weighing balance and pH meter were not available.*
19.	Are the equipment in product development section qualified?	Firm has performed only internal qualification of qc lab equipments used in product development. *Moreover, the firm was advised to qualify the equipments / instruments from authorized bodies* (external calibration)
20.	Whether firm has proper maintenance / calibration / re-qualification program for the equipment used in PD section?	The calibration of equipments was performed by external body but the external body was not accreditated by PNAC. *Tachometer used for qualification of RPM of dissolution apparatus was not functional.* *Daily verification of HPLC by Caffeine check method was not performed.*
21.	Whether firm has qualified staff in product development section with proper knowledge and training in product development?	Training record of product development staff was not available.
22.	Whether firm has manufactured three stability batches for the stability studies of finished product tablets as required?	Yes, firm has manufactured three stability batches for the stability studies of Xetine 10mg Tablet with batch no V001, V002 & V003 having batch size of 2500 tablets each.
23.	What was the criteria for fixing the batch size of stability batches?	As stated by firm's management, the criteria for fixing the batch size of stability batches was based on testing intervals and record of production.
24.	Whether firm has complete record of production of stability batches?	Firm has trial BMRs of all three stability batches available.
25.	Whether firm have protocols for stability testing of stability batches?	Yes, firm has protocols for testing of stability batches.
26.	Whether firm has developed and validated the method for testing of stability batches?	Yes
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?	As the Firm is using in house developed method hence no method transfer protocol needed.
28.	Whether firm has documents confirming the qualification of equipment / instruments being used in the test and analysis of API and the finished drug?	Equipment used in testing of API and finished product were qualified. Equipment calibration was performed biannually from external body which is not accreditated with PNAC. *Moreover, the firm was advised to qualify the equipments / instruments from authorized bodies only.*
29.	Whether firm has stability indicating method of analysis?	*No. The firm has not developed stability indicating method.*
30.	Whether firm has HPLC software 21CFR compliant?	Yes, certificate of conformity of Lab solution Software version 6.82 was available.
31.	Whether firm could show audit trail reports on vortioxetine testing?	Yes, Audit trail record for testing of product was available in Shimadzu LC20A Lab solution Software version 6.82.
32.	Whether firm has some remaining quantities of degradation product and stability batches?	Yes, firm has some remaining quantities of stability batches Trial B. No V001 = 122 packs Trial B. No V002 = 122 packs Trial B. No V003 = 122 packs
33.	Whether firm has commitment batches kept on stability testing?	Firm has kept all three trial batches kept for stability testing.
34.	Whether firm has valid calibration status for the equipment used in vortioxetine tablets	*Calibration certificates were available from 3rd party (which was not accreditated with PNAC) for*

	production and analysis?	*equipments used in QC and production.*
35.	Do proper and continuous monitoring and controls are available for stability chambers?	Digital data loggers are available for continuous monitoring and controls of stability chambers.
36.	Do related manufacturing area, equipments, personnel and utilities be rated as GMP compliant?	Related manufacturing area, equipment, personnel and utilities are GMP compliant. GMP Certificate issued on basis of GMP inspection conducted on 01-3- 2019.

Conclusion:

Based on the area inspected, the technical personnel met and the documents reviewed, and considering the findings of inspection, it is concluded that stability data submitted by M/s. Horizon Healthcare (Pvt) Ltd. Plot No.35-A, Small industrial Estate, Taxila, Pakistan for registration of said product is verifiable. However, few points are being recorded for the kind perusal of the Drug Registration Board, against questions 6, 9, 14, 18, 19, 20, 28, 34 of the check list.The said stability is invalid keeping in view the comments no. 6, 9, 14, 18, 19, 20, 28, 34.

Dr. MuzzamilWaheed, Director DTL, Rawalpindi

Ms. Mahvish Ansari, Area FID

Mr. Hafiz Ahsan, Assistant Director PE&R, DRAP, Islamabad.

Decision: Deferred for taking clarification from applicant regarding the stability studies points at Sr.No. 6, 14, 18.

Firm Response (Xetine Tablet 10mg)

Sr#	Questions	Observations	Reply
1	Point No:6 Whether firm use API manufacturer method of testing?	No.Firm has developed in-house method for testing of API	Firm has been tested Raw material according to Manufacturer's Method and performed Method Verification Now We updated the COA and SAP according to Drug substance Manufacturer's Method .Results are also verified.
2	Point No:14 Whether firm has written and authorized protocols for the development of tablet?	Firm has written and authorized protocol for Development of applied product.However ,product development protocol to be updated for roles and responsibilities	Product Development Protocol has been updated for roles and responsibilities clearly mention the responsibilities involved in Product Development
3	Point No :18 Whether firm has necessary equipment available in product development (R&D)section for Development of	Yes ,firm has necessary equipment available in product development (R&D) section for Development of finished product including Balance , Sieves,Single punch compression Machine,Cone mixer,Ribbon Mixer and Coating Pan However, logbook record of weighing balance and PH meter were not available.	Logbook record of only Excipients analysis was not available . Now we are maintaining all log book record regularly..

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**

d. Exemption from onsite verification of stability data

166.	Name and address of manufacturer / Applicant	M/s Jenner Pharmaceuticals (Pvt.) Ltd. 26- km Lahore Sharaqpur Road Sheikhupura
	Brand Name +Dosage Form + Strength	Neocomb Tablets 500/20mg
	Composition	*Each enteric film coated Tablet Contains:* Naproxen (as enteric coated inner core) : 500 mg Esomeprazole (As Magnesium Trihydrate as film coated outer core): 20mg

	Diary No. Date of R& I & fee	Dy:912, 30-09-2015 , Rs.50,000/- (29-09-2015)
	Pharmacological Group	Anti-inflammatory and Anti-rheumatic
	Type of Form	Form-5D
	Finished product Specification	Innovators's
	Pack size & Demanded Price	10's, 20's, 30's As per SRO
	Approval status of product in Reference Regulatory Authorities.	Vimovo Tablets Manufactured by AstraZeneca UK
	Me-too status	---
	GMP status	Last GMP/Panel inspection conducted on 23-12-2020 for renewal of DML
	Remarks of the Evaluator.	

Now the firm has submitted stability data detailed as under:

STABILITY STUDY DATA

Drug	Neocomb Tablets 500/20mg			
Name of Manufacturer	M/s Jenner Pharmaceuticals (Pvt.) Ltd. 26- km Lahore Sharaqpur Road Sheikhupura			
Manufacturer of API	Naproxen: Divi's Laboratories India Esomeprazole Magnesium: Everest Organics India			
API Lot No.	Naproxen: 2-M-B-0730319 Esomeprazole Magnesium: ESM/E-077/19			
Description of Pack (Container closure system)	10's, 20's and 30's tablets packed in 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: 0,1,2,3,4,5 & 6 months		Real Time: 0,3,6 months	
Product name	Batch Nos.	Batch size	Date of Mfg.	Date of initiation
Neocomb 500/20mg tablets	NCB-PB-018001	1000 tablets	10-2019	12-10-2019
Neocomb 500/20mg tablets	NCB-PB-018002	1000 tablets	10-2019	12-10-2019
Neocomb 500/20mg tablets	NCB-PB-018003	1000 tablets	10-2019	12-10-2019
Date of submission	Dy no 3094, Dated 2-7-2020			

REQUEST OF EXEMPTION ROM ON SITE INSPECTION

Now the firm has requested for Exemption from On-site Investigation of their submitted stability data of Neocomb 500/20mg tablets and provided the following documents in conjunction with the checklist approved by the Registration Board in its 278th Meeting:

Administrative Portion

1.	Reference of last onsite panel inspection for instant dosage form conducted duringlast two years.	Firm has referred to onsite inspection report of their products "Lansodex Capsule 60mg and 30mg, Sofopas Tablet 400/90", which were presented in 287th meeting of Registration board. Registration Board decided to approve registration of Lansodex Capsule 60mg and 30mg, Sofopas Tablet 400/90 of M/s Jenner Pharmaceuticals (Pvt) Ltd,. Sheikupura. Date of inspection : 10-12-2018 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 two separate Memmert (Germany) stability chambers

<table>
<tr><td></td><td></td><td>for real time and accelerated stability studies which are equipped with data loggers.</td></tr>
<tr><td>2.</td><td>Documents for the procurement of API with approval from DRAP (in case ofimport).</td><td>Copy of commercial invoices to import Naproxen (6.200kg) and Esomeprazole Magnesium (325gm) attested by AD, I&E DRAP, Lahore 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>2-M-B-0730319
ESM/E-077/19</td><td>5319500023
EXP/187/18-19</td><td>11-02-2019
11-02-2019</td></tr></table></td></tr>
<tr><td>3.</td><td>Documents for the procurement of reference standard and impurity standards.</td><td>Firm has declared that manufacturer of API of Naproxen and Esomeprazole magnesium has supply impurities and working standard along with the material</td></tr>
<tr><td>4.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by regulatory authority of country of origin.</td><td>Copy of WHO-GMP certificate of M/s Divi’s Laboratories India for Naproxen (Certificate# L.Dis.No. 816/DCA/AP/2018) issued by Director and licensing authority Drugs Control Administration, Andhra Pradesh India valid upto 6-2024.
Copy of DML of M/s Everest Organics India for Esomeprazole Magnesium (Certificate# L.Dis.No. 2034/E1/2019) issued by Drugs Control Administration, Govt of Telangana India valid upto 12-2022.</td></tr>
<tr><td>5.</td><td>Mechanism for Vendor pre-qualification</td><td>The firm has submitted copy of document with title “Rationale for selection of Manufacturing of the API „ Naproxen and Esomeprazole separately“”</td></tr>
<tr><td>6.</td><td>Certificate of analysis of the API, reference standards and impurity standards</td><td>The firm has submitted certificate of analysis for API (Naproxen Batch# 2-M-B-0730319), (Esomeprazole Batch# ESM/E-077/19), working standards and impurity standards.</td></tr>
<tr><td>7.</td><td>Documents for the procurement</td><td>The firm has submitted photocopy of Purchase Order/Invoices for the procurement of excipients used in product development.</td></tr>
<tr><td>8.</td><td>List of qualified staff involved in product development with relevant experience.</td><td>The firm has submitted photocopy of List of R& D technical staff comprising of 3 technical members.</td></tr>
<tr><td colspan="3">Production Data</td></tr>
<tr><td>9.</td><td>Authorized Protocols/SOP for the development & stability testing of trial batches.</td><td>The firm has submitted copy of Product Development Protocol & Stability study protocols for the Neocomb 500/20mg tablets.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Record of three stability batches for the stability studies of Neocomb 500/20mg tablets such as.<table><tr><td colspan="3">Neocomb 500/20mg tablets</td></tr><tr><th>Batch No.</th><th>Date of Mfg.</th><th>Batch Size</th></tr><tr><td>NCB-PB-018001</td><td>10-2019</td><td>1000 tablets</td></tr><tr><td>NCB-PB-018002</td><td>10-2019</td><td>1000 tablets</td></tr><tr><td>NCB-PB-018003</td><td>10-2019</td><td>1000 tablets</td></tr></table></td></tr>
<tr><td>11.</td><td>Record of remaining quantities of stability batches.</td><td>Firm has submitted reconciliation sheet mentioning followingdetails:<table><tr><td colspan="3">Neocomb 500/20mg tablets</td></tr><tr><th rowspan="2">Batch No.</th><th colspan="2">Remaining Quantity</th></tr><tr><th>Accelerated</th><th>Long Term</th></tr><tr><td>NCB-PB-018001</td><td>0 tablets</td><td>260 tablets</td></tr></table></td></tr>
</table>

		NCB-PB-018002	0 tablets	260 tablets
		NCB-PB-018003	0 tablets	260 tablets
QA / QC DATA				
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted photocopies of digital graphs for Real Time and Accelerated Conditions for complete stability studies of applied formulations. The firm has two separate Memmert (Germany) stability chambers for real time and accelerated stability studies which are equipped with data loggers.		
13.	Method used for analysis of API alongwith COA.	The firm has submitted photocopy of raw material specifications, raw material testing procedures for Naproxen and Esomeprazole Magnesium		
14.	Method used for analysis of FPP & complete record of testing of stability batches (i.e. chromatograms, lab reports, raw data sheets etc.)	The firm has submitted photocopy of Testing Method of Finished Product for Neocomb 500/20mg Tablets along with relevant analytical record for stability studies.		
15.	Reports of stability studies of API from manufacturer.	The firm has submitted stability studies reports on API as per Zone-IV-a conditions.		
16.	Analysis reports for excipients used.	The firm has submitted photocopies of its Analytical reports for all excipients used in product development of Neocomb 500/20mg Tablets.		
17.	Drug-excipients compatibility studies.	The firm has submitted that drug excipient compatibility studies data is not applicable since firm has used qualitative innovator formulation.		
18.	Record of comparative dissolution data.	Firm has performed comparative dissolution study against reference product Vimovo Tablets 500/20mg (Astra Zeneca Canada) at 0.1N HCl, pH 1.2, Buffer pH 6.8 and Buffer pH 7.4		
19.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted audit trail reports of stability studies of applied formulations.		
Remarks of Evaluator (VI)		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: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches of both products on long term stability studies throughout the 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 of both products as per the commitment submitted in the registration application.**

Item No. I: Agenda of Evaluator PEC-VII

Case no. 01 Registration applications for local manufacturing of (Human) drug

a. Deferred cases

167.	Name and address of manufacturer / Applicant	M/s Fynk Pharmaceuticals. 19km G.T. Road Kalashah Kaku, Lahore, Pakistan
	Brand Name + Dosage Form + Strength	Quitapine ST Tablets 300mg
	Composition	Each extended release film coated tablet contains: Quetiapine fumarate…300mg
	Diary No. Date of R&I & Fee	Dy.No 6795 dated 15-02-2019 Rs.20,000/- Dated 15-02-2019 (0836583)
	Pharmacological Group	Atypical antipsychotic
	Type of Form	Form-5
	Finished product Specification	Inno Specification
	Pack size & Demanded Price	10's, 20's, 30's : As per SRO
	Approval status of product in reference regulatory authorities	Approved in USFDA

	Me-too status	Qusel XR 300mg Tablet of Hilton Pharma Karachi
	GMP status	GMP inspection conducted on 21-11-17 concluded that firm is operating at satisfactory level of GMP compliance.
	Remarks of the Evaluator	Reference product is approved as Quetiapine as fumarate…300mg extended release tablet.
	Previous Decision	Deferred for submission of label claim/composition of applied formulation in line with reference product i.e. Quetiapine as fumarate…300mg extended release tablet.
	Evaluation by PEC AD	In original dossier the firm applied as Quetiapine as fumarate…300mg extended release tablet.
	Decision: Approved with innovator's specification. 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	
168.	Name and address of manufacturer / Applicant	M/s Convell Laboratories. Swat, KPK
	Brand Name +Dosage Form + Strength	Quetil 100mg Tablet
	Composition	Each Film coated Tablet Contains: Quetiapine as fumarate…100mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 11446 dated 05-03-2019 Rs.20,000/- Dated 04-03-2019 (#0508175)
	Pharmacological Group	Neuroleptic/dopamine receptor antagonist
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Quetiapine film coated tablet (25mg, 100mg, 150mg, and 200mg) by M/s Aurobindo pharma, MHRA Approved.
	Me-too status	Qusel Tablet (25mg, 100mg, 200mg) by M/s Hilton pharma, Reg No. (37684, 37685, 37690)
	GMP status	M/S Convell: Panel inspection dated 02-3-2019 for renewal of DML
	Remarks of Evaluator [VII]	The firm revised their formulation from Quetiapine fumarate uncoated tablet to Quetiapine as fumarate film coated tablet. Without the provision of fee.
	Previous Decision (296)	Deferred for submission of requisite fee for revision of formulation as per the reference product
	Remarks of Evaluator [VII]	The firm has submitted fee challan of Rs. 7500/- (Deposit slip # 774912722828) dated 3-08-2021 for change of formulation from uncoated to: Each film coated Tablet Contains: Quetiapine as fumarate…..100 mg
	Decision: Approved.	
169.	Name and address of manufacturer / Applicant	M/s Convell Laboratories. Swat, KPK
	Brand Name +Dosage Form + Strength	Quetil 25mg Tablet
	Composition	Each Film coated Tablet Contains: Quetiapine fumarate…25mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 11445 dated 05-03-2019 Rs.20,000/- 04-03-2019 (#0508174)
	Pharmacological Group	Neuroleptic/dopamine receptor antagonist
	Form	Form-5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO

	Approval status of product in Reference Regulatory Authorities	Quetiapine film coated tablet (25mg, 100mg, 150mg, and 200mg) by M/s Aurobindo pharma, MHRA Approved.
	Me-too status	Qusel Tablet (25mg, 100mg, 200mg) by M/s Hilton pharma, Reg No. (37684, 37685, 37690)
	GMP status	M/S Convell: Panel inspection dated 02-3-2019 for renewal of DML
	Remarks of Evaluator [VII]	The firm revised their formulation from Quetiapine fumarate uncoated tablet to Quetiapine as fumarate film coated tablet. Without the provision of fee.
	Previous Decision (296)	Deferred for submission of requisite fee for revision of formulation as per the reference product
	Remarks of Evaluator [VII]	The firm has submitted fee challan of Rs. 7500/- (Deposit slip # 72744539) dated 3-08-2021 for change of formulation from uncoated to: Each film coated Tablet Contains: Quetiapine as fumarate…..25 mg
	Decision: Approved.	
170.	Name and address of manufacturer / Applicant	M/s Mediate Pharmaceutical Pvt Ltd. Plot No. 150-151, Sector 24, Korangi Industrial Area, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Cetra-Med 200mg/ml Oral Solution
	Composition	Each ml Contains: Piracetam…200mg
	Diary No. Date of R& I & fee	Form-5 Dy.No 8329 dated 25-02-2019 Rs.20,000/- Dated 25-02-2019. Duplicate File bearing Dy No 8562 R & I dated 22-04-2020 (#0818199)
	Pharmacological Group	Antiprotozoal
	Form	Form-5
	Finished product Specifications	Manufacture specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	NA (In ANSM it is archived and repealed)
	Me-too status	Piractim 1gm/5ml Syrup M/s Global
	GMP status	M/S Mediate Pharma Last GMP inspection conducted on 02-04-2019 and report concludes was considered to be operating at acceptable level of compliance with GMP guidelines .
	Remarks of Evaluator [VII]	Evidence of approval of applied formulation in reference regulatory authorities/agencies as adopted by the Registration Board in its 275th meeting.
	Previous 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.
	Remarks [VII]	Firm provides the evidence of NOOTROPYL 20%, oral solution in ANSM France which is valid
	Decision: Approved with innovator's specification. 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	
171.	Name and address of manufacturer / Applicant	M/s. Libra (Private) Ltd., 77, Peshawar industrial estate, Hayatabad Peshawar
	Brand Name +Dosage Form + Strength	Metzole V Gel
	Diary No. Date of R& I & fee	Dy.No. 171, 20-3-2015, Rs.20,000/-
	Composition	Each gm of vaginal gel contains: - Metronidazole…….7.5 mg

	Pharmacological Group	Antimicrobial
	Type of Form	Form-5
	Finished Product Specification	Innovator
	Pack size & Demanded Price	75gm / Rs.105
	Approval status of product in Reference Regulatory Authorities.	Vendazole 0.75% gel (USFDA)
	Me-too status	Metni-V shaigan
	GMP status	Last GMP Inspection of Libra Pharma GMP certificate dated 14-12-2020 was provided
	Remarks of Evaluator VII	• Latest GMP inspection report (which should have been conducted within the period of last one year). • Evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • 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 273	Deferred due to paucity of time
	Remarks of Evaluator VII	**Query** / **Response** Evidence of approval of applied formulation in reference regulatory authorities/ agencies — Vendazole 0.75% gel (USFDA) Latest GMP inspection report (which should have been conducted within the period of last one year). — GMP certificate dated 14-12-2020 was provided, GMP shows the suspension of production in Cream/ ointment, injection general and capsule section 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. — Cream/ointment section available but production suspended Justification of overage in master formulation. — Revised formulation is submitted Methylene chloride and Sodium cyclamate are discontinued/ banned excipients. For this reason, you have to revise the formulation and re-submit same. — Revised formulation is submitted
	Previous Decision 312	Deferred. For the confirmation of manufacturing facility, as GMP shows the suspension of production in Cream/ointment, injection general and capsule section
	Remarks of Evaluator VII	Firm submitted the licensing division letter stated that "keeping in view the recommendation of panel in their inspection conducted on 12-08-2020 in compliance with the decision of 270 meeting board decide to allow resumption of production I following three sections 1. Dry powder injection (Cephalosporin) 2. Capsule (general/antibiotics) 3. Cream/ointment (General/antibiotics)

	Decision: **Approved with innovator's specification. 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**	
172.	Name and address of manufacturer / Applicant	M/s. Libra (Private) Ltd., 77, Peshawar industrial estate, Hayatabad Peshawar
	Brand Name +Dosage Form + Strength	Silver Cream
	Diary No. Date of R& I & fee	Dy.No. 173, 20-3-2015, Rs.20,000/-
	Composition	Each gm contains:- Silver sulphadiazine….. 10mg
	Pharmacological Group	Antibiotics and Chemotherapeutics for Dermatological
	Type of Form	Form-5
	Finished Product Specification	USP
	Pack size & Demanded Price	50gm Rs,500
	Approval status of product in Reference Regulatory Authorities.	Silvadene 1% cream (USFDA approved).
	Me-too status	Silver-S Cream, Shaigan Pharma, Reg No. 030060Dermazin by Novartis
	GMP status	Last GMP Inspection of Libra Pharma GMP certificate dated 14-12-2020 was provided
	Remarks of Evaluator VII	• Latest GMP inspection report (which should have been conducted within the period of last one year). • Evidence of pharmacopoeia reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • 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 273	Deferred due to paucity of time
	Remarks of Evaluator VII	

S. No	Query	Response
1.	Latest GMP inspection report (which should have been conducted within the period of last one year).	GMP certificate dated 14-12-2020 was provided
2.	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.	Cream/ointment section available but production suspended
3.	Justification of overage in master formulation.	Revised formulation is submitted
4.	Methylene chloride and Sodium cyclamate are discontinued/ banned excipients. For this reason, you have to revise the formulation and re-submit same.	Revised formulation is submitted

	Previous Decision 312	Deferred. For the confirmation of manufacturing facility, as GMP shows the suspension of production in Cream/ointment, injection general and capsule section

	Remarks of Evaluator VII	Firm submitted the licensing division letter stated that "keeping in view the recommendation of panel in their inspection conducted on 12-08-2020 in compliance with the decision of 270 meeting board decided to allow resumption of production I following three sections 1. Dry powder injection (Cephalosporin) 2. Capsule (general/antibiotics) 3. Cream/ointment (General/antibiotics)
	Decision: Approved	
173.	Name and address of manufacturer / Applicant	M/s. Libra (Private) Ltd., 77, Peshawar industrial estate, Hayatabad Peshawar
	Brand Name +Dosage Form + Strength	Xamic 250mg Capsule
	Diary No. Date of R& I & fee	Dy.No. 175, 20-3-2015, Rs.20,000/-
	Composition	Each capsule contains:- Tranexamic acid……..250mg
	Pharmacological Group	Antifibrinolytic.
	Type of Form	Form-5
	Finished Product Specification	Manufacture
	Pack size & Demanded Price	2x10's/ Rs.90.00 per 20's
	Approval status of product in Reference Regulatory Authorities.	TRANEX 250 mg capsule, AIFA approved.
	Me-too status	Texamic Capsule 250mg, Nimrall Pharma Reg. No. 068502
	GMP status	Last GMP Inspection of Libra Pharma GMP certificate dated 14-12-2020 was provided
	Remarks of Evaluator VII	• Latest GMP inspection report (which should have been conducted within the period of last one year). • Evidence of pharmacopoeia reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • 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 273	Deferred due to paucity of time
	Remarks of Evaluator VII	

S#	Query	Response
1.	Latest GMP inspection report (which should have been conducted within the period of last one year).	GMP certificate dated 14-12-2020 was provided
2.	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.	Capsule genal section available but production suspended
3.	Justification of overage in master formulation.	Revised formulation is submitted

	Previous Decision 312	Deferred. For the confirmation of manufacturing facility, as GMP shows the suspension of production in Cream/ointment, injection general and capsule section
	Remarks of Evaluator VII	Firm submitted the licensing division letter stated that "keeping in view the recommendation of panel in their inspection conducted on 12-08-2020 in compliance with the decision of 270 meeting board decided to allow resumption of production I following three sections 1. Dry powder injection (Cephalosporin) 2. Capsule (general/antibiotics) 3. Cream/ointment (General/antibiotics)
	Decision: Approved with innovator's specification. 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	
174.	Name and address of manufacturer / Applicant	M/s. Libra (Private) Ltd., 77, Peshawar industrial estate, Hayatabad Peshawar
	Brand Name +Dosage Form + Strength	Xamic 500mg Capsule
	Diary No. Date of R& I & fee	Dy.No. 172, 20-3-2015, Rs.20,000/-
	Composition	Each capsule contains:- Tranexamic acid……..500mg
	Pharmacological Group	Antifibrinolytic
	Type of Form	Form-5
	Finished Product Specification	Manufacturer
	Pack size & Demanded Price	2x10's Rs.120.00 per 20's
	Approval status of product in Reference Regulatory Authorities.	TRANEX 500 mg capsule, AIFA approved.
	Me-too status	Texamic Capsule 500mg, Nimrall Pharma Reg. No. 068503
	GMP status	Last GMP Inspection of Libra Pharma GMP certificate dated 14-12-2020 was provided
	Remarks of Evaluator VII	• Latest GMP inspection report (which should have been conducted within the period of last one year). • Evidence of pharmacopoeia reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • 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 273	Deferred due to paucity of time

	Remarks of Evaluator VII	<table><tr><th>S.#</th><th>Query</th><th>Response</th></tr><tr><td>1.</td><td>Latest GMP inspection report (which should have been conducted within the period of last one year).</td><td>GMP certificate dated 14-12-2020 was provided</td></tr><tr><td>2.</td><td>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.</td><td>Capsule genal section available but production suspended</td></tr><tr><td>3.</td><td>Justification of overage in master formulation.</td><td>Revised formulation is submitted</td></tr></table>
	Previous Decision 312	Deferred. For the confirmation of manufacturing facility, as GMP shows the suspension of production in Cream/ointment, injection general and capsule section
	Remarks of Evaluator [VII]	Firm submitted the licensing division letter stated that "keeping in view the recommendation of panel in their inspection conducted on 12-08-2020 in compliance with the decision of 270 meeting board decide to allow resumption of production I following three sections 1. Dry powder injection (Cephalosporin) 2. Capsule (general/antibiotics) 3. Cream/ointment (General/antibiotics)
	Decision: Approved with innovator's specification. 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	
175.	Name and address of manufacturer / Applicant	M/S High –Q Pharmaceuticals, Plot No ; 224/23 Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	Platlo Plus 75mg/75mg Tablet
	Composition	Each film coated tablet contain Clopidogrel (as bisulfate) (USP)…….75mg Acetylsalicylic acid (as enteric coated pellets)….75mg
	Diary No. Date of R& I & fee	Dy.No.10448; 31-07-2017; Rs.20,000/- (31-07-2017)
	Pharmacological Group	Anti-Platelet aggregation
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	10's, 14's, 28's, ; As per SRO
	Approval status of product in Reference Regulatory Authorities	CoPlavix Tablet Of (TGA Approved)
	Me-too status	Clodril Plus Tablet M/s Macter International
	GMP status	Last GMP inspection was conducted on 30 June 2021 and the report shows good GMP.
	Remarks of the Evaluator	1st letter: 04th June, 2018 Reminder letter: 9th October, 2018 Latest GMP inspection report (conducted within the period of last one year).

		Source of pellets of Acetyl salicylic acid (In case of imported source remaining Rs: 80000/- fee) GMP certificate of source of pellets Stability study of 3 batches of pellets Certificate of analysis of pellets
	Previous decision(s) 296	Deferred for following: Registration Board deferred the case for: • Latest GMP inspection report (conducted within the period of last three year). • Source of pellets of Acetyl salicylic acid (In case of imported source remaining Rs: 80000/- fee) • GMP certificate of source of pellets, stability data and COA of pellets. • Clarification of the dosage of the Innovator product, whether bilayer tablet or otherwise.
	Remarks of evaluator	

S#	Query	Response
	Latest GMP inspection report (conducted within the period of last three year).	Last GMP inspection was conducted on 30 June 2021 and the report shows good GMP.
	Source of pellets of Acetyl salicylic acid (In case of imported source remaining Rs: 80000/- fee)	Source is Surge lab Pakistan
	GMP certificate of source of pellets, stability data and COA of pellets. GMP certificate of source of pellets, stability data and COA of pellets	Source is Surge lab Pakistan
	Clarification of the dosage of the Innovator product, whether bilayer tablet or otherwise.	Highnoon is making this table by compression and then film coating is done, in TGA biconcave coated tablet is mentioned.

	Previous Decision 312	Deferred for revision of formulation and manufacturing method as per reference product and confirmation of availability of bilayered machine
	Remarks of Evaluator [VII]	The Inspection report dated 6 July 2021 confirms the availability of bilayer machine. In TGA Australia the dosage form is described as biconvex tablet film coated not bilayered detailed method of manufacturing is also submitted by the firm.
	Decision: Deferred for deliberation in forthcoming meeting regarding approval of the applied formulation as bi-layered and /or plain tablet.	

Sr.#	Name and address of manufacturer / Applicant	Brand Name (Proprietary name + Dosage Form + Strength) Composition Pharmacological Group Finished product Specification	Type of Form Initial date, diary Fee including differential fee Demanded Price / Pack size	Remarks on the formulation (if any) including International status in stringent drug regulatory agencies / authorities Me-too status GMP status as depicted in latest inspection report (with date) by the Evaluator	Previous Remarks of the Evaluator.	Previous Decision

176.	M/s Gulf Pharmaceuticals Rawat.	Ascab 5% Cream Each tube contains:- Permethrin…..5.0 % (Scabicides, Pediculocides)	Form 5 11-07-2012 Rs.8000/= (Photocopy attached) 30-10-2014 Rs.12,000/= Dy.No.6931 30gm As Per SRO	Elimite of Mylan Pharms, (USFDA) Lotrix of GSK Pharma Inspection conducted on 18-05-2016 showed that the firm is found complying GMP as of today	Firm claims manufacturer's specs. Composition table contains Acyclovir as active ingredient in the submitted corrections	Deferred in 268: Deferred for correction of API in master formulation .
Remarks of evaluator [VII]: The API is corrected as Cream Each tube contains:- Permethrin…..5.0% with the fee of 7500 dated 03 September 2021 (#76692145723) **Decision: Approved with innovator's specification with formulation as** **Each tube contains cream: -** **Permethrin…..5.0%** **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**						
177.	M/s Gulf Pharmaceuticals Rawat.	Odium 2mg Capsules Each capsule contains:- Loperamide hydrochloride …….2mg (Opiate) USP specifications)	Form 5 11-07-2012 Rs.8000/= (Photocopy attached) 30-10-2014 Rs.12,000/= Dy.No.6934 1x10's As Per SRO	Loperamide hydrochloride of Mylan (USFDA) Floramex of Zafa Pharma Inspection conducted on 18-05-2016 showed that the firm is found complying GMP as of today	Needs to clarify pharmacological group as WHOATC code states pharmacological group as anti-propulsive or anti-diarrhoeal	Deferred in 268: Deferred for clarification of pharmacological group.
Remarks of evaluator [VII]: Firm clarify their pharmacological group as anti-propulsive or anti-diarrhoeal **Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee for correction of pharmacological group as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**						
178.	M/s Gulf Pharmaceuticals Rawat.	Simfoni 100mg Suspension Each 5ml contains:- Dexibuprofen (MS) ……...100 mg (Non-steroidal Anti-inflammatory)	Form 5 11-07-2012 Rs.8000/= (Photocopy attached) 30-10-2014 Rs.12,000/= Dy.No.6973 120ml As Per SRO	Not Provided Tercica of Sami Pharma Inspection conducted on 18-05-2016 showed that the firm is found complying GMP as of today	Reference of regulatory agency not provided Firm claims manufacturer's specs within dossier. However, the label states USP specifications but the product is not present in available pharmacopoeia	Deferred in 268: Deferred for evidence of approval by reference regulatory authorities as reference submitted/provided is incorrect
Remarks of evaluator [VII]: Firm provided the me too reference of Tercica 100mg/5 ml suspension by sami pharma instead of RRA Evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting still needed **Decision: Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.**						

179.	M/s Gulf Pharmaceuticals Rawat.	Orthovis 500mg Capsules Each capsule contains: - Glucosamine Sulphate as KCl ……500mg (Amino Acid)	Form 5 Dy.No.6918 11-07-2012 Rs.8000/= (Photocopy attached) Rs.12,000/= 30-10-2014 2×10's Rs.250	Not provided Gevoflox by Hilton Pharma Inspection conducted on 18-05-2016 showed that the firm is found complying GMP as of today	Clarify the pharmacological group as WHOATC code states pharmacological group as anti-inflammatory, anti-rheumatics Confirm price of product	Deferred in 268: Deferred for evidence of approval by reference regulatory authorities & clarification of Pharmacological group.
Remarks of evaluator [VII]**:** In RRA firm provide the reference of Malaysia which is not included in RRA. Evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting still needed **Decision: Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.**						

b. Vet Deferred

180.	Name and address of manufacturer / Applicant	M/s Mylab Pvt Ltd. Khankah Sharif Bahawalpur
	Brand Name +Dosage Form + Strength	Oxycart spray
	Diary No. Date of R& I & fee	Dy.No 44228 dated 28-12-2018 Rs. 20,000 (26/12/2018)
	Composition	Each ml Contains: Oxytetracyclin….. 750 mg Oxycartisone 240 mg
	Pharmacological Group	Antibiotic/steroidal solution
	Type of Form	Form-5
	Finished Product Specification	In house
	Pack Size & Demanded Price	250 ml / As per brand leader
	Approval Status of Product in Reference Regulatory Authorities.	NA
	Me-too Status	NA
	GMP status	Last GMP inspection conducted on and operating at satisfactory compliance with GMP guidelines as of today
	Remarks of the Evaluator **VII**	Me too not available
	Previous 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.
	Remarks of the Evaluator **VII**	The Me too Oxycort spray by star lab Registration # 014143. With composition EACH 300ML Contains: - Oxytetracycline HCL 1500MG Which is not same as applied
	Decision: Deferred for following • **Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.** • **Confirmation of manufacturing facility of spray section from licencing division.**	

Case no. 02: Registration applications of drugs for which Form 5F is submitted

181.	Name, address of Applicant / Marketing Authorization Holder	M/s Indus Pharma (Pvt.) Ltd Plot No. 26-27 & 63/67, Sector 27, Korangi Industrial Area, Karachi-74900.
	Name, address of Manufacturing site.	M/s Indus Pharma (Pvt.) Ltd Plot No. 26-27 & 63/67, Sector 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. 7451 dated 08/03/2021
	Details of fee submitted	PKR 20,000/- dated 19/10/2020 (#1932559)
	proposed proprietary name / brand name	Lecetam Oral Solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Levetiracetam……100mg
	Pharmaceutical form of applied drug	A clear, colourless or almost colourless, apple flavoured solution filled in amber glass bottle.
	Pharmacotherapeutic Group of (API)	Antiepileptics
	Reference to Finished product specifications	USP
	Proposed Pack size	10ml, 15ml, 30ml, 60ml, 120ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Levetiracetam Oral Solution, USP by ACI Healthcare USA, Inc., USFDA Approved.
	For generic drugs (me-too status)	Lerace Oral Solution by Hilton Pharma (pvt) Ltd., Reg. No. 061224
	GMP status of the Finished product manufacturer	GMP inspection dated 28-11-2019 concludes as under: "After reviewing their QA System, QC & Manufacturing, relevant documents, utilities and personal capacity the current GMP are rated as GOOD."
	Name and address of API manufacturer.	Zhejiang Huahai Pharmaceutical Co. Ltd. Chuannan, Duqiao, Linhai, Zhejiang, 317016, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template
	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. (assay by HPLC with PDA detector, limit 98to 101%), residual solvent by GC
	Stability studies	Levetiracetam (Batches: C5146-09-016, C5146-09-017, C5146-

		09-018) Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH
	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
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader **Lumark Oral Solution** by **Searle Pakistan Limited** by performing quality tests.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Huahai Pharmaceutical Co. Ltd.		
API Lot No.	D5294-18-127		
Description of Pack (Container closure system)	Printed unit carton containing 1 Amber glass bottle of 60ml with aluminium PP Cap Pack also contains 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.	TR-1/LVT 60ml	TR-2/LVT 60ml	TR-3/LVT 60ml
Batch Size	2000 bottles	2000 bottles	2000 bottles
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	18-02-2020	18-02-2020	18-02-2020
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 previous inspection report of "Canazin tablets (Canagliflozin)", which was presented in 289th meeting of Registration Board. Registration Board approved the application of Canazin tablets and wherein HPLC system was declared as 21 CFR 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 EU-GMP certificate (Certificate# IT/E/API/10/2019 REV.1) in the name of M/s Zhejiang Huahai Pharmaceutical Co., Ltd China, valid up to 14/03/2022 issued by Italian Medicine Agency
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (Invoice# HH2020169) specifying the quantity of 124Kg of Levetiracetam HCl from M/s Zhejiang Huahai Pharmaceutical Co., Ltd 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	Submitted

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

Remarks OF Evaluator:

S. No	Section #	Observations/Deficiencies/ Short-comings	Remarks of the firm
01	3.2.S.4.4	The submitted COA from drug substance manufacturer mentions the reference for specs as USP but drug product manufacturer is claiming BP specification. Clarification is needed	The API and Finished product both were tested as per the pharmacopeia monograph of USP, for which the COA of API (tested by manufacturer) USP specification is provided
02	3.2.P.1	Composition is different from reference product of USFDA	Formulation of Lecetam oral solution is as per the formulation of *USFDA approved products* of following *ACI Healthcare USA, Inc., Marlex Pharmaceuticals Inc and Roxane Laboratories, Inc.* Comparison table is provided
03	2.3.P.2.5	Discussion of microbiological attributes of the Drug Product (e.g., preservative effectiveness studies to be performed as per recommendation of pharmacopoeia) not provided.	The preservative effectiveness study of Lecetam Oral Solution is performed and the results are found satisfactory till 14th day (Results Attached). The study will be completed on 23-11-21 and the results till 28th day will be shared accordingly The firm follow the USP 43 for Finished product testing and followed the same specification and covered all quality attributes and specification as mentioned in USP.
04	2.3.P.4	Control of excipients is missing	We have used Pharmacopeia standard excipients for which monographs and Analytical Procedures are attached, however for inhouse excipient, analytical procedure is attached along with the COA of all excipients used in formulation.

Decision: Deferred for the submission of microbiological attributes of the Drug Product i.e. complete 28-day preservative effectiveness study.

182.	Name, address of Applicant / Marketing Authorization Holder	M/s Opal Laboratories Pvt Ltd. LC-41, L.I.T.E., Landhi, Karachi
	Name, address of Manufacturing site.	M/s Opal Laboratories Pvt Ltd. LC-41, L.I.T.E., Landhi, 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
	Details of fee submitted	Form-5F Dy.No 7676 dated 09-03-2021 Rs.20,000/- dated 02-11-2020 (#2039392)
	proposed proprietary name / brand name	Nift Capsule 250 mg
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Cephradine…250 mg
	Pharmaceutical form of applied drug	Capsule Blue colour Body and Blue colour Cap “0” size capsule

	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	2 x 6's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Velosef 250 mg Capsule by M/s Glaxosmithkline, USFDA Approved
	For generic drugs (me-too status)	Dicef 250 mg Capsule by M/s ICI Pharma (#043849)
	GMP status of the Finished product manufacturer	New license granted on 27/05/2021 Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Pharmagen limited Kot Nabi Bukhswala, 34 Km 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):	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. 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 Velosef 250 mg Capsule (#2158) by Glaxosmithkline Pharma performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Velosef 250mg Capsule by Glaxosmithkline Pharma 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, specificity.
	Remarks: Cephradine is manufactured locally in Pakistan by Pharmadex by acylation of 7 aminodesacetoxycephalospranic acid with mix anhydride. It consists of series of chemical reactions crystallization, filtration, drying milling and compacting then packaging.	

STABILITY STUDY DATA			
Manufacturer of API	M/s Pharmagen limited Kot Nabi Bukhswala, 34 Km Ferozpur, Road, Lahore		
API Lot No.	No. Cephradine / 126 / 2020		
Description of Pack (Container closure system)	Alu-Alu blister of 2 x 6's packed in printed unit Carton along 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: 0,1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Tr-002	Tr-003	Tr-004
Batch Size	200,000 Capsules	200,000 Capsules	200,000 Capsules
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	04-06-2020	10-06-2020	15-06-2020
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

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.	GMP certificate for Parmagen Ltd Lahore # 06/209-DRAP (AD/607409-530) issued by DRAP Pakistan issued on 08-01-2019 was provided
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice from Pharmagen Ltd specifying purchase of cephradine 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 & accelerated)	Submitted

Remarks

Sr.#	Section #.	Deficiencies	Remarks of the firm
1.	***3.2.S.4.4***	The submitted COA from drug substance manufacturer mentions the reference for specs as BP but drug product manufacturer is claiming USP specifications. Clarification is needed	The USP/NF is a drug compendium officially recognized in USA. The equivalent standards i.e. BP have the same acceptance criteria based on similar principles (chromatographic, spectroscopic, titration) and performance characteristics (specificity, accuracy, precision). Claim for drug product is taken from pharmacopeia reference as USP, and test carried out at acceptance criteria on the critical steps of manufacturing. The process has been validated and ensured that it is controlled. Reference on competitors also claimed as GlaxoSmithKline/ Velosef/USP and Indus Pharma/ Vericef/ USP.

2.	***3.2.S.5***	Justification is needed that why specifications of reference standard is USP but the API specification on COA is BP	The USP/NF is a drug compendium officially recognized in USA. So, the product is tested for compliance with USP monograph. While the BP have equivalent alternative standard having same acceptance criteria and make use of analytical procedures based on similar principles and performance characteristics.
3.	***3.2.S.7.3***	Stability data of drug substance for real time study provided by API manufacture is at 25 °C ± 2°C / 60% ± 5%RH for accelerated study and 5 °C ± 3°C is provided but the stability study by drug product manufacturer is at 30 °C ± 2°C / 60% ± 5%RH and 45 °C ± 2°C / 60% ± 5%RH. Clarification is needed	• The Stability Study conducted by Drug Substance (API) manufacturer at 25°C±2°C, 60% ± 5% RH for Accelerated study and 5°C ± 3°C for Real time study as per ICH guidelines accordance with the Zone-IV A conditions. Record of data logger for the storage conditions throughout the transportation herewith enclosed. • The Stability Study conducted by drug product manufacturer at 30°C±2°C, 65% ± 5% RH for Real time study and 40°C ± 2°C / 75% ± 5% RH for Accelerated study as per ICH guideline accordance with the Zone-IV A conditions. • Stability Study of drug substance has been performed by manufacturer (Pharmagen) as per conditions required for API stability, while, the stability of drug product kept at guided conditions.
4.	***3.2.P.3***	Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacturer shall also be submitted	Provided
5.	***2.3.P.4***	Control of excipients, details of method of assay and dissolution are not provided.	We have used Pharmacopeia standard excipients for which monographs and Analytical Procedures are attached, however for inhouse excipient, analytical procedure is attached along with the COA of all excipients used in formulation.
6.	***3.2.P.3.4***	Tests and acceptance criteria should be provided (with justification, including experimental data) performed at the critical steps identified in 3.2.P.3.3 of the manufacturing process, to ensure that the process is controlled	Provided
7.	***3.2.P.6***	COA of primary / secondary reference standard including source and lot number shall be provided	Provided
8.	***3.2.P.8***	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
9.	***3.2.P.8***	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Decision: Approved.

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

183.	Name, address of Applicant / Marketing Authorization Holder	M/s Opal Laboratories Pvt Ltd. LC-41, L.I.T.E., Landhi, Karachi
	Name, address of Manufacturing site.	M/s Opal Laboratories Pvt Ltd. LC-41, L.I.T.E., Landhi, 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
	Details of fee submitted	Form-5F Dy.No 7677 dated 09-03-2021 Rs.20,000/- dated 02-11-2020 (#2039390)
	proposed proprietary name / brand name	Nift Capsule 500 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Cephradine…500 mg
	Pharmaceutical form of applied drug	Capsule Blue color Body and Blue colour Cap of "0" size capsule
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	2 x 6's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefradine 500mg capsule by M/s Kent Pharmaceuticals UK, MHRA Approved
	For generic drugs (me-too status)	Cefrinex 500 mg Capsule by M/s Bosch Pharmaceuticals (Pvt.) Ltd Karachi
	GMP status of the Finished product manufacturer	New license granted on 27/05/2021 Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Pharmagen limited Kot Nabi Bukhswala, 34 Km 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):	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. 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 Velosef 500 mg Capsule (#2158) by Glaxosmithkline Pharma performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Velosef 250mg Capsule by Glaxosmithkline Pharma 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, specificity.
	Remarks: Cephradine is manufactured locally in Pakistan by Pharmadex by acylation of 7 amino desacetoxy-cephalospranic acid with mix anhydride. It consists of series of chemical reactions crystallization, filtration, drying milling and compacting then packaging.	

STABILITY STUDY DATA			
Manufacturer of API	M/s Pharmagen limited Kot Nabi Bukhswala, 34 Km Ferozpur, Road, Lahore		
API Lot No.	No. Cephradine / 126 / 2020		
Description of Pack (Container closure system)	NIFT Capsules 500mg are proposed to be supplied as follows: Alu-Alu blister of 2 x 6's packed in printed unit Carton along 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: 0,1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Tr-002	Tr-003	Tr-004
Batch Size	200,000 Capsules	200,000 Capsules	200,000 Capsules
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	04-06-2020	10-06-2020	15-06-2020
No. of Batches	03		
REQUEST OF EXEMPTION FROM ON SITE INSPECTION			
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.	GMP certificate for Parmagen Ltd Lahore # 06/209-DRAP (AD/607409-530) issued by DRAP Pakistan issued on 08-01-2019 was provided
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Invoice from Pharmagen Ltd specifying purchase of cephradine 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 & accelerated)	Submitted

Remarks

Sr.#	Section #.	Deficiencies	Remarks of the firm
1.	***3.2.S.4.4***	The submitted COA from drug substance manufacturer mentions the reference for specs as BP but drug product manufacturer is claming USP specifications. Clarification is needed	The USP/NF is a drug compendium officially recognized in USA. The equivalent standards i.e. BP have the same acceptance criteria based on similar principles (chromatographic, spectroscopic, titration) and performance characteristics (specificity, accuracy, precision). Claim for drug product is taken from pharmacopeial reference as USP, and test carried out at acceptance criteria on the critical steps of manufacturing. The process has been validated and ensured that it is controlled. Reference on competitors also claimed as GlaxoSmithKline/Velosef/USP and Indus Pharma/Vericef/USP.
2.	***3.2.S.5***	Justification is needed that why specifications of reference standard is USP but the API specification on COA is BP	The USP/NF is a drug compendium officially recognized in USA. So, the product is tested for compliance with USP monograph. While the BP have equivalent alternative standard having same acceptance criteria and make use of analytical procedures based on similar principles and performance characteristics. Reference standard are harmonized as to be used USP, BP or Ph.Eur. if justified with reference to the similarity in IUPAC Nomenclature or chemical abstract of standard taken as primary standard.
3.	***3.2.S.7.3***	Stability data of drug substance for real time study provided by API manufacture is at 25 °C ± 2°C / 60% ± 5%RH for accelerated study and 5 °C ± 3°C is provided but the stability study by drug product manufacturer is at 30 °C ± 2°C / 60% ± 5%RH and 45 °C ± 2°C / 60% ± 5%RH. Clarification is needed	• The Stability Study conducted by Drug Substance (API) manufacturer at 25°C±2°C, 60% ± 5% RH for Accelerated study and 5°C ± 3°C for Real time study as per ICH guidelines accordance with the Zone-IV A conditions. Record of data logger for the storage conditions throughout the transportation herewith enclosed. • The Stability Study conducted by drug product manufacturer at 30°C±2°C, 65% ± 5% RH for Real time study and 40°C ± 2°C / 75% ± 5% RH for Accelerated study as per ICH

			guideline accordance with the Zone-IV A conditions. • Stability Study of drug substance has been performed by manufacturer (Pharmagen) as per conditions required for API stability, white, the stability of drug product kept at guided conditions.
4.	***3.2.P.3***	Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacturer shall also be submitted	Provided
5.	***2.3.P.4***	Control of excipients, details of method of assay and dissolution are not provided.	We have used Pharmacopeia standard excipients for which monographs and Analytical Procedures are attached, however for inhouse excipient, analytical procedure is attached along with the COA of all excipients used in formulation.
6.	***3.2.P.3.4***	Tests and acceptance criteria should be provided (with justification, including experimental data) performed at the critical steps identified in 3.2.P.3.3 of the manufacturing process, to ensure that the process is controlled	Provided
7.	***3.2.P.6***	COA of primary / secondary reference standard including source and lot number shall be provided	Provided
8.	***3.2.P.8***	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
9.	***3.2.P.8***	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Decision: Approved.

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

New Section:

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 / 03 Products

184.	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,6 7/2,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. 24522 dated 30/08/2021
	Details of fee submitted	PKR 30,000/-: dated 18/06/2021
	proposed proprietary name / brand name	Zolnex 0.5mg tablet
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Alprazolam…….0.5mg
	Pharmaceutical form of applied drug	White, Round shaped, bisect oral tablet
	Pharmacotherapeutic Group of (API)	Benzodiazepine
	Reference to Finished product specification	USP
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Xanax 0.5mg tablet by M/s Upjohn, USFDA Approved.
	For generic drugs (me-too status)	Zolam 0.5 mg Tablet by M/s Saydon, Reg. No. 060002
	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 Alprazolam 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 substances (2-Amino-5-Chlorobenzophenone), 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 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (541921),(551318), (560670)
	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 Xanax 0.5mg tablet by Pfizer by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).

		CDP has been performed against the innovator brand that is Xanax 0.5mg tablet by Pfizer 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 uniformity of contents missing

STABILITY STUDY DATA

Manufacturer of API	M/s Cambrex Profarmaco Milano S.R.L Via Curiel,34-20067 Paullo-Milano,Italy.		
API Lot No.	801012		
Description of Pack (Container closure system)	Alu-PVC 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: 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 tab47	
Manufacturing Date	02-2021	02-2021	
Date of Initiation	09-02-2021	23-02-2021	
No. of Batches	02		

Administrative Portion

19.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
20.	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.
21.	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
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	Submitted
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#	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
3.	3.2.P.5	In assay the injection volume prescribed inn USP is 25 ul but firm used 100 ul. justification is needed	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)
4.	3.2.P.5	The USP monograph for this dosage form includes content uniformity test. Justify the exemption of these tests.	In the content uniformity test internal standard TRIAZOLAM is used (Reference USP 43) which was not received with the shipment. We used alternate method for uniformity of dosage units by way of weight variation.
5.		• 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.	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

Strength	Formulation development analysis finished date	CDP end date
0.5 mg	01/03/2021	03/03/2021
0.25 mg	17/03/2021	19/03/2021
1 mg	24/03/2021	25/03/2021

Decision: Approved.

- **Firm shall submit content uniformity test data as per USP monograph before issuance of letter.**
- **Manufacturer will place first three production batches on long term stability studies throughoutproposed 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.**

185.	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,6 7/2,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. 28574 dated 18/Oct/2021
	Details of fee submitted	PKR 30,000/-: (35985451) dated 18/06/2021
	The proposed proprietary name / brand name	Zolnex 1 mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Alprazolam…….1 mg
	Pharmaceutical form of applied drug	White, Round shaped, bisect oral tablet
	Pharmacotherapeutic Group of (API)	Benzodiazepine
	Reference to Finished product specifications	USP
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xanax 1 mg tablet by M/s Upjohn, USFDA Approved.
	For generic drugs (me-too status)	Zolam 1 mg Tablet by M/s Saydon, Reg. No. 079392
	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 Alprazolam 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 substances (2-Amino-5-Chlorobenzophenone), 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 72 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (541921), (551318), (560670)
	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 Xanax 1 mg tablet by Pfizer by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the innovator brand that is Xanax 1 mg tablet by Pfizer 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 uniformity of contents missing

STABILITY STUDY DATA

Manufacturer of API	M/s Cambrex Profarmaco Milano S.R.L Via Curiel,34-20067 Paullo-Milano,Italy.		
API Lot No.	801012		
Description of Pack (Container closure system)	Alu-PVC 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: 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	
Manufacturing Date	03-2021	03-2021	
Date of Initiation	3-2021	3-2021	
No. of Batches	02		

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 No. II-API/44/H/2019 issued by Italian Medicine Agency.
3.	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
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 #	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 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
3.	3.2.P.5	In assay the injection volume prescribed inn USP is 25 ul but firm used 100 ul. justification is needed	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)
4.	3.2.P.5	The USP monograph for this dosage form includes content uniformity test. Justify the exemption of these tests.	In the content uniformity test internal standard TRIAZOLAM is used (Reference USP 43) which was not received with the shipment. We used alternate method for uniformity of dosage units by way of weight variation.
5.		• 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.	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 **Strength** | **Formulation development analysis finished date** | **CDP end date** 0.5 mg | 01/03/2021 | 03/03/2021 0.25 mg | 17/03/2021 | 19/03/2021 1 mg | 24/03/2021 | 25/03/2021

Decision: Approved.

- **Firm shall submit content uniformity test data as per USP monograph before issuance of letter.**
- **Manufacturer will place first three production batches on long term stability studies**

throughoutproposed 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.**

186.	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. 7455 dated 08 March 2021
	Details of fee submitted	PKR 50,000/- (#2028870) dated 21/04/2020
	proposed proprietary name / brand name	Ultragesic DS Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tramadol HCl …….....75mg Paracetamol..... 650mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Analgesic/NSAID
	Reference to Finished product specification	USP
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Tramadol/Paracetamol 75mg/650mg Tablets Aspire Pharma Ltd, MHRA Approved UK
	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.	**Paracetamol** M/s. Zafa Chemie Raiwind Manga Bypass Near Sunder Industrial Estate Gate No.3, Lahore **Tramadol HCl** Supriya Lifescience Ltd A-5/2, Lote-Parshuram Industrial Area, M.I.D.C, Taluka-Khed, District-Ratnagriri, Maharashtra, India 415 722
	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 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 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: **Tramadol HCl:** Real time: 30˚C ± 2˚C / 65% ± 5%RH for 48 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months **Paracetamol:** Real time: 30˚C ± 2˚C / 65% ± 5%RH for 54 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: **Tramadol HCl:** SLL/TDM/0715011, SLL/TDM/0715012, SLL/TDM/0715014 **Paracetamol:** 1331, 1332, 1333
	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 **Tramadol/ Paracetamol 75mg/650mg** tablet by **Teva Pharma** by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is **Tramadol/ Paracetamol 75mg/650mg** tablet by **Teva Pharma** in Acid media (0.1 N HCL) & Phosphate Buffer (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 linearity, range, accuracy, precision, specificity.
	Remarks: • The formulation is developed using similar excipients as reference which uses Povidone (E1201), magnesium stearate (E572), anhydrous colloidal silica, sodium, starch glycolate (type A) and pregelatinized maize starch. But Firm use pregelatinized corn starch, cross-povidone , povidone and magnesium stearate as firm claims that we used pregelatinized starch in 3 different role as binder, diluent and disintigrent instead magnesium stearate is increased instead of stearic acid so applied product has less excipients but no excipient outside the reference is added.	

STABILITY STUDY DATA	
Manufacturer of API	**Paracetamol** M/s. Zafa Chemie Raiwind Manga Bypass Near Sunder Industrial

	Estate Gate No.3, Lahore **Tramadol HCl** Supriya Lifescience Ltd A-5/2, Lote-Parshuram Industrial Area, M.I.D.C, Taluka-Khed, District-Ratnagriri, Maharashtra, India 415 722		
API Lot No.	**Tramadol HCl:** SLL/TDM/0715011, SLL/TDM/0715012, SLL/TDM/0715014 **Paracetamol:** 1331, 1332, 1333		
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-090419	TF-100419	TF-110419
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	04-2019	04-2019	04-2019
Date of Initiation	09-04-2019	10-04-2019	11-04-2019
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.	**Tramadol HCl:** Copy of GMP certificate No. NEW-WHO-GMP/CERT/KD/67649/2018/11/25185 issued by FDA Maharashtra valid till 04/10/2021. **Paracetamol:** Copy of GMP certificate No. 211/2018-DRAP (AD/735850-228) issued by DRAP LAHORE valid till 02/10/2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Attested invoice from ADC attached for Tramadol HCl Invoice No. SLL/EXP/1310-17-18 • Paracetamol is locally purchased
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 & 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 translated for tramadol Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country) for both API's	Valid drug manufacturing licence and Valid GMP Certificate for supriya pharma (valid till 4- 2022) and Zafa Pharma (Valid till 10-2022) is provided
2.	3.2.S.4.4	The submitted COA from drug substance manufacturer mention BP specifications with titration method of assay but COA of dug product manufacturer adopted USP method for assay although all other tests are according to BP. clarification is needed.	Alternative test method other than compendial can be used and BP/USP both allow with certain conditions However, in our case, we do not use non-compendial test method. we have used USP test method (HPLC based) for determination of assay content because HPLC technique is more modern, reliable, specific and accurate in comparison of titration. In chromatography, retention time of analyte is specific for an analyte but titration technique is not specific for a particular analyte. We had done analytical method verification studies on assay method and submitted the same;
3.	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	"Magnesium stearate" is from plant source as declared by manufacturer "Peter Greven" therefore it is not applicable for BSE and TSE.
4.		• 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.	We have carried out CDP after stability because the stability study are the part of formulation development if a trail batches do no meet the specification after 03 months it mean formulation development is not appropriate and has to be address, so multiple trails have to be done to reach conclusive formulation in that case if CDP performed earlier then it must be performed again and again secondly both the actives in this case are from BCS class 1 so chance of dissolution failer was very low so that's why CDP was performed after commencement of stability study

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.

Case No.04: Registration applications of drugs for which stability study data is submitted

c. Verification of stability study data/Exemption

a. New cases

187.	Name and address of manufacturer / Applicant	M/s Wilshire Laboratories Pvt Ltd. 124/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Regus 97/103 mg Tablet
	Composition	Each film coated tablet contains: Sacubitril…..97mg Valsartan…..103mg
	Diary No. Date of R& I & fee	Dy. No. 113, 1/1/2018, Rs: 50,000/- 20/12/2019 (#0619510),
	Pharmacological Group	Angiotensin Receptor Neprilysin Inhibitor
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10, 20, 30, 60's/ As per SRO
	Approval status of product in Reference Regulator Authorities	Entresto Tablet of Novartis pharms (USFDA Approved)
	Me-too status	NA
	GMP status	Last GMP inspection conducted on 08-08-2019, and the report concludes that the firm was operating at an acceptable compliance of cGMP. The firm was further advised to submit CAPA report with respect to the current inspection proceedings.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Regus 97/103 mg Tablet		
Name of Manufacturer	M/s Wilshire Laboratories Pvt Ltd. 124/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore		
Manufacturer of API	M/s Zhuhai Rundu Pharmaceutical Co., Ltd, No 6-airport north road, Sanzao town, Jinwan district Zhuhai Guangdong, China,		
API Lot No.	**Sacubitril/Valsartan:** 57318060102		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30˚C ± 2˚ C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
Time Period	Real time: 24 months Accelerated:6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (month) Real Time: 0,3,6, 9,12, 18, 24 (month)		
Batch No.	T001	T002	T003
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	01-2019	01-2019	01-2019
Date of Initiation	24-03-2019	24-03-2019	24-03-2019
No. of Batches	03		
Date of Submission	7/08/2020 (19268)		

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	Inspection dated 20-07-2019 for verification of authenticity of stability data submitted for registration of

		velbuvir 400 mg/100 mg tablet
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Sacubitril/Valsartan**: Copy of COA (Batch# 57317080101 from Zhuhai Rundu Pharmaceutical Co., Ltd China is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Yes
4.	Stability study data of API from API manufacturer	Yes (for zone IV-B)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of certificate of cGMP: Valid Dated: 21-12-2021 from office of the Zhuhai Food and drug administration (City not a provincial)
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Commercial invoice/ air way bill for Sacubitril/Valsartan from M/s Zhuhai Rundu Pharmaceutical Co., Ltd, Guangdong, China, has been submitted NOT attested by AD, DRAP I&E Lahore.
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes (same as API manufacturer)
9.	Drug-excipients compatibility studies (where applicable)	NA (Formulation of applied drug product is qualitatively similar to that of innovator Brand)
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** T001 / 1.5 kg / 01-2019 T002 / 1.5 kg / 01-2019 T003 / 1.5 kg / 01-2019
11.	Record of comparative dissolution data (where applicable)	Comparative dissolution studies have been performed with competitor product Enteresto (Novartis) batch # EW2457 in following mediums: a. pH 6.8 buffer b. pH 4.5 buffer c Water d. pH 0.1 N HCl buffer F2 factor value has calculated which is within acceptance range for 0.1 HCL in other medium the dissolution is more than 85% within 15 min so no F2 calculation needed.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Yes
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Yes

REMARKS OF EVALUATOR

S#	Deficiency	Response
1.	Firm has to submit valid copy of cGMP for M/s Zhuhai Rundu Pharmaceuti`1cal Co., Ltd,	Firm has submitted the valid GMP of Zuhai rundu pharma issued by Guangdong food and

	Guangdong, China, issued by Guangdong Food and Drug Administration not city.	drug administration China (#YUE20160246) valid till 2024
2.	On air way bill no batch number or AD attestation is there. Provide some evidence (like Form 7 etc.) that same batch was used in the stability study for which import documents had been submitted	The commercial invoice for the batch number 57318060102 attested by AD DRAP Lahore is provided along with form 3 and 7.
3.	The applicant has not performed impurity testing for NDMA or NDEA. The COA provided by the API manufacturer do not confirm impurity testing for NDMA or NDEA as well.	The API manufacturer Zhuhai Rundu has conducted impurity testing for NMDA and NDEA as per results the NDMA has been found under the limit i.e. NMT 0.3ppm and NDEA was not detected. Declaration, Detailed method and results provided
4.	Justify the formula used to calculate the assay and dissolution. Formula for assay it does not have potency of standard LC and wt. of tablet etc.	Formula used to calculate assay Abd dissolution is the ratio between absorption of sample to absorption of standard taking potency equivent to 100%. Whereas the tablet taken is as per prescribes in the testing method
5.	Reference standard is as cocrystals complex sacubitril/ valsartan or both are separate, provide COA of reference standard. Need detail of reference standard used for the performance of identification tests by comparing the IR spectra of the API shall be submitted.	The Reference standard used by manufacturer for identification test by comparing the IR spectra of API is a cocrystal complex sacubitril/ valsartan COA with batch # 160405 was provided
6.	The API manufacturer and Finished product manufacturer have not performed powder X-ray diffraction analysis to differentiate the co-crystals from coprecipitate etc.	The manufacture evaluates the said product for structure elucidation from instrument analysis and research center of sunyatsen university china. They also done evaluation for crystal form but x ray diffraction was not done. The firm also claims that some other renowned pharma is also purchasing API from the same source)
7.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Provided
8.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Decision: The Board deferred the case for submission of characterization studies of drug substance performed to differentiate co-crystal from coprecipitate by drug substance manufacturer.

188.	Name and address of manufacturer / Applicant	M/s Wilshire Laboratories Pvt Ltd. 124/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Regus 24/26 mg Tablet
	Composition	Each film coated tablet contains: Sacubitril…..24 mg Valsartan…..26 mg
	Diary No. Date of R& I & fee	Dy. No. 111, 1/1/2018, Rs: 50,000/- 20/12/2019 (#0619524),
	Pharmacological Group	Angiotensin Receptor Neprilysin Inhibitor
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10, 20, 30, 60's/ As per SRO
	Approval status of product in Reference Regulator Authorities	Entresto Tablet of Novartis pharms (USFDA Approved)
	Me-too status	NA

	GMP status	Last GMP inspection conducted on 08-08-2019, and the report concludes that the firm was operating at an acceptable compliance of cGMP. The firm was further advised to submit CAPA report with respect to the current inspection proceedings.
	Remarks of the Evaluator	

STABILITY STUDY DATA			
Drug	Regus 24/26 mg Tablet		
Name of Manufacturer	M/s Wilshire Laboratories Pvt Ltd. 124/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore		
Manufacturer of API	M/s Zhuhai Rundu Pharmaceutical Co., Ltd, No 6-airport north road, Sanzao town, Jinwan district Zhuhai Guangdong, China,		
API Lot No.	**Sacubitril/Valsartan:** 57318060102		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
Time Period	Real time: 24 months Accelerated:6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (month) Real Time: 0,3,6, 9,12, 18, 24 (month)		
Batch No.	T001	T002	T003
Batch Size	2500 tablet	2500 tablet	2500 tablet
Manufacturing Date	02-2019	02-2019	02-2019
Date of Initiation	15-05-2019	15-05-2019	15-05-2019
No. of Batches	03		
Date of Submission	7/08/2020 (19268)		

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	Inspection dated 20-07-2019 for verification of authenticity of stability data submitted for registration of velbuvir 400 mg/100 mg tablet
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Sacubitril/Valsartan**: Copy of COA (Batch# 57317080101 from Zhuhai Rundu Pharmaceutical Co., Ltd China is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Yes
4.	Stability study data of API from API manufacturer	Yes (for zone IV-B)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of certificate of cGMP: Valid Dated: 21-12-2021 from office of the Zhuhai Food and drug administration (City not a provincial)
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Commercial invoice/ air way bill for Sacubitril/Valsartan from M/s Zhuhai Rundu Pharmaceutical Co., Ltd, Guangdong, China, has been submitted NOT attested by AD, DRAP I&E Lahore.
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes (same as API manufacturer)

9.	Drug-excipients compatibility studies (where applicable)	NA (Formulation of applied drug product is qualitatively similar to that of innovator Brand)
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** T001 / 1.5 kg / 01-2019 T002 / 1.5 kg / 01-2019 T003 / 1.5 kg / 01-2019
11.	Record of comparative dissolution data (where applicable)	Comparative dissolution studies have been performed with competitor product Enteresto (Novartis) batch # EW2457 in following mediums: a. pH 6.8 buffer b. pH 4.5 buffer c Water d. pH 0.1 N HCl buffer F2 factor value has calculated which is within acceptance range for 0.1 HCL in other medium the dissolution is more than 85% within 15 min so no F2 calculation needed.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Yes
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Yes

REMARKS OF EVALUATOR

S#	Deficiency	Response
1.	Firm has to submit valid copy of cGMP for M/s Zhuhai Rundu Pharmaceuti`1cal Co., Ltd, Guangdong, China, issued by Guangdong Food and Drug Administration not city.	Firm has submitted the valid GMP of Zuhai rundu pharma issued by Guangdong food and drug administration China (#YUE20160246) valid till 2024
2.	On air way bill no batch number or AD attestation is there. Provide some evidence (like Form 7 etc.) that same batch was used in the stability study for which import documents had been submitted	The commercial invoice for the batch number 57318060102 attested by AD DRAP Lahore is provided along with form 3 and 7.
3.	The applicant has not performed impurity testing for NDMA or NDEA. The COA provided by the API manufacturer do not confirm impurity testing for NDMA or NDEA as well.	The API manufacturer Zhuhai Rundu has conducted impurity teting for NMDA and NDEA as per results the NDMA has been found under the limit i.e. NMT 0.3ppm and NDEA was not detected. Declaration, Detailed method and results provided
4.	Justify the formula used to calculate the assay and dissolution. Formula for assay it does not have potency of standard LC and wt. of tablet etc.	Formula used to calculate assay Abd dissolution is the ratio between absorption of sample to absorption of standard taking potency equivent to 100%. Whereas the tablet taken is as per prescribes in the testing method
5.	Reference standard is as cocrystals complex sacubitril/ valsartan or both are separate, provide COA of reference standard. Need detail of reference standard used for the performance of identification tests by comparing the IR	The Reference standard used by manufacturer for identification test by comparing the IR spectra of API is a cocrystal complex sacubitril/ valsartan COA with batch # 160405 was provided

	spectra of the API shall be submitted.	
6.	The API manufacturer and Finished product manufacturer have not performed powder X-ray diffraction analysis to differentiate the co-crystals from coprecipitate etc.	The manufacture evaluate the said product for structure elucidation from instrument analysis and research center of sunyatsen university china. They also done evaluation for crystal form but x ray diffraction was not done. The firm also claims that some other renowned pharma are also purchasing API from the same source)
7.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Provided
8.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Decision: The Board deferred the case for submission of characterization studies of drug substance performed to differentiate co-crystal from coprecipitate by drug substance manufacturer.

b. Deferred Cases:

189.	Name and address of manufacturer / Applicant	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Glitab 5/850 mg Tablet
	Composition	Each Film Coated Tablet Contains: Dapagliflozin Propanediol Monohydrate Eq. to Dapagliflozin…5mg Metformin HCl…..…850 mg"
	Diary No. Date of R& I & fee	Dy. No 2271 dated 10-11-2016 Rs.50,000/- (#0569345) 09-09-2016
	Pharmacological Group	Selective sodium glucose co-transporter subtype-2 (SGLT2) Inhibitor and Biguanides
	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 Regulator Authorities	Xigduo 5 mg/850 & 5/1000 mg film coated tablets of AstraZeneca approved by EMA
	Me-too status	NA
	GMP status	03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.
	Remarks of the Evaluator	Assay of both is by HPLC method Dissolution is as per reference product

STABILITY STUDY DATA

Drug	Glitab 5/850 mg Tablet
Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
Manufacturer of API	Dapagliflozin Propanediol monohydrate: M/S Jiangsu Yongan Pharmaceuticals Co., Lt China 18, Provincial Highway 237, Huaian Economic Development Zone, Jiangsu China Metformin: Aarti Drugs Pvt Ltd Mahendra Industrial Estate, Ground Floor, Road No. 29, Plot No. 109-D Sion (East) Mumbai India.
API Lot No.	Dapagliflozin Propanediol monohydrate: DGF-20110011 Metformin: MEF/19081807
Description of Pack (Container closure system)	As per SRO

Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
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.	367DS01	367DS02	367DS03
Batch Size	2000	2000	2000
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	14-09-2020	14-09-2020	14-09-2020
No. of Batches	03		
Date of Submission	08-07-2021 (19138)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	For Dapagliflozin The firm has submitted COA from both API M/S Jiangsu Yongan Pharmaceuticals Co., Lt China 18, Provincial Highway 237, Huaian Economic Development Zone, Jiangsu China For Metformin: The firm has submitted COA from both API Aarti Drugs Pvt Ltd Mahendra Industrial Estate, Ground Floor, Road No. 29, Plot No. 109-D Sion (East) Mumbai and FPP manufacturer
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Yes
4.	Stability study data of API from API manufacturer	Provided (for zone IV-B)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Dapagliflozin: Copy of GMP Certificate No # … for M/s Jiangsu Yongan Pharmaceuticals Co., Lt China issued by China Food and Drug Administration, is submitted. valid till 14-1-2024. For Metformin: Copy of GMP Certificate No # 6095581 issued by FDA Maharashtra for M/s Aarti industries limited plot # K. 17/18/19, MIDC Tarapur dist Thane zone 4 valid till 31-12-2022
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Dapagliflozin: Copy of commercial invoice has been submitted issued by ADC, Karachi DRAP. Address of Exporter (Head office): M/s Jiangsu Yongan Pharmaceuticals China

Batch No.	Invoice No.	Quantity	Date
DGF-201811001	ZY18120402G/W	500 g	4/1/19

Metformin:

<table>
<tr><td></td><td></td><td>Copy of commercial invoice has been submitted issued by ADC, Karachi DRAP.
Address of Exporter (Head office): M/s
M/S Aarti industries India
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity</th><th>Date</th></tr>
<tr><td>MEF/1907 074</td><td>1907074</td><td>1000 kg</td><td>7-Nov-2019</td></tr>
</table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes (same as API manufacturer)</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA
(Formulation of applied drug product is qualitatively similar to that of innovator Brand)</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>367DS01</td><td>2000</td><td>09-2020</td></tr>
<tr><td>367DS02</td><td>2000</td><td>09-2020</td></tr>
<tr><td>367DS03</td><td>2000</td><td>09-2020</td></tr>
</table></td></tr>
<tr><td></td><td>Record of comparative dissolution data (where applicable)</td><td>No
Firm has submitted Comparative dissolution study of their product with “Xigdu” 5/1000mg
The details are as follows:
<table>
<tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr>
<tr><td>Product name</td><td>Xigduo</td><td>Product name</td><td>Dapagliflozin 10 mg</td></tr>
<tr><td>Batch #</td><td>137421</td><td>Batch #</td><td>371DS01</td></tr>
<tr><td>Mfg date</td><td>01-2021</td><td>Mfg date</td><td>09-2020</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
Comparative dissolution studies for other strengths not performed. It has been performed with competitor product Xigduo by Hilton for higher strength i.e. as formulation is dose proportional)</td></tr>
<tr><td>11.</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>Yes</td></tr>
<tr><td>12.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Provided</td></tr>
<tr><td>13.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Yes</td></tr>
</table>

REMARKS OF EVALUATOR

Sr. No.	Observations/Documents Required	Status of Document/Justifications
1.	Valid copy of DML of FPP should be provided as provided one is expired.	The valid DML # 000105 (by way of formulation) of Nabiqasim Industries renewed w.e.f. 12-07-2019 and valid upto 11-07-2024 is Provided

2.	Firm has not submitted the documents for procurement of reference and impurity standards.	Metformin HCL working standard and impurity standard record is Provided For Dapagliflozin, As there is no specified impurities mention on COA and DMF of API manufacturer so there is no impurity standard required in impurity testing. There are no documents of procurement of Working standard of Dapagliflozin API B#DGF-201812001.Although working standard of Dapagliflozin API received to us from manufacturer with shipment sample of "Lurasidone HCl", Batch No. 201909001.
3.	In Reference of previous approval of application with stability study data firm provides the panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail of the testing reports cannot be made as audit trail was not activated. So, on that base exemption could be granted.	There is mistake incurred in the Panel Inspection Report of Sofosbuvir 400mg tablet at Point No.31wherein by mistake it was mentioned that "the Audit trail on the testing records cannot be made as audit trail was not activated". While on the same date by the same Panel Inspection Team during the inspection for our another new drug "Novasept Gel" the panel has mentioned "Audit trail reports were available and randomly checked" in Inspection Report at Point No.31 of Novasept Gel. Copy of Inspection Report of Novasept Gel is attached as Annexure – C.
4.	Please submit clarification for difference in the address of the manufacturer of metformin Hydrochloride on invoice, stability data & on GMP certificate moreover submit the GMP Certificate of relevant site, also provide list of drugs for which GMP certificate is issued to M/s Aarti Pharma.	Please note that on invoice, mention address is of manufacturer corporate office while on stability data , GMP Certificate , Retention of Licence certificate manufacturing facility address for Metformin HCl is mention. On COA address of manufacturing facility of Metformin HCl and Corporate Office is mentioned. Declaration from Aarti Drugs Limited regarding confirmation of address is Provided GMP certificate of Relevant Site for Metformin HCl API and list of drugs for which GMP certificate is issued to M/s Aarti Pharma attached is Provided
5.	Record of comparative dissolution data is missing.	Record of comparative dissolution data is provided for higher strength
6.	Compliance record of HPLC software 21 CFR & audit trail reports on product testing.	Compliance record of HPLC software 21 CFR & audit trail reports on product testing is Provided
7.	Record of Digital data logger for temperature and humidity monitoring of stability chambers(real time and accelerated)	The record of Digital data logger for temperature and humidity monitoring of stability chambers is Provided

Decision of 312: Deferred for comparative dissolution data as the provided data is for different formulation

Remarks of evaluator:

Comparative dissolution studies for this strength was performed. It has been performed with competitor product Daplozmet 5/850 mg by Highnoon Lab at pH 1.2, 4.5 and 6.8 (dated 10-2021)

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.

190.	Name and address of manufacturer / Applicant	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Daplozin 5 mg Tablet

	Composition	Each Film coated tablet contains: Dapagliflozin propanediol monohydrate eq. to dapagliflozin….5 mg
	Diary No. Date of R& I & fee	Dy. No 2235 dated 2-11-2016 Rs.50,000/- (#0313883) 29-4-2016
	Pharmacological Group	Selective sodium glucose co-transporter subtype-2 (SGLT2) Inhibitor
	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 Regulator Authorities	Farxiga tablet 5 & 10mg by Astrazeneca AB (USFDA approved)
	Me-too status	NA
	GMP status	03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.
	Remarks of the Evaluator	Assay of ……..is by HPLC method Dissolution is as per reference product,

STABILITY STUDY DATA

Drug	Daplozin 5 mg Tablet		
Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi		
Manufacturer of API	Dapagliflozin Propanediol monohydrate: M/S Jiangsu Yongan Pharmaceuticals Co., Lt China 18, Provincial Highway 237, Huaian Economic Development Zone, Jiangsu China		
API Lot No.	Dapagliflozin Propanediol monohydrate: DGF-20110011		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
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.	370DS01	370DS02	370DS03
Batch Size	2000	2000	2000
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	27-09-2020	27-09-2020	27-09-2020
No. of Batches	03		
Date of Submission	5 July 2021 (18810)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	For Dapagliflozin The firm has submitted COA from both API Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road, Sanzao Town, Jinwan District,

<table>
<tr><td></td><td></td><td>Guangdong, China and FPP manufacturer</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer</td><td>Yes</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Provided (for zone IV-B)</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>Dapagliflozin:
Copy of GMP Certificate No # … for M/s Jiangsu Yongan Pharmaceuticals Co., Lt China issued by China Food and Drug
Administration, is submitted. valid till 14-1-2024.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice has been
submitted issued by ADC, Karachi DRAP.
<table>
<tr><td>Batch No.</td><td>Invoice No.</td><td>Quantity</td><td>Date</td></tr>
<tr><td>DGF-201811001</td><td>ZY18120402G/W</td><td>500 g</td><td>4/1/19</td></tr>
</table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes (same as API manufacturer)</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA
(Formulation of applied drug product is qualitatively similar to that of innovator Brand)</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches:
<table>
<tr><td>Batch No.</td><td>Batch Size</td><td>Mfg. Date</td></tr>
<tr><td>370DS01</td><td>2000</td><td>09-2020</td></tr>
<tr><td>370DS02</td><td>2000</td><td>09-2020</td></tr>
<tr><td>370DS03</td><td>2000</td><td>09-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>No
Firm has submitted Comparative dissolution study of their product with “Dapa 10 mg by Hilton Pharma” The details are as follows:
<table>
<tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr>
<tr><td>Product name</td><td>Dapa 10 mg tablets</td><td>Product name</td><td>Dapagliflozin 10 mg</td></tr>
<tr><td>Batch #</td><td>137421</td><td>Batch #</td><td>371DS01</td></tr>
<tr><td>Mfg date</td><td>01-2021</td><td>Mfg date</td><td>09-2020</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
Comparative dissolution studies for other strengths not performed. It has been performed with competitor product Dapa 10 mg by Hilton for higher strength i.e. as formulation is dose proportional)</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>Yes</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Provided</td></tr>
</table>

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

REMARKS OF EVALUATOR

Sr. No.	Observations/Documents Required	Status of Document/Justifications
1.	Firm has not submitted documents for procurement of reference and impurity standards.	Reference Standard COA is provided As there is no specified impurities mention on COA and DMF of API manufacturer so there is no impurity standard required in impurity testing. *There are no documents of procurement of Working Standard of Dapaglifozin API B # DGF-201812001. Although working standard of Dapaglifozin API is received to us from manufacturer with shipment sample of "Lurasidone HCl", Batch No. 201909001.
2.	Valid copy of DML of FPP should be provided as provided one is expired.	The valid DML # 000105 (by way of formulation) of Nabiqasim Industries renewed w.e.f. 12-07-2019 and valid upto 11-07-2024 is provided
3.	COA of API from API manufacturer is needed.	COA of API from API manufacturer is provided
4.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is provided
5.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The record of Digital data logger for temperature and humidity monitoring of stability chambers in soft copy (CD) is provided. While we have already submitted a file to DRAP containing the hard copy of data logger.
6.	In reference of previous approval of applications with stability study data firm provides the panel inspection of Sofosbuvir 400mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail on the testing records cannot be made as audit trail was not activated. So on that base exemption could be granted.	There is mistake incurred in the Panel Inspection Report at Point No.31wherein by mistake it was mentioned that "the Audit trail on the testing records cannot be made as audit trail was not activated". While on the same date by the same Panel Inspection Team during the inspection for our another new drug "Novasept Gel" the panel has mentioned "Audit trail reports were available and randomly checked" in Inspection Report at Point No.31 of Novasept Gel. Copy of Inspection Report of Novasept Gel is provided.

Decision of 312: Deferred for comparative dissolution data as the provided data is for different formulation

Remarks of evaluator:

Comparative dissolution studies for this strength was performed. It has been performed with competitor product Dapa 5 mg (Batch # 136537) at pH 1.2, 4.5 and 6.8 (dated 9-2021)

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.

191.	Name and address of manufacturer / Applicant	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Glytec-M XR 50/1000 mg Tablet
	Composition	Each Film Coated Tablet Contains: Sitagliptin as phosphate Monohydrate …50mg Metformin HCl (extended release) …1000mg

	Diary No. Date of R& I & fee	Dy. No 14274 dated 17-04-2018 Rs.20,000/- Dated 17-04-2018
	Pharmacological Group	Anti- diabetic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 14"s As per SRO
	Approval status of product in Reference Regulator Authorities	JANUMET® XR 50/500 mg, 50/1000 mg, 100/1000 mg (sitagliptin and metformin HCl) Extended-Release Tablets (USFDA)
	Me-too status	Tagipmet XR tablets by Highnoon Lab limited. 084651
	GMP status	03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Glytec-M XR 50/1000 mg Tablet		
Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi		
Manufacturer of API	**For Sitagliptin phosphate monohydrate:** M/s Zheijiang Yengtai Pharmaceutical Co., Ltd, China Address: No1 Donghai 4th avenue zheijiang provincial chemical and medical raw material base Linhai zone, Linhai city Zhejiang province China **For Metformin hydrochloride:** Aarti industries LTD. Address: Plot No. K-17/18/19 MIDC Tarapur 401506, Dist Thane zone 4 Maharashtra, India.		
API Lot No.	**Sitagliptin phosphate monohydrate:** 1827-0001-20009 **Metformin hydrochloride**: MEF/1901807		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
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.	316DS01	316DS02	316DS03
Batch Size	1500	1500	1500
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	07-2020	07-2020	07-2020
No. of Batches	03		
Date of Submission	25/02/2021 (6326)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

S.#	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting.

<table>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>For Sitagliptin:
The firm has submitted COA for from both API and FPP manufacturer
For Metformin hydrochloride:
The firm has submitted COA for from both API and FPP manufacturer</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer</td><td>Yes</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Provided (for zone IV-B)</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>Sitagliptin:
The firm has provided copy of Certificate (Certificate# 201807039) of GMP compliance issued to M/s Zheijiang Yongtai Pharmaceutical Co., Ltd., Zheijiang province by CFDA valid Up to june-30-2021.
For Metformin hydrochloride:
The firm has submitted copy of GMP certificate declaring following information:
Certificate No. 6095581
Issued to: I Aarti industries LTD.
Address: Plot No. K-17/18/19 MIDC Tarapur 401506, Dist Thane zone 4 Maharashtra, India.
Issued by: Food & Drugs Administration, Maharashtra.
Validity: Valid Till 24-09-2021.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The Proof of Purchase of API Sitagliptin as Phosphate from M/s. Zheijang Yongtai Pharmaceutical Co., Ltd and Metformin HCl from M/s. Aarti Drugs Ltd., duly attested by AD- Karachi is provided.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes (same as API manufacturer)</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>316DS01</td><td>1500</td><td>07-2020</td></tr>
<tr><td>316DS01</td><td>1500</td><td>07-2020</td></tr>
<tr><td>316DS01</td><td>1500</td><td>07-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution studies for this strength not performed. It has been performed with competitor product Janumet tablet XR (Merck) for higher strength i.e. Sita/Met XR 100/1000 mg as formulation is dose proportional.</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>Yes</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Provided</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>Provided</td></tr>
</table>

Remark of Evaluator:

S.#	Observations/Documents Required	Status of Document/Justifications
1.	Firm has to submit valid copy of cGMP for M/s. Zheijang Yongtai Pharmaceutical Co., Ltd., Zheijiang Province. As provided one is valid only till 2021.	The valid copy of cGMP Certificate valid up to 28-06-2023 for M/s. Zheijang Yongtai Pharmaceutical Co., Ltd., Zheijiang Province is provided.
2.	Documents for the procurement of API with approval from DRAP.	The Proof of Purchase of API Sitagliptin as Phosphate from M/s. Zheijang Yongtai Pharmaceutical Co., Ltd and Metformin HCl from M/s. Aarti Drugs Ltd., duly attested by AD- Karachi is provided.
3.	Stability study data of API from API manufacturer.	Stability Data of API Manufacturer Sitagliptin as Phosphate from M/s. Zheijang Yongtai Pharmaceutical Co., Ltd and Metformin HCl from M/s. Aarti Drugs Ltd., is provided.
4.	Since API of Sitagliptin is being incorporated via coating solution so how it is possible to ensure that proper amount of active has been incorporated in dosage form while using 100% quantity in master formulation.	To ensure proper amount of Sitagliptin API incorporated in dosage form we have taken 100% excess quantity of API in master formulation i.e. 200% Master formulation is provided.
5.	Documents for the procurement of reqference and impurity standards missing for sitagliptin phosphate monohydrate.	Documents for the procurement of reference and impurity standards missing for Stagliptin Phosphate Monohydrate is provided.
6.	In innovator product approved in USFDA propyl gallate assay was performed (https:/www.accessdata.fda.gov/ drugsaftfda_docs/nda/2012/ 202270 Orig1s000ChemR.pdf) as propyl gallate is carcinogenic and is permissible in certain limits. Justify the exemption of this test by applicant.	We have not use propyl gallate in our formulation so there is no need to perform its testing.
7.	The GMP, Quality Control Department analysis report is from Zheijiang Yengtai Pharmaceutical Co., Ltd, China and on many documents including Commercial Invoice name is mentioned as Zhejiang Hengdian Apeloa China. Provide the relationship.	The Zheijiang Yengtai Pharmaceutical Co., Ltd, China is the manufacturer of API Sitagliptin Phosphate while M/s. Zhejiang Hengdian Apeloa Imp & Exp. Co., Ltd., China is their authorized agent to export Sitagliptin Phosphate to Pakistan. The Letter from the API Manufacturer is provided.
8.	Compliance Record of HPLC software 21CFR & audit trial reports on product testing.	Compliance Record of HPLC software 21CFR & audit trial reports on product testing is provided.
9.	In reference of previous approval of applications with stability study data firm provides the panel inspection of Sofosbuvir 400mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail on the testing records cannot be made as audit trail was not activated. So on that base exemption could be granted.	There is mistake incurred in the Panel Inspection Report at Point No.31wherein by mistake it was mentioned that "the Audit trail on the testing records cannot be made as audit trail was not activated". While on the same date by the same Panel Inspection Team during the inspection for our another new drug "Novasept Gel" the panel has mentioned "Audit trail reports were available and randomly checked" in Inspection Report at Point No.31 of Novasept Gel. Copy of Inspection Report of Novasept Gel is provided.

Decision of 312: Deferred for comparative dissolution data as the provided data is for different formulation

Remarks of evaluator:

Comparative dissolution studies for this strength was performed. It has been performed with competitor product Trvimet XR (Batch # 185FA) at pH 1.2, 4.5 and 6.8 (dated 9-2021)

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.		
192.	Name and address of manufacturer / Applicant	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Glytec-M XR 50/500 mg Tablet
	Composition	Each Film Coated Tablet Contains: Sitagliptin as phosphate Monohydrate …50mg Metformin HCl (extended release) …500mg
	Diary No. Date of R& I & fee	Dy. No 14273 dated 17-04-2018 Rs.20,000/- Dated 17-04-2018
	Pharmacological Group	Anti- diabetic
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 14"s As per SRO
	Approval status of product in Reference Regulator Authorities	JANUMET® XR 50/500 mg, 50/1000 mg, 100/1000 mg (sitagliptin and metformin HCl) Extended-Release Tablets (USFDA)
	Me-too status	Tagipmet XR tablets by Highnoon Lab limited. 084651
	GMP status	03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.
	Remarks of the Evaluator	Assay of both Sitagliptin and Metformin is by HPLC method

STABILITY STUDY DATA

Drug	Glytec-M XR 50/500 mg Tablet		
Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi		
Manufacturer of API	For Sitagliptin phosphate monohydrate: M/s Zheijiang Yengtai Pharmaceutical Co., Ltd, China Address: No1 Donghai 4th avenue zheijiang provincial chemical and medical raw material base Linhai zone, Linhai city Zhejiang province China For Metformin hydrochloride: Aarti industries LTD. Address: Plot No. K-17/18/19 MIDC Tarapur 401506, Dist Thane zone 4 Maharashtra, India.		
API Lot No.	**Sitagliptin phosphate monohydrate:** 1827-0001-20009 **Metformin hydrochloride**: MEF/1901807		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
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.	315DS01	315DS02	315DS03
Batch Size	1500	1500	1500
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	07-2020	07-2020	07-2020
No. of Batches	03		
Date of Submission	25/02/2021 (6326)		

<table>
<tr><th colspan="3">DOCUMENTS / DATA PROVIDED BY THE APPLICANT</th></tr>
<tr><th>S.#</th><th>Documents to Be Provided</th><th>Status</th></tr>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm</td><td>A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting.</td></tr>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>For Sitagliptin:
The firm has submitted COA for from both API and FPP manufacturer
For Metformin hydrochloride:
The firm has submitted COA for from both API and FPP manufacturer</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer</td><td>Yes</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Provided (for zone IV-B)</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>Sitagliptin:
The firm has provided copy of Certificate (Certificate# 201807039) of GMP compliance issued to M/s Zheijiang Yongtai Pharmaceutical Co., Ltd., Zheijiang province by CFDA valid Up to june-30-2021.
For Metformin hydrochloride:
The firm has submitted copy of GMP certificate declaring following information:
Certificate No. 6095581
Issued to: I Aarti industries LTD.
Address: Plot No. K-17/18/19 MIDC Tarapur 401506, Dist Thane zone 4 Maharashtra, India.
Issued by: Food & Drugs Administration, Maharashtra.
Validity: Valid Till 24-09-2021.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The Proof of Purchase of API Sitagliptin as Phosphate from M/s. Zheijang Yongtai Pharmaceutical Co., Ltd and Metformin HCl from M/s. Aarti Drugs Ltd., duly attested by AD- Karachi is provided.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes (same as API manufacturer)</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>315DS01</td><td>1500</td><td>07-2020</td></tr>
<tr><td>315DS01</td><td>1500</td><td>07-2020</td></tr>
<tr><td>315DS01</td><td>1500</td><td>07-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Janumet XR Tablets” The details are as follows:
<table>
<tr><th colspan="2">Reference product</th><th colspan="2">Test Product</th></tr>
<tr><td>Product name</td><td>Janumet XR100/1000mg</td><td>Product name</td><td>Sitagliptin/Metformin XR</td></tr>
<tr><td>Batch #</td><td>S028886</td><td>Batch #</td><td>317DS01</td></tr>
<tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>07-2020</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:</td></tr>
</table>

		1. pH 1.2 HCl buffer 2. pH 4.5 Acetate buffer 3. pH 6.8 Phosphate buffer Comparative dissolution studies for other strengths not performed. It has been performed with competitor product Janumet tablet XR (Merck) for higher strength i.e. Sita/Met XR 100/1000 mg as formulation is dose proportional)
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Provided
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

REMARKS OF EVALUATOR

S.#	Observations/Documents Required	Status of Document/Justifications
1.	Firm has to submit valid copy of cGMP for M/s. Zheijang Yongtai Pharmaceutical Co., Ltd., Zheijiang Province. As provided one is valid only till 2021.	The valid copy of cGMP Certificate valid up to 28-06-2023 for M/s. Zheijang Yongtai Pharmaceutical Co., Ltd., Zheijiang Province is provided.
2.	Documents for the procurement of API with approval from DRAP.	The Proof of Purchase of API Sitagliptin as Phosphate from M/s. Zheijang Yongtai Pharmaceutical Co., Ltd and Metformin HCl from M/s. Aarti Drugs Ltd., duly attested by AD- Karachi is provided.
3.	Stability study data of API from API manufacturer.	The Stability Data of API Manufacturer Sitagliptin as Phosphate from M/s. Zheijang Yongtai Pharmaceutical Co., Ltd and Metformin HCl from M/s. Aarti Drugs Ltd., is provided.
4.	Since API of Sitagliptin is being incorporated via coating solution so how it is possible to ensure that proper amount of active has been incorporated in dosage form while using 100% quantity in master formulation.	To ensure proper amount of Sitagliptin API incorporated in dosage form we have taken 100% excess quantity of API in master formulation i.e. 200% Master formulation is provided.
5.	Documents for the procurement of reqference and impurity standards missing for sitagliptin phosphate monohydrate.	Documents for the procurement of reference and impurity standards missing for Stagliptin Phosphate Monohydrate is provided.
6.	In innovator product approved in USFDA propyl gallate assay was performed (https:/www.accessdata.fda.gov/ drugsaftfda_docs/nda/2012/ 202270Orig1s000ChemR.pdf) as propyl gallate is carcinogenic and is permissible in certain limits. Justify the exemption of this test by applicant.	We have not use propyl gallate in our formulation so there is no need to perform its testing.
7.	The GMP, Quality Control Department analysis report is from Zheijiang Yengtai Pharmaceutical Co., Ltd, China and on many documents including Commercial Invoice name is mentioned as Zhejiang Hengdian Apeloa China. Provide the relationship.	The Zheijiang Yengtai Pharmaceutical Co., Ltd, China is the manufacturer of API Sitagliptin Phosphate while M/s. Zhejiang Hengdian Apeloa Imp & Exp. Co., Ltd., China is their authorized agent to export Sitagliptin Phosphate to Pakistan. The Letter from the API Manufacturer is provided.
8.	Compliance Record of HPLC software 21CFR & audit trial reports on product testing.	Compliance Record of HPLC software 21CFR & audit trial reports on product testing is provided.

9.	In reference of previous approval of applications with stability study data firm provides the panel inspection of Sofosbuvir 400mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail on the testing records cannot be made as audit trail was not activated. So on that base exemption could be granted.	There is mistake incurred in the Panel Inspection Report at Point No.31wherein by mistake it was mentioned that "the Audit trail on the testing records cannot be made as audit trail was not activated". While on the same date by the same Panel Inspection Team during the inspection for our another new drug "Novasept Gel" the panel has mentioned "Audit trail reports were available and randomly checked" in Inspection Report at Point No.31 of Novasept Gel. Copy of Inspection Report of Novasept Gel is provided.

Decision of 312: Deferred for comparative dissolution data as the provided data is for different formulation

Remarks of evaluator:

Comparative dissolution studies for this strength was performed. It has been performed with competitor product Trvimet XR (Batch # 185FA) at pH 1.2, 4.5 and 6.8 (dated 9-2021)

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.

Item No. I: Agenda of Evaluator PEC-IX

Case no. 01 Registration applications for local manufacturing of (Human) drugs

a. New cases

193.	Name and address of manufacturer/ Applicant	M/s Navegal Laboratories. 41/1-A2, Phase-1, Industrial Estate, Hattar
	Brand Name + Dosage Form + Strength	Modagil 200mg Tablet
	Composition	Each Tablet Contains: Modafinil…200mg
	Diary No. Date of R & I & fee	Dy. No.39404; 30.11.2018 PKR. 20,000/-; 30.11.2018
	Pharmacological Group	Folic acid analogs (not in ATC)
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	1x10's, 2x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities.	PROVIGIL® (modafinil) 100mg and 200mg tablets, for oral use, C-IV. TGA approved
	Me-too status	Monalert 200mg Tablet. Reg. No. 47171
	GMP status	Staisfactory GMP level on 11.03.2017
	Remarks of the Evaluator(IX)	• The firm revised the formulation from film-coated tablet to uncoated tablet along with submission of Rs. 7,500/- fee (Challan 173132402) dated 20.09.2021.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
194.	Name and address of manufacturer/ Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road, Lahore
	Brand Name + Dosage Form + Strength	Linkacin 300mg Injection
	Composition	Each 1ml ampoule contains: Lincomycin as HCL monohydrate…300mg
	Diary No. Date of R & I & fee	Dy. No. 41292; 07.12.2018 PKR. 20,000/-; 07.12.2018
	Pharmacological Group	Lincosamide
	Type of Form	Form 5
	Finished product Specification	The firm has claimed USP specs.
	Pack size & Demanded Price	1ml; As per SRO
	Approval status of product in Reference Regulatory Authorities.	LINCOMYCIN LWS lincomycin (as hydrochloride monohydrate) 300 mg/1 mL solution for injection ampoule. TGA approved
	Me-too status	Lincofac 300Mg/1Ml Injection. Reg. No. 39658 (does not depict

		monohydrate form)
	GMP status	GMP certificate issued on the basis of inspection dated 28.02.2019.
	Remarks of the Evaluator(IX)	• The firm submitted Form 5. • The firm revised Lincomycin as HCL to Lincomycin as HCL monohydrate in the label claim and adjusted its weight as per salt factor.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
195.	Name and address of manufacturer/ Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road, Lahore
	Brand Name + Dosage Form + Strength	Desvin XR 50mg Tablet
	Composition	Each extended release tablet contains: Desvenlafaxine as succinate……50mg
	Diary No. Date of R & I & fee	Dy. No. 41271; 07.12.2018 PKR. 20,000/-; 07.12.2018
	Pharmacological Group	Other antidepressants
	Type of Form	Form-5
	Finished product Specification	The firm has claimed manufacturer's specifications
	Pack size & Demanded Price	14's, 28's, 56's, 168's; As per SRO
	Approval status of product in Reference Regulatory Authorities.	Pristiq extended release tablets 50mg (film-coated). USFDA approved
	Me-too status	Denla XR 50mg Tablet. Reg. No. 70433 (Does not depict coating)
	GMP status	GMP certificate issued on the basis of inspection dated 28.02.2019.
	Remarks of the Evaluator(IX)	• The firm submitted Form 5. • The firm revised Desvenlafaxine as succinate to Desvenlafaxine as succinate monohydrate and adjusted its weight in Master formula as per salt factor. • The firm revised the formulation to film-coated tablet from uncoated tablet without fee.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	
196.	Name and address of manufacturer/ Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road, Lahore
	Brand Name + Dosage Form + Strength	Picso 5mg Tablets
	Composition	Each uncoated tablet contains: Sodium picosulfate as monohydrate…5mg
	Diary No. Date of R & I & fee	Dy. No. 41263; 07.12.2018 PKR. 20,000/-; 07.12.2018
	Pharmacological Group	Contact laxatives
	Type of Form	Form 5
	Finished product Specification	The firm has claimed manufacturer's specifications.
	Pack size & Demanded Price	10x10's, 100's, 300's; As per SRO
	Approval status of product in Reference Regulatory Authorities.	Laxoberal® laxative tablets 5 mg tablets. DIMDI Germany approved
	Me-too status	U-Salax Tablet R.No.075548 (deos not depict monohydrate form).
	GMP status	GMP certificate issued on the basis of inspection dated 28.02.2019.
	Remarks of the Evaluator(IX)	• The firm submitted Form 5. • The firm adjusted the quantity of API as per salt factor in Master Formula.
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	

b. Deferred cases

197.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Arte Plus Tablet 80mg/480mg
	Composition	Each Tablet Contains: Artemether…80mg Lumefantrine…480mg
	Diary No. Date of R & I & fee	Dy. No. 40355; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Drugs for urinary frequency and incontinence
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	14's, 28's; Each tablet Rs. 60/-
	Approval status of product in Reference Regulatory Authorities.	WHO Approved formulation
	Me-too status	Eptrim-X 80/480mg Tablets. Reg. No. 75828
	GMP status	The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported.
	Remarks of the Evaluator(IX)	• The firm revised the product from Film Coated Tablet to plain tablet without submission of applicable fee. • The cover letter was meant for 80/480mg strength. However, all other documents were meant for 20mg and rivaroxaban has been mentioned. The firm submitted enclosure of Form 5 with correct label claim and other contents without submission of applicable fee. • First page of Form 5 is still missing.
	Decision of 296th meeting of RB	Deferred for: • Fee for revision of formulation. • Submission of Form 5 and Latest GMP inspection report.
	Evaluation by PEC	The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. The firm submitted the following: • Form 5 • Rs, 7,500/- fee (Challan: 58272632322)
	Decision: Approved with innovator's specifications.	
198.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Rivakem Tablet 15mg
	Composition	Each Film Coated Tablet Contains: Rivaroxaban…15mg
	Diary No. Date of R & I & fee	Dy. No. 40385; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Factor Xa inhibitor
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	14's, 28's; Rs. 7270/- per 14 tablets
	Approval status of product in Reference Regulatory Authorities.	Rivaroxaban 15 mg film-coated tablets. MHRA approved
	Me-too status	Rivaxo 15mg film-coated Tablet. Reg. No. 80790
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	
	Decision of 296th meeting of RB	Deferred for submission of latest GMP inspection report.
		The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported.
	Decision: Approved with innovator's specifications.	

199.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemyfenac 100mg Tablet
	Composition	Each Tablet Contains: Aceclofenac…100mg
	Diary No. Date of R & I & fee	Dy. No. 40382; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Antiinflammatory and antirheumatic products, non-steroids
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	10's; As per SRO
	Approval status of product in Reference Regulatory Authorities.	Aceclofenac 100 mg film-coated Tablets. MHRA approved
	Me-too status	Anac 100mg Tablet. Reg. No. 81502
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	The firm has applied for plain tablet. Coating composition are mentioned thereof. However, the manufacturing outlines does not depict coating process. The firm revised the manufacturing outlines. Revision of label claim to film-coated tablet is required.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Revision of label claim to film-coated tablet along with submission of applicable fee.
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm did not revise the label claim, but resubmitted the master formula. • The firm submitted Rs. 7,500/- fee (Challan: 3050179428)
	Decision: Deferred for revision of label claim.	
200.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemsartan Tablet 5mg/160mg
	Composition	Each Film Coated Tablet Contains: Amlodipine as besilate…5mg Valsartan…160mg
	Diary No. Date of R & I & fee	Dy. No. 40384; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Antihypertensives
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	14's; Rs. 340/-
	Approval status of product in Reference Regulatory Authorities.	Exforge film-coated tablet 5/160mg. USFDA approved
	Me-too status	VALTAN -M 165 PLUS TABLET. Reg. No. 77206
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	• The firm had applied for film-coated tablet. The firm revised the label claim and mentioned the coating composition in master formula. • In master formula, the label claim is amlodipine as besilate. However, in Form 5 it is amlodipine. The firm did not clarify the same. • The firm shall submit properly filled enclosure of Form 5. • The firm shall also revise amlodipine as besilate to amlodipine besilate in master formula only.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Submission of applicable fee for revision of label claim to

		film-coated tablet. • Revision of amlodipine to amlodipine as besilate in Form 5. • Submission of enclosure of Form 5. • Revision of amlodipine as besilate to amlodipine besilate in master formula only. • Pack size & Demanded Price
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm submitted Rs. 7,500/- fee (Challan: 131899163). • The firm did not adjust the weight of amlodipine besilate in master formula as salt factor.
	Decision: Deferred for adjustment of weight of amlodipine besilate in master formula as salt factor.	
201.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemsartan Tablet 10mg/160mg
	Composition	Each Film Coated Tablet Contains: Amlodipine as besilate…10mg Valsartan…160mg
	Diary No. Date of R & I & fee	Dy. No. 40383; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Antihypertensives
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	14's; Rs. 448/-
	Approval status of product in Reference Regulatory Authorities.	Exforge film-coated tablet 10/160. USFDA approved
	Me-too status	VALTAN -M 170 PLUS TABLET. Reg. No. 77207
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	• The firm has applied for film-coated tablet. The firm revised label claim and mentioned the coating composition in master formula. • In master formula, the label claim is amlodipine as besilate. However, in Form 5 it is amlodipine. The firm did not clarify the same. • The firm shall submit properly filled enclosure of Form 5. • The firm shall also revise amlodipine as besilate to amlodipine besilate in master formula only.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Submission of applicable fee for revision of label claim to film-coated tablet. • Revision of amlodipine to amlodipine as besilate in Form 5. • Submission of enclosure of Form 5. • Revision of amlodipine as besilate to amlodipine besilate in master formula only. • Pack size & Demanded Price
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm submitted Rs. 7,500/- fee (Challan: 17055425) • The firm did not adjust the weight of amlodipine besilate in master formula as salt factor.
	Decision: Deferred for adjustment of weight of amlodipine besilate in master formula as salt factor.	
202.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kem- Mont 10mg Tablet
	Composition	Each chewable tablet Contains: Montelukast (as sodium)…….10mg

	Diary No. Date of R & I & fee	Dy. No. 40388; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Leukotriene receptor antagonists
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 20's, 14's, 30's, 40's, 50's,60's, 70's, 80's, 90's, 100; Rs. 100 per tablet
	Approval status of product in Reference Regulatory Authorities.	Singulair Tablet 10 mg of M/S MSD (USFDA Approved)
	Me-too status	Montiget 10 mg tablets of M/s Getz Pharma (Reg.# 034838)
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	• Proof of international availability of same formulation and same strength in reference regulatory authorities as defined in 275th meeting of the registration board is required. • Provide proof of approval of me-too product (name registration number and name of company) by DRAP. • Revise "Montelukast sodium eq. to. Montelukast" to "Montelukast sodium" in master formula only.
	Decision of 296th meeting of RB	Deferred for: • Proof of international availability of same formulation and same strength in reference regulatory authorities as defined in 275th meeting of the registration board. • Proof of approval of me-too product (name registration number and name of company) by DRAP. • Revision of Montelukast sodium eq. to. Montelukast" to "Montelukast sodium" in master formula only.
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm submitted Rs. 7,500/- fee (Challan: 9322242273) • The firm did not adjust the weight of monteleukast sodium in master formula as salt factor. • The firm included film-coating in the master formula and manufacturing outlines. The firm shall submit all the required documents (Form 5, master formula with adjustment of the weight of monteleukast sodium as salt factor, complete specifications including testing method) for film-coated tablet.
	Decision: Deferred for submission of all the required documents (Form 5, master formula with adjustment of the weight of monteleukast sodium as salt factor, complete specifications including testing method) for film-coated tablet	
203.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kem- Mont 5mg Tablet
	Composition	Each chewable tablet Contains: Montelukast (as sodium)…….5mg
	Diary No. Date of R & I & fee	Dy. No. 40387; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Leukotriene receptor antagonists
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 20's, 14's, 30's, 40's, 50's,60's, 70's, 80's, 90's, 100; Rs. 100 per tablet
	Approval status of product in Reference Regulatory Authorities.	SINGULAIR® (montelukast sodium) Chewable Tablets. USFDA approved
	Me-too status	Nohist Chewable Tablet 5mg. Reg. No. 85712
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	Revise "Montelukast sodium eq. to. Montelukast" to "Montelukast sodium" in master formula only.
	Decision of 296th meeting of RB	Deferred for:

		• Submission of latest GMP inspection report. • Revision of Montelukast sodium eq. to. Montelukast" to "Montelukast sodium" in master formula only.
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm submitted Rs. 7,500/- fee (Challan: 126310600433) • The firm did not adjust the weight of monteleukast sodium in master formula as salt factor.
	Decision: Deferred for adjustment of the weight of monteleukast sodium as salt factor in master formula.	
204.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemyflox 400mg Tablet
	Composition	Each Film-coated tablet Contains: Moxifloxacin HCl…400mg
	Diary No. Date of R & I & fee	Dy. No. 40380; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Fluoroquinolones
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	5's; Rs. 465/-
	Approval status of product in Reference Regulatory Authorities.	AVELOX (moxifloxacin as hydrochloride) 400mg tablets, film-coated. USFDA approved
	Me-too status	Moxizyan 400mg Tablets, film-coated. Reg. No. 77252
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	Undertaking at the end of Form 5 is missing.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Submission of undertaking at the end of Form 5.
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm submitted Rs. 7,500/- fee (Challan: 126310600433) • The firm submitted the required undertaking.
	Decision: Approved.	
205.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemylid 600mg Tablet
	Composition	Each film-coated tablet Contains: Linezolid…600mg
	Diary No. Date of R & I & fee	Dy. No. 40381; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Other antibacterials
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	12's; Rs. 980/-
	Approval status of product in Reference Regulatory Authorities.	ZYVOX® (linezolid) 600mg tablets (film-coated) for oral use by Pharmacia and Upjohn. US-FDA approved
	Me-too status	Ozlin 600 mg Tablet by Linta Pharmaceuticals. Reg No. 78179
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	
	Decision of 296th meeting of RB	Deferred for submission of latest GMP inspection report.
	Evaluation by PEC	The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported.
	Decision: Approved with innovator's specifications.	
206.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemadol-P 37.5/325mg Tablet
	Composition	Each Film Coated Tablet Contains:

		Tramadol hcl….37.5mg Paracetamol…325mg
	Diary No. Date of R & I & fee	Dy. No. 40379; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Opioids in combination with non-opioid analgesics
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's; Rs. 190/-
	Approval status of product in Reference Regulatory Authorities.	ULTRACET (tramadol hydrochloride and acetaminophen) tablets, for oral use by Janssen Pharms US-FDA approved
	Me-too status	Tril-P Tablet. Reg. No. 78181
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	First page of Form 5 is missing. Revise tramadol as HCl to tramadol HCl and mention correct quantity of tramadol HCl, i.e., 37.5mg in Master formula.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Submission of Form 5 (first page). • Revision of tramadol as HCl to tramadol HCl (label claim and composition) and mentioning the correct quantity of tramadol HCl, i.e., 37.5mg in Master formula.
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm did not submit Form 5. • The firm revised tramadol as HCl to tramadol HCl in the composition and mentioned the correct quantity of tramadol HCl, i.e., 37.5mg in Master formula. Revision of label claim is required. • The firm submitted Rs. 7,500/- fee (Challan: 35326160)
	Decision: Deferred for revision of label claim.	
207.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemroxen-E Tablet 500/20mg
	Composition	Each Delayed Release Tablet Contains: Naproxen…500mg Esomeprazole…20mg
	Diary No. Date of R & I & fee	Dy. No. 40377; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Opioids in combination with non-opioid analgesics
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	VIMOVO (naproxen and esomeprazole magnesium trihydrate) delayed-release tablets, for oral use (375 mg enteric-coated naproxen /20 mg immediate-release esomeprazole film-coated or 500 mg enteric-coated naproxen /20 mg immediate-release esomeprazole film-coated). US-FDA approved
	Me-too status	Tril-P Tablet. Reg. No. 78181
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	• First page of Form 5 is missing. • The manufacturing process starts with producing a core tablet with naproxen. This core tablet is manufactured by a conventional wet granulation process. The core tablet is coated with six layers of film-coating. An enteric coat and barrier coat are applied prior to the active coat. The fourth coat is the esomeprazole magnesium trihydrate coat. Revise the composition and manufacturing outlines accordingly. • Revise esomeprazole to esomeprazole as magnesium Trihydrate

		in the label claim along with submission of applicable fee, and adjust its weight in Master formula as per salt factor. • Clarification is required regarding the pack size and demanded price.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Clarification of formulation in line with the reference product. • Revision of esomeprazole to esomeprazole as magnesium Trihydrate in the label claim along with submission of applicable fee, and adjustment of its weight in Master formula as per salt factor. • Clarification regarding the pack size and demanded price.
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The firm did not submit Form 5. • The firm claimed pack and price as per SRO • The firm submitted Rs. 7,500/- fee (Challan: 7443248912). • The firm did not revise esomeprazole to esomeprazole as magnesium Trihydrate in the label claim.
	Decision: Deferred for submission of stability data of three batches as per Zone IV-A.	
208.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Kemfylin Syrup 100mg/5ml
	Composition	Each 5ml contains: Doxofylline…100mg
	Diary No. Date of R & I & fee	Dy. No. 40378; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Other systemic drugs for obstructive airway diseases
	Type of Form	Form 5
	Finished product Specification	The firm has claimed in-house specifications
	Pack size & Demanded Price	30ml; Rs. 170/-, 60ml; Rs. 180/-, 90ml; Rs. 170/-, 100ml; Rs. 220/-, 120ml; Rs. 350/-, 450ml; Rs. 500/-
	Approval status of product in Reference Regulatory Authorities.	DOXOFILLINA ABC "200 mg/10 ml Sciroppo" Flacone da 200 ml. AIFA approved
	Me-too status	Unifyline Syrup. Reg. No. 47180
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	First page of Form 5 is missing.
	Decision of 296th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Submission of Form 5 (first page).
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported. • The frim submitted Form 5 (first page).
	Decision: Approved with innovator's specifications.	
209.	Name and address of manufacturer/ Applicant	M/s Alkemy Pharmaceuticals Labs Pvt Ltd, P/9, SITE, Hyderabad
	Brand Name + Dosage Form + Strength	Zaridine Syrup 5mg/5ml
	Composition	Each 5ml contains: Loratadine …5mg
	Diary No. Date of R & I & fee	Dy. No. 40376; 05.12.2018 PKR. 20,000/-; 05.12.2018
	Pharmacological Group	Other systemic drugs for obstructive airway diseases
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	30ml; Rs. 45/-
	Approval status of product in Reference Regulatory Authorities.	Loratadine 5 mg/ 5 ml syrup. MHRA approved

	Me-too status	Histagon Syrup 5mg/5ml. Reg. No. 28188
	GMP status	Latest GMP inspection report is required.
	Remarks of the Evaluator(IX)	First page of Form 5 is missing.
	Decision of 312th meeting of RB	Deferred for: • Submission of latest GMP inspection report. • Submission of Form 5 (first page).
	Evaluation by PEC	• The firm was inspected on 06.10.2021, wherein acceptable level of GMP compliance was reported.
	Decision: Approved with innovator's specifications.	
210. 211. 212. 213. 214.	Deleted as these cases were already considered in 293rd meeting.	
215.	Name and address of manufacturer / Applicant	M/s Bosch Pharmaceuticals (Pvt.) Ltd. Bosch House 221, Sector 23, Korangi Industrial Area, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Bkay 250mg/2ml Injection
	Composition	Each 2ml Contains: Amikacin as sulphate…250mg
	Diary No. Date of R& I & fee	Dy No. 27974: 16.08.2018 PKR 20,000/-: 16.08.2018
	Pharmacological Group	Aminoglycosides
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack size & Demanded Price	1's, 5's ampule; as per PRC
	Approval status of product in Reference Regulatory Authorities.	AMIKACIN 250mg/mL (as sulfate) injection vial (2ml). MHRA approved
	Me-too status	Aimwel 250mg Injection. Reg. No. 68218
	GMP status	The firm was inspected on 13.04.2021, wherein renewal of DML was recommended.
	Remarks of the Evaluator(IX).	• The firm has submitted Form 5 with 31 points. • The firm has claimed 36 months of shelf life.
	Decision of 291ST meeting of RB	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	• The firm submitted a cover letter for revision of BKay 250mg/2ml to BKay 250mg/ml. • The firm submitted Rs. 30,000/- fee (Challan:428647442636). • The firm shall submit fresh Form 5 along with all supported documents as per enclosure thereof. • Clarification is required about the filled volume / pack size per vial.
	Decision: Deferred for: • **Submission of fresh Form 5 along with all supported documents as per enclosure thereof.** • **Clarification about the filled volume / pack size per vial.**	
216.	Name and address of manufacturer / Applicant	M/s Inventor Pharma. Plot No. K/196, S.I.T.E. (SHW) Phase II, Karachi
	Brand Name +Dosage Form + Strength	Pantovetor 40mg Tablet
	Composition	Each gastro resistant tablet Contains: Pantoprazole as sodium sesquihydrate…40mg
	Diary No. Date of R& I & fee	Dy.No 6321 dated 13-02-2019 Rs.20,000/- Dated 12-02-2019
	Pharmacological Group	Proton pump inhibitors
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack size & Demanded Price	As per SRO

	Approval status of product in Reference Regulatory Authorities.	Pantoprazole 40 mg gastro-resistant tablets (MHRA Approved)
	Me-too status	Protium Gastro Resistant Tablets 40mg by Abbott (Reg# 021039)
	GMP status	Last GMP inspection report dated 03-09-2019 concludes GOOD compliance to GMP
	Remarks of the Evaluator(IX)	• Firm has applied the formulation of film coated tablet since the reference product is gastro resistant tablet. Firm need to revise the formulation to gastro resistant tablet as per the reference product along with submission of requisite fee for revision of formulation.
	Previous decision	The Board in its 295th meeting deferred the case for revision of formulation as per reference product along with submission of requisite fee.
	Evaluation by PEC	The firm revised the formulation from film coated tablet to gastro resistant tablet without submission of fee. Moreover, revision of master formula is still required
	Decision of 307th meeting of RB	Deferred for: • Submission of fee of Rs. 30000/- for revision of formulation from film coated tablet to gastro resistant tablet. • Revision of master formula.
	Evaluation by PEC	• The firm did not submit any fee. • The firm did not mention the gastro-resistant coating composition in the master formula. • The firm shall revise Pantoprazole as sodium sesquihydrate to Pantoprazole sodium sesquihydrate in master formula and shall adjust its per tablet weight as per salt factor. • The firm shall submit the method of manufacturing and drug product specifications.
	Decision: Deferred for: **• Submission of fee of Rs. 30000/- for revision of formulation from film coated tablet to gastro resistant tablet.** **• Mentioning the gastro-resistant coating composition in the master formula.** **• Revision of Pantoprazole as sodium sesquihydrate to Pantoprazole sodium sesquihydrate in master formula and adjustment of its per tablet weight as per salt factor.** **• Submission of method of manufacturing and drug product specifications.**	
217.	Name and address of manufacturer / Applicant	M/s Inventor Pharma. Plot No. K/196, S.I.T.E. (SHW) Phase II, Karachi
	Brand Name +Dosage Form + Strength	Hepakil 120ml Syrup
	Composition	Each 5ml contains: L-Ornithine L-Aspartate…300mg Nicotinamide…24mg Riboflavin sodium phosphate…0.24mg
	Diary No. Date of R& I & fee	Dy.No 8167 dated 25-02-2019 Rs.20,000/- Dated 25-02-2019
	Pharmacological Group	Vitamins & amino acid supplement
	Type of Form	Form 5
	Finished Product Specification	Innovator's specs
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Could not be confirmed
	Me-too status	Could not be confirmed
	GMP status	Last GMP inspection report dated 03-09-2019 concludes GOOD compliance to GMP
	Remarks of the Evaluator(IX)IX	• Firm has submitted the request to revise their formulation to following composition: Each 5ml contains: L-Ornithine L-Aspartate…300mg

		Nicotinamide…24mg Riboflavin Sodium phospate…0.76mg • Firm has also submitted fee Rs. 20,000/- for revision of formulation • Me-too status of this formulation has been verified: Levijon Syrup by Sami Pharma (Reg # 015063) • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting, since the submitted reference of Germany could not be verified.
	Decision of 307th meeting of RB	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	The firm submitted reference of DMDI Germany, which could not be verified.
	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.	

Case No. 02 Registration applications for local manufacturing of (veterinary) drugs

a. New Cases

b. Deferred Cases

218.	Name and address of Manufacturer / Applicant	M/s Vetz Pharmaceutical (Pvt) Ltd Plot # Q-1, S.I.T.E, Kotri, Sindh
	Brand Name +DosageForm+Strength	Aminovetz injection 500ml
	Composition	Each ml contains Dextrose …….50 mg Calcium chloride ……0.15mg Potassium chloride……. 0.2mg Magnesium Sulfate…….. 0.2mg Sodium acetate trihydrate ……2.5mg L-Histidine HCl …..……..0.34mg DL-Methionine ……0.34mg DL-Tryptophan ……0.34mg L-Cysteine HCl ……0.34mg L-Threonine ……0.68mg DL-Isoleucine ……0.68mg L-Arginine HCl ……0.85mg DL-Phenylalanine ……1.02mg DL-Valine ……..1.7mg L-Lysin HCl ……..1.02mg L-Leucine ……1.36mg Monosodium glutamate ……1.36mg Vitamin B1 (Thiamin HCl) ……0.10mg Vitamin B2 (Riboflavin-5-Phosphate).. 0.04mg Vitamin B6 (Pyridoxine Hydrochloride)..0.1mg Vitamin B12 (Cyanocobalamin) …..0.05mcg Nicotinamide ……..1.5mg
	Diary No. Date of R & I & fee	Dy. No. 42892; 17.12.2018 PKR. 20,000/-; 17.12.2018
	Pharmacological Group	Amino Acid/ Electrolytes/ Vitamins
	Types of Form	Form-5
	Finished Product Specification	In-house specifications
	Pack Size & Demanded Price	500 ml Decontrolled
	Me-too status	Could not be confirmed
	GMP status	The firm was inspected on 26 & 27-7-2019 with the following

		conclusion: Based on the above observation their current GMP compliance level is rated as good.	
	Remark of Evaluator	The composition do not match with the provided me-too. Terminal sterilization is missing in the manufacturing outlines.	
	Previous decision	The Board in its 295th meeting deferred the case for: • Clarification of method of terminal sterilization/ sterile filling process in manufacturing outlines. • 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:	• The firm submitted revised manufacturing outlines. • The firm revise the composition as follow along with submission of Rs. 20000/- dated 18.08.2020	
		Each ml contains Dextrose ……50 mg Calcium chloride ……0.15mg Potassium chloride…… 0.2mg Magnesium Sulfate…… 0.2mg Sodium acetate trihydrate …2.5mg L-Histidine HCl …..…0.34mg DL-Methionine ……0.34mg DL-Tryptophan ……0.34mg L-Cysteine HCl ……0.34mg L-Threonine ……0.68mg DL-Isoleucine ……0.68mg L-Arginine HCl ……0.85mg DL-Phenylalanine ……1.02mg DL-Valine ……1.7mg L-Lysin HCl ……1.02mg L-Leucine ……1.36mg Monosodium glutamate …1.36mg Vitamin B1 (Thiamin HCl) …0.10mg Vitamin B2 (Riboflavin-5-Phosphate).. 0.04mg Vitamin B6 (Pyridoxine Hydrochloride)..0.1mg Vitamin B12 (Cyanocobalamin) …..0.05mcg Nicotinamide ……1.5mg	Each 100ml contains Dextrose …….5.5 mg Calcium chloride ……15mg Potassium chloride… 20mg Magnesium Sulfate… 20mg Sodium acetate trihydrate ……250mg L-Histidine HCl..……34mg DL-Methionine ……34mg DL-Tryptophan ……34mg L-Cysteine HCl ……34mg L-Threonine ……68mg DL-Isoleucine …68mg L-Arginine HCl …85mg DL-Phenylalanine…102mg DL-Valine ……170mg L-Lysin HCl ……102mg L-Leucine ……136mg Monosodium glutamate ……136mg Vitamin B1 (Thiamin HCl) …10mg Vitamin B2 (Riboflavin-5-Phosphate).. 4mg Vitamin B6 (Pyridoxine Hydrochloride)..10mg Vitamin B12 (Cyanocobalamin) …..5mcg Nicotinamide ……150mg Benzyl alcohol…1.5mg Sterile water QS…100ml
		The firm submitted the following me-too product, the composition of varies from our me-too database.	

		
	Decision in 296th meeting of RB	The case was 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:	The firm again submitted the same reference.
	Decision: The Board referred the case to registration section (Import & veterinary) with the direction to confirm the registration status of generic drug product referred by the firm.	
219.	Name and address of Manufacturer / Applicant	M/s Vetz Pharmaceutical (Pvt) Ltd Plot # Q-1, S.I.T.E, Kotri, Sindh
	Brand Name +DosageForm+Strength	Aminovetz injection 250ml
	Composition	Each ml contains Dextrose …….50 mg Calcium chloride ……0.15mg Potassium chloride……. 0.2mg Magnesium Sulfate…….. 0.2mg Sodium acetate trihydrate ……2.5mg L-Histidine HCl …..……..0.34mg DL-Methionine ……0.34mg DL-Tryptophan ……0.34mg L-Cysteine HCl ……0.34mg L-Threonine ……0.68mg DL-Isoleucine ……0.68mg L-Arginine HCl ……0.85mg DL-Phenylalanine …….1.02mg DL-Valine ……..1.7mg L-Lysin HCl ……..1.02mg L-Leucine …….1.36mg Monosodium glutamate ……1.36mg Vitamin B1 (Thiamin HCl) ……0.10mg Vitamin B2 (Riboflavin-5-Phosphate).. 0.04mg Vitamin B6 (Pyridoxine Hydrochloride)..0.1mg Vitamin B12 (Cyanocobalamin) …..0.05mcg

		Nicotinamide ……..1.5mg
	Diary No. Date of R & I & fee	Dy. No. 42896; 17.12.2018 PKR. 20,000/-; 17.12.2018
	Pharmacological Group	Amino Acid/ Electrolytes/ Vitamins
	Types of Form	Form-5
	Finished Product Specification	In-house specifications
	Pack Size & Demanded Price	250 ml Decontrolled
	Me-too status	Could not be confirmed
	GMP status	The firm was inspected on 26 & 27-7-2019 with the following conclusion: Based on the above observation their current GMP compliance level is rated as good.
	Remark of Evaluator	The composition do not match with the provided me-too. Terminal sterilization is missing in the manufacturing outlines.
	Previous decision	The Board in its 295th meeting deferred the case for: • Clarification of method of terminal sterilization/ sterile filling process in manufacturing outlines. • 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:	• The firm submitted revised manufacturing outlines. • The revise the composition as follow along with submission of Rs. 20000/- dated 18.08.2020

Each ml contains	Each 100ml contains
Dextrose ……50 mg	Dextrose …….5.5 mg
Calcium chloride ……0.15mg	Calcium chloride ……15mg
Potassium chloride…… 0.2mg	Potassium chloride…… 20mg
Magnesium Sulfate…… 0.2mg	Magnesium Sulfate…… 20mg
Sodium acetate trihydrate …2.5mg	Sodium acetate trihydrate …250mg
L-Histidine HCl …..…0.34mg	L-Histidine HCl …..…34mg
DL-Methionine ……0.34mg	DL-Methionine ……34mg
DL-Tryptophan ……0.34mg	DL-Tryptophan ……34mg
L-Cysteine HCl ……0.34mg	L-Cysteine HCl ……34mg
L-Threonine ……0.68mg	L-Threonine ……68mg
DL-Isoleucine ……0.68mg	DL-Isoleucine ……68mg
L-Arginine HCl ……0.85mg	L-Arginine HCl …85mg
DL-Phenylalanine ……1.02mg	DL-Phenylalanine …102mg
DL-Valine ……1.7mg	DL-Valine ……170mg
L-Lysin HCl ……1.02mg	L-Lysin HCl ……102mg
L-Leucine ……1.36mg	L-Leucine ……136mg
Monosodium glutamate …1.36mg	Monosodium glutamate ……136mg
Vitamin B1 (Thiamin HCl) …0.10mg	Vitamin B1 (Thiamin HCl) …10mg
Vitamin B2 (Riboflavin-5-Phosphate).. 0.04mg	Vitamin B2 (Riboflavin-5-Phosphate).. 4mg
Vitamin B6 (Pyridoxine Hydrochloride)..0.1mg	Vitamin B6 (Pyridoxine Hydrochloride)..10mg
Vitamin B12 (Cyanocobalamin) …..0.05mcg	Vitamin B12 (Cyanocobalamin) …..5mcg
Nicotinamide ……1.5mg	Nicotinamide ……150mg
	Benzyl alcohol…1.5mg
	Sterile water QS…100ml

The firm submitted the following me-too product, the composition of varies from our me-too database.

		
	Decision in 296th meeting of RB	The case was 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:	• The firm again submitted the same reference.
	Decision: The Board referred the case to registration section (Import & veterinary) with the direction to confirm the registration status of generic drug product referred by the firm.	
220.	Name and address of Manufacturer / Applicant	M/s Vetz Pharmaceutical (Pvt) Ltd Plot # Q-1, S.I.T.E, Kotri, Sindh
	Brand Name +DosageForm+Strength	Vetzphos Injection
	Composition	Each ml contains: Sodium acid phosphate……400 mg
	Diary No. Date of R & I & fee	Dy. No. 43742; 24.12.2018 PKR. 20,000/-; 24.12.2018
	Pharmacological Group	Phosphate deficiency (general tonic)
	Types of Form	Form-5
	Finished Product Specification	In-house specifications. Avaialable in USP as (Each mL contains: Monobasic sodium phosphate, monohydrate, 276 mg; dibasic sodium phosphate, anhydrous, 142 mg (equivalent to dibasic sodium phosphate, heptahydrate, 268 mg); Water for Injection q.s. In the 5 mL and 15 mL product, phosphoric acid and/or NaOH may have been added for pH adjustment.)
	Pack Size & Demanded Price	250 ml Decontrolled
	Me-too status	Alphos-40 Injection (10ml, 20ml, 50ml, 100ml). Reg. No. 046573
	GMP status	The firm was inspected on 26 & 27-7-2019 with the following conclusion: Based on the above observation their current GMP compliance level is rated as good.
	Remarks of Evaluator[IX]	Provide me-too product (Name and registration number) with same strength and filled volume approved by DRAP. Terminal sterilization is missing in the manufacturing outlines.
	Previous decision	• The Board in its 295th meeting deferred the case for justification and evidence of applied pack size.
	Evaluation by PEC:	The firm submitted the following dosage:

		• Cattle / buffalo / horses: 200-250ml (IV single use for 250 ml) • Sheep goat: 50-70ml • Dogs/ cats: 10-20ml • Camels: 300-350ml Provide me-too product (Name and registration number) with same strength and filled volume approved by DRAP.
	Decision in 296th meeting of RB	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:	The firm submitted that 250 ml pack size is not registered in DRAP, but we apply for the first time to meet our business requirements.
	Decision: Deferred for evidence of approval of the applied formulation by DRAP in same filled volume (250ml) as applied.	
221.	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	TYFENIC-30 Oral Liquid
	Composition	Each 100 ml contains Florfenicol…….30g
	Diary No. Date of R & I & Fee	Dy No.11644: 06.03.2019 Rs. 20,000/-: 01.03.2019
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished Product Specification	Firm has claimed In-house specification
	Pack Size & Demanded Price	100 ml, 500 ml, 1 Litre, 2.5 Litre, 5 Litre : As per Policy of MoH
	Approval Status of product in Reference Regulatory Authorities	N/A
	Me-too Status	Could not be confirmed
	GMP Status	New License (Inspection Date: 04.10.2018 & 05.11.2018)
	Remarks of the Evaluator(IX)	The firm has submitted pictures of label and packing of me-too product Florofen oral solution by Leads Pahrma (Reg. No. 43160), which is registered in the me-too data as injection.
	Previous decision	The board in its 290th meeting deferred the case for confirmation of me-too product
	Evaluation by PEC	The firm revised the formulation from Each 100 ml contains Florfenicol…….30g To Each 100 ml contains Florfenicol…….25g Colistin sulphate… 50 MIU without submission of fee. The firm submitted the following me too: Florotin-25. Reg. No. 93840, which is not available in the database. The firm did not revise the manufacturing outlines and finished product specifications.
	Decision in 296th meeting of RB	Deferred for the following: Submission of fresh Form 5 along with all supported documents as per annexure and submission of fee. Confirmation of me-too status.The case was 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:	The firm submitted POLIFLOR LIQUID Registration No. 78383 (each ml contains:-florfenicol (USP)……250mg, colistin

		sulphate (BP)..0.5 MIU). The frim did not submit any fee for revision of the formulation / strength and imparting another API in it. The frim only submitted Form 5, master formula, manufacturing outlines and specifications for the drug product.
	Decision: Registration Board rejected the case since the firm has changed its application and included Colistin sulphate in the applied formulation.	
222.	Name and address of manufacturer / Applicant	Mylab Pvt. Ltd Khankah Shareef Bahawalpur
	Brand Name +Dosage Form + Strength	Klavimox WSP
	Composition	Each 100 grams contain: Amoxicillin as trihydrate…….16g clavulanic acid as potassium salt ……..4g
	Diary No. Date of R& I & fee	Dy No. 2021: 16.01.2018 PKR 20,000/-: 15.01.2018
	Pharmacological Group	Amoxicillin and beta-lactamase inhibitor
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed innovator's specifications
	Pack size & Demanded Price	100g, 500g, 1 kg, 10kg, 25kg,; As per SRO (10% less than the brand leader)
	Me-too status	PRIMOX-PLUS WATER Soluble Powder. Reg. No. 074026
	GMP status	The firm has been granted additional section Oral powder (penicillin) on the basis of inspection dated 13-14.09.2018.
	Remarks of the Evaluator(IX)	• The firm has mentioned in master Formula that "appropriate overage is added to compensate the potency loss on storage". The firm was asked for clarification. However, the firm did not reply. • The firm was asked to submit complete updated Form 5 duly signed by all concerned persons. However, the firm submitted incomplete Form 5. • The firm was asked to submit complete finished product specifications and testing method. However, the firm did not submit the same. • Details of environmental control processing including waste disposal management. • The product is intended for oral use. In the proposed dosage, the firm has mentioned 1ml/20kg body weight, which is submitted for Clavimox Injection. Clarification is was asked from the firm. The firm did not reply. • Correction of 'clavulanic acid as potassium' to 'potassium clavulanate' is required in Master Formula. • The firm changed clavulanic acid to clavulanic acid as potassium salt without submission of fee. • Available in USP, wherein the monograph is for "for oral suspension'.
	Previous decision	The Board in its 288th meeting deferred the case for the following: Justification on scientific basis for addition of overage in master formulation. The firm was asked to submit complete updated Form 5 duly signed by all concerned persons. However, the firm submitted incomplete Form 5. The firm was asked to submit complete finished product specifications and testing method. However, the firm did not submit the same. Correction of amoxicillin as trihydrate to amoxicillin trihydrate in Master Formula is required. Details of environmental control processing including waste

		disposal management is needed. The product is intended for oral use. In the proposed dosage, the firm has mentioned 1ml/20kg body weight, which is submitted for Clavimox Injection. Clarification is required from the firm. Correction of 'clavulanic acid as potassium' to 'potassium clavulanate' is required in Master Formula. The firm changed clavulanic acid to clavulanic acid as potassium salt without submission of fee.
	Evaluation by PEC	• The firm removed overage. • Updated Form 5 submitted. • The firm has claimed innovator's specifications • The firm changed clavulanic acid to clavulanic acid as potassium salt without submission of fee. • The product is intended for oral use. In the proposed dosage, the firm has mentioned 1ml/20kg body weight, which is submitted for Clavimox Injection. • Available in USP, wherein the monograph is for "for oral suspension'.
	Previous decision	The Board in its 289th meeting deferred the case for the following: Submission of fee for revision of salt form. Submission of correct dosage clarifications about the dosage form.
	Evaluation by PEC	The firm submitted Rs. 5,000/- fee. Submission of correct dosage is required clarification about the dosage form is required.
	Previous decision	The Board in its 290th meeting deferred the case for the following: Submission of correct dosage (in terms of mg per kg body weight) is required. Clarification about the dosage form is required.
	Evaluation by PEC	The firm submitted the revised dosage (in terms of mg per kg body weight) and submitted that the dosage form is WSP.
	Decision of 307th meeting of RB	Deferred for clarification from the firm regarding the dosage form as water soluble powder, because the product is available in USP, wherein the monograph is for "for oral suspension'.
		The firm submitted that the product is available in USP for human use, not veterinary. The firm submitted that they have followed me-too product (Primox-Plus water soluble powder, Reg. No. 74026), which is registered as drug by DRAP
	Decision: Deferred for clarification as their claim is for water soluble drug product while its a suspension in the monograph present in USP.	

Case No. 04 Registration applications of drugs for which stability study data is submitted

a. Verification of stability study data

b. Deferred Cases

223.	Name and address of manufacturer / Applicant	M/s Shaigan Pharmaceutical (Pvt) Ltd., 14 km Adyala road, Post office Dahgal, Rawalpindi
	Brand Name +Dosage Form + Strength	ESSO PLUS TABLET
	Composition	Each modified release tablet contains: Naproxen ……375mg Esomeprazole as magnesium trihydrate……..20mg
	Diary No. Date of R& I & fee	Duplicate, 21-01-2011, Rs.15000/-, 21-01-2011, Rs. 12,000/-, 25-03-2015, Rs. 23,000/-, 04-01-2017

	Pharmacological Group	NSAID + PPI
	Type of Form	Form-5D
	Finished product Specification	In-house specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	VIMOVO (naproxen and esomeprazole magnesium trihydrate) delayed-release tablets, for oral use (USFDA approved)
	Me-too status	N/A
	GMP status	25-9-2019 Panel recommended the renewal of DML. Liquid injectable section (ampoule & vials) available.
	Remarks of the Evaluator(IX)	

STABILITY STUDY DATA

Name of Manufacturer	M/s Shaigan Pharmaceutical (Pvt) Ltd., 14 km Adyala road, Post office Dahgal, Rawalpindi		
Manufacturer of API	**Naproxen:** M/s DIVI's Laboratories limited, Unit-2, Chippada Village, Annavaram (post), Bheemunipatnam Mandal, Visakhapatnam district, Andhra Pradesh – 531162, INDIA **Esomeprazole magnesium trihydrate:** M/s Metrochem API Private Limited, Flat No. 302, Bhanu Enclave, Sundar Nagar, Erragadda, Hyderabad – 500 038. T.S. India		
API Lot No.	**Naproxen:** 2-M-B-0390119 **Esomeprazole magnesium trihydrate:** ESM/1606239		
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, 4, 6 months Real Time: 0, 3, 6 months		
ESSO PLUS TABLET			
Batch No.	T-001	T-002	T-003
Batch Size	1900 tablets	1900 tablets	1900 tablets
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	01-2020	01-2020	01-2020
No. of Batches	03		
Date of Submission	30-11-2020 (Dy. No. 31808)		

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.	The firm has provided reference of already approved product Tikanox-60 and Tikanox-90 Tablets in 291st meeting of Registration board.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Naproxen:** The firm has submitted copy of COA of naproxen (batch # 2-M-B-0390119) from M/s DIVI's Laboratories limited., India. Copy of COA from FPP manufacturer also submitted. **Esomeprazole magnesium trihydrate:** The firm has submitted copy of COA of Esomeprazole (batch # ESM/1606239) from M/s Metrochem API Private Limited, India. Copy of COA from FPP manufacturer also

<table>
<tr><td></td><td></td><td>submitted.</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Naproxen: The firm has submitted details of its analytical method for testing of API as well as from API manufacturer.
Esomeprazole magnesium trihydrate: The firm has submitted details of its analytical method for testing of API as well as from API manufacturer.</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer.</td><td>Naproxen: The firm has submitted 6 months accelerated and 60 months real time stability study data of API as per zone IVA.
Esomeprazole magnesium trihydrate: The firm has submitted 6 months accelerated and 60 months real time stability study data of API. Long term stability data are not as per Zone IVA.</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by regulatory authority of country of origin.</td><td>Naproxen: The firm has submitted copy of GMP certificate for M/s DIVI’s Laboratories Limited, India issued by Drugs Control Administration, Government of Telangana, India. It is valid till 23-07-2021.
Esomeprazole magnesium trihydrate: The firm has submitted copy of License Retention certificate for M/s Metrochem API private limited, Unit-I, India issued by Drugs Control Administration, Government of Telangana, India. It is valid till 29-09-2024.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Naproxen: The firm has submitted copy of commercial invoice specifying import of Naproxen API (10Kg) attested by AD (I & E) DRAP, Islamabad dated 26-04-2019.
Esomeprazole magnesium trihydrate: The firm has submitted copy of invoice for the purchase of Esomeprazole magnesium trihydrate (5 Kg) attested by Assistant Director (I & E) DRAP, Lahore dated 15-09-2016.</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>The firm has submitted copy of method used for analysis of finished Product “ESSO PLUS Tablet 375mg / 20mg ”.</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>The qualitative formulation of Esso plus Tablets 375/20 is same as innovator product.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted 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>T-001</td><td>1900 Tablet</td><td>01-2020</td></tr>
<tr><td>T-002</td><td>1900 Tablet</td><td>01-2020</td></tr>
<tr><td>T-003</td><td>1900 Tablet</td><td>01-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>The firm has submitted comparative dissolution profile of Esso plus tablet (batch # T-001) with reference product Vimovo tablet (batch # KA0175) in media in pH 7.4, 0.1 M HCl, and phosphate buffer pH 6.8). The results show that dissolution profile of the test and the reference product are almost similar.</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw</td><td>The firm has submitted stability study data of 03 batches alongwith chromatograms, raw data sheets, COA, and</td></tr>
</table>

	data sheets, COA, summary data sheets etc.	summary data sheet.
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted audit trail reports of applied product.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted photocopies of data logger record for chambers used in Real Time & Accelerated stability studies of applied product

- The firm has submitted 06 months Accelerated and 06 months Real Time Stability Data for 03 Batches.

Sr.No.	Observations	Response by the Firm
1.	Real time stability data of Naproxen is not as per Zone -IV A.	The firm has submitted copies real time stability study data sheets of 3 batches of Naproxen for 60months at zone IVA storage conditions.
2.	Address mentioned on license of Naproxen API is different from that mentioned on GMP certificate and certificate of analysis.	The firm has submitted GMP certificate with correct address of API manufacturer.
3.	Documents for the procurement of API (Naproxen) in case of import alongwith endorsement from DRAP office shall be submitted.	The firm has submitted copy of commercial invoice specifying import of Naproxen API (10Kg) attested by AD (I & E) DRAP, Islamabad dated 26-04-2019.

Previous Decision: Registration Board deferred the case till the decision of Health Task force (M-307).
Evaluation by PEC: The firm requested that the case may be reconsidered

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.

Case no. 06 Registration applications of drugs submitted on Form 5F

a. New cases

224.	Name, address of Applicant / Marketing Authorization Holder	M/s Sami Pharmaceuticals Pvt Limited. F-95, S.I.T.E, Karachi, Pakistan
	Name, address of Manufacturing site.	M/s Sami Pharmaceuticals Pvt Limited. F-95, 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. 7085 dated 03.03.2021
	Details of fee submitted	PKR 50,000/-: dated 22.02.2021
	proposed proprietary name / brand name	SUGAT 200mg/2ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml contains: Sugammadex Sodium equivalent to Sugammadex……..200mg
	Pharmaceutical form of applied drug	Injectable
	Pharmacotherapeutic Group of (API)	Reversal of Neuromuscular Blockers, Antidotes
	Reference to Finished product specifications	Innovator's specs
	Proposed Pack size	1's

	Proposed unit price	As per SRO
	status in reference regulatory authorities	BRIDION 200mg/2ml Injection, USFDA Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	Apicore Pharmaceuticals Private Limited Block no. 252 – 253, village: dhobikuva 391440, opp: Jain Irrigation, Padra – Jambusar highway, Tal. Padra, District Vadodara, 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, 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)	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 verification of assay analysis, 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 18 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (API-233/19/02/04, API-233/19/02/05 API-233/19/06/09)
	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 A BRIDION 200mg/2ml Injection by Merck Sharp & Dohme Corp by performing quality tests (Identification, composite Assay, pH, osmolality, sterility and endotoxin test).
	Analytical method validation/verification of product	Method validation studies for assay have submitted including linearity, accuracy, precision, robustness, specificity.

Manufacturer of API	Apicore Pharmaceuticals Private Limited Block no. 252 – 253, village: Dhobikuva 391440, Opp: Jain Irrigation, Padra – Jambusar Highway, Tal. Padra, District Vadodara, Gujrat India
API Lot No.	API-233/ 19/01/03
Description of Pack (Container closure system)	Glass Vial Type-I Clear Colorless Chlorobutyl Rubber Stopper Aluminum Crimp-Caps and Flip-Off Seals
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	600 vials	600 vials	600 vials
Manufacturing Date	09-2019	09-2019	09-2019
Date of initiation	09-2019	09-2019	09-2019
No. of Batches	03		

7.	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.
8.	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/20011774 is issued by CFDA valid till 01/01/2022.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	copy of commercial invoice (Invoice# TG9121801295 19.03.2019 with received quantity i.e. 1 kg) for the purchase of Sugammaex Sodium from M/s. Apicore Pharmaceuticals Private Limited attested by AD (I&E) DRAP, Karachi (08.04.2019).
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 & accelerated)	Submitted

Remarks:

Deficiencies		**Reply of the firm**
2.3.S.4.2	For determination of suga-chloro content, you have mentioned two different RI detectors, i.e., Perkin Elmer and Waters 2414. Clarification is required about the use of either detector.	The firm submitted that they have used only one detector. The firm did not submit the name of the detector in the revised method.
3.2.P.3.2	• In the drug product specifications, you have specified the osmolality to be 300–500. However, the composition does not depict the use of excipient for osmolality adjustment.	• The firm submitted that the osmolality of the reference product was 300 – 500 mOsm/Kg. Osmolality of our product was also in the range of 300 – 500 mOsm/Kg.

	Clarify the same. • Moreover, the pH has been adjusted with HCl, and not with a base. Provide rationale for the alkaline pH before its adjustment.	• The firm submitted that the pH of the sugammadex sodium 10% solution is 7.8 – 9.0. Therefore, the pH was adjusted with hydrochloric acid.
2.3.S.4.3	The firm has performed impurity testing by simultaneous method in the drug substance. The firm did not perform the method validation/verification for the same.	The firm submitted the method validation for impurities performed by the drug substance manufacturer.
3.2.P.5.1	• The PMDA has specified the identification (HPLC, ultraviolet-visible spectrum), extractable volume, foreign insoluble matter, insoluble particulate matter, and assay (the free acid of Org48302, sugammadex + the free acid of Org48302) tests for the drug product, which have not been tested in the applied product. • You have not performed the filled volume / weight variation test. • You shall provide a discussion and justification for incomplete analyses of the drug product.	The firm submitted that they followed the FDA specifications as the product is approved in FDA. They submitted that they have already performed the extractable volume, clarity, visible particles and particulate matter, but not submitted to DRAP as these are part of our in-process testing.
3.2.P.5.3	• The firm has performed impurity testing by simultaneous method in the drug product. The firm did not perform the method validation for the same.	The firm submitted the analytical method validation report for the assay. • The firm did not perform analytical method validation by simultaneous method. • The firm did not perform the specificity test in the presence of impurities.
3.2.P.6	• Provide the procedure of standardization of the working standard and detail along with CoA of the reference standard used, and complete traceability. • In the CoA of the working standard, you have mentioned the precaution "once vial is opened it should be used within three months". Provide the rationale behind such precaution. Furthermore, the same working standard has been even at 6-month stability data. Justify its use beyond three months.	The firm submitted they have standardized their own working standard against the working standard of the drug substance manufacturer. • The firm submitted that there were multiple vials after standardization.
3.2.P.8.3	• The PMDA specifies that the attributes tested in stability studies include identification, extractable volume, foreign insoluble matter, insoluble particulate matter, and container/closure integrity testing, which have not been tested in the applied product. Clarification is required. • You shall clarify whether the stability was conducted placing the vial erect or inverted.	• The firm submitted that they followed the FDA specifications as the product is approved in FDA. They submitted that they have already performed the extractable volume, clarity, visible particles and particulate matter, but not submitted to DRAP as these are part of our in-process testing. • The vials were placed in inverted position. Revised stability protocol is attached.

Decision: The Board deferred the application for submission of:

- **Analytical method validation by simultaneous method.**
- **Specificty test in the presence of impurities.**
- **Justification for not performing test for filled volume for the drug product.**
- **Discussion along with the justification for incomplete analyses of the drug product.**

225.	Name, address of Applicant / Marketing Authorization Holder	M/s Sami Pharmaceuticals Pvt Limited. F-95, S.I.T.E, Karachi, Pakistan
	Name, address of Manufacturing site.	M/s Sami Pharmaceuticals Pvt Limited. F-95, 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. 7086 dated 03.03.2021
	Details of fee submitted	PKR 50,000/-: dated 22.02.2021
	proposed proprietary name / brand name	SUGAT 500mg/5ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Sugammadex Sodium equivalent to Sugammadex..500mg
	Pharmaceutical form of applied drug	Injectable
	Pharmacotherapeutic Group of (API)	Reversal of Neuromuscular Blockers, Antidotes
	Reference to Finished product specifications	Innovator's specs
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	BRIDION 500mg/5ml Injection, USFDA Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	Apicore Pharmaceuticals Private Limited Block no. 252 – 253, village: dhobikuva 391440, opp: Jain Irrigation, Padra–Jambusar highway, Tal. Padra, District Vadodara, 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, 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)	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 verification of assay analysis, 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 18 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (API-233/19/02/04, API-233/19/02/05 API-233/19/06/09)
	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 A BRIDION 200mg/2ml Injection by Merck Sharp & Dohme Corp by performing quality tests (Identification, composite Assay, pH, osmolality, sterility and endotoxin test).
	Analytical method validation/verification of product	Method validation studies for assay have submitted including linearity, accuracy, precision, robustness, specificity.

Manufacturer of API	Apicore Pharmaceuticals Private Limited Block no. 252 – 253, village: Dhobikuva 391440, Opp: Jain Irrigation, Padra – Jambusar Highway, Tal. Padra, District Vadodara, Gujrat India		
API Lot No.	API-233/ 19/01/03		
Description of Pack (Container closure system)	Glass Vial Type-I Clear Colorless Chlorobutyl Rubber Stopper Aluminum Crimp-Caps and Flip-Off Seals		
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	600 vials	600 vials	600 vials
Manufacturing Date	09-2019	09-2019	09-2019
Date of initiation	09-2019	09-2019	09-2019
No. of Batches	03		

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.	Copy of GMP certificate No. S-GMP/20011774 is issued by CFDA valid till 01/01/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	copy of commercial invoice (Invoice# TG9121801295 19.03.2019 with received quantity i.e. 1 kg) for the purchase of Sugammaex Sodium from M/s. Apicore Pharmaceuticals Private

		Limited attested by AD (I&E) DRAP, Karachi (08.04.2019).
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 & accelerated)	Submitted
Remarks: As for above strength		
Decision: The Board deferred the application for submission of: • **Analytical method validation by simultaneous method.** • **Specificty test in the presence of impurities.** • **Justification for not performing test for filled volume for the drug product.** • **Discussion along with the justification for incomplete analyses of the drug product.**		
226.	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. 8048: dated 11.03.2021
	Details of fee submitted	PKR 50,000/-: dated 01.02.2021
	proposed proprietary name / brand name	OBTIX 5mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Obeticholic acid …..5mg
	Pharmaceutical form of applied drug	Light green to green colored, round shape film coated tablets plain from both side Immediate release
	Pharmacotherapeutic Group of (API)	Bile and liver therapy
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	OCALIVA 5mg Tablets by M/s. Intercept Pharma UK & Ireland, EMA Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020

	Name and address of API manufacturer.	VIRUPAKSHA ORGANICS LIMITED Survey No. 10, Gaddapotharam Village, Jinnaram Mandal,Sangareddy District – 502319,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 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, tests for impurities & related substances, 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 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: AOBTC0217001,AOBTC0217002, AOBTC0217003
	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 OCALIVA 5mg Tablets by M/s. Intercept Pharma UK & Ireland by performing quality tests (Identification, Assay, Dissolution etc). CDP has been performed against the same brand that is OCALIVA 5mg Tablets by M/s. Intercept Pharma UK & Ireland in Acid media (pH 1.2), Phosphate Buffer (pH 6.8) & acetate buffer(pH 4.5).
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision, robustness, specificity.

STABILITY STUDY DATA

Manufacturer of API	VIRUPAKSHA ORGANICS LIMITED Survey No. 10, Gaddapotharam Village, Jinnaram Mandal,Sangareddy District – 502319,Telangana, India.
API Lot No.	AOBTC0118001
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, 4, 6 (Months) Real Time: 0, 3, 6 (Months)

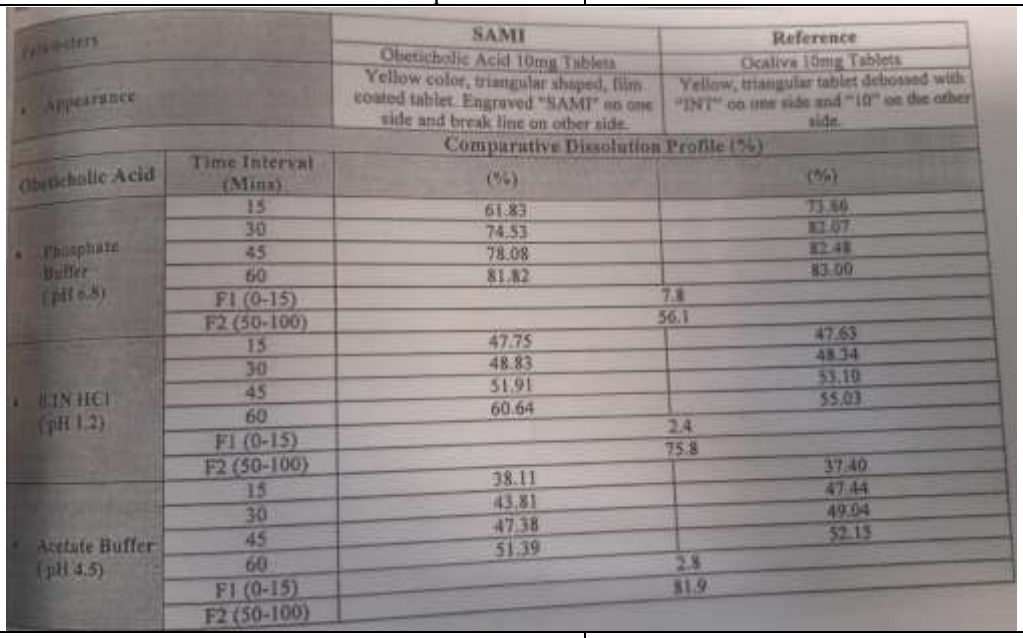
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	03.04.2020	03.04.2020	03.04.2020
No. of Batches	03		

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. 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. • 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 GMP certificate No. 5884/E1/2018 issued by FAC valid till 27/03/2023 in respect of nine drugs (not containing obetichoic acid).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice (Invoice# AEX/052/2019-20 Sep 25 2019 with received quantity i.e. 250 gm) for the purchase Obeticholic acid from VIRUPAKSHA ORGANICS LIMITED attested by AD (I&E), Karachi dated 02-10-2019
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 & accelerated)	Submitted

Remarks OF Evaluator:

2 3.S.4 1	• The European public assessment report has specified the palladium and microbial test for the drug substance, which has not been performed the drug substance and drug product manufacturers. Justification is required. • Since the semisynthetic drug substance originates from human/animal source, a certificate shall be provided, confirming that the drug substance is free from BSE and TSE	• We developed the product as per FDA. Tests for Palladium and microbial tests are not mentioned in FDA Chemistry review for this product • Certificate of BSE and TSE for Obeticholic Acid attached
2 3.S.4.3	The firm has performed impurity testing by simultaneous method in the drug substance. The drug product manufacturer did not perform the method validation/verification for the same.	We performed analytical method validation for assay method as per CTD requirement. Method validation of impurity method performed by drug substance manufacturer submitted.
3.2.S.4.5	A discussion/justification shall be provided on the inclusion of certain tests, evolution of tests	Justification of specification attached

	analytical procedures and acceptance criteria	
3.2.S.7	The European public assessment report has specified the conditions for real time and accelerated stability studies as 5°C ± 3°C and 25 °C/60% RH, respectively. The drug substance manufacturer has provided the data as per Zone IV-A. Justification is required about the stability of the drug substance in Zone IV-A as compared to 5°C ± 3°C	We developed the product as per FDA. In FDA Chemistry review of this product, the stability parameters / storage conditions of drug substance is not mentioned. The drug substance is stable at Zone IV-A stability conditions which is much more stringent therefore we accepted this
3.2.P.2.2.1	The appendix I of WHO for CDP specifies that a maximum of one time-point should be considered after 85% dissolution of the reference (comparator) product has been reached. The appendix I of WHO for CDP also specifies that in the case where 85% dissolution cannot be reached owing to poor solubility of the API or the release mechanism of the dosage form, the dissolution should be conducted until an asymptote (plateau) has been reached. The drug product manufacturer has used 15, 30, 45 and 60 minutes time points without fulfilling the above criteria. Justification is required.	We performed CDP at 15, 30, 45 and 60 minutes time points in which plateau has reached after 30 minutes in all three mediums. CDP report along with graphical representation is attached for your kind perusal.
		
3.2.P.3.3	Tests and acceptance criteria shall be provided (with justification, including experimental data) performed at the critical steps identified. in the manufacturing Process to ensure that the process is controlled	Revised section 3.2.P.3.3 is attached BPIs submitted in dossier in Module 2 (Annexure 05) for OBTIX 10mg tablet & in PSI file under annexure 10 for OBTIX 5mg tablet, have all experimental data details
3.2.P.3.4.1	You have claimed in-house specifications for the excipients. For excipients of non-compendial standards, specifications as well as analytical procedures shall be provided. Moreover, validation information for the analytical procedures for in-house standard excipients shall be submitted. Justification of the specifications for the analytical procedures for in-house standard excipients shall also be provided.	Specifications and analytical procedures for Apple green Lake color, Iron oxide yellow, and sheffcoat PVA white are submitted. The firm submitted validation of assay method of Apple green Lake color and Iron oxide yellow. The firm submitted the justification of specifications as in-house. The performed tests (in the absence of CoA from excipients manufacturer) could not justify the quality of the excipients.

Parameters		SAMI	Reference
• Appearance		Obeticholic Acid 10mg Tablets Yellow color, triangular shaped, film coated tablet. Engraved "SAMI" on one side and break line on other side.	Ocaliva 10mg Tablets Yellow, triangular tablet debossed with "INT" on one side and "10" on the other side.
		Comparative Dissolution Profile (%)	
Obeticholic Acid	Time Interval (Mins)	(%)	(%)
• Phosphate Buffer (pH 6.8)	15	61.83	73.86
	30	74.53	82.07
	45	78.08	82.48
	60	81.82	83.00
	F1 (0-15)	7.8	
	F2 (50-100)	56.1	
• 0.1N HCl (pH 1.2)	15	47.75	47.63
	30	48.83	48.34
	45	51.91	53.10
	60	60.64	55.03
	F1 (0-15)	2.4	
	F2 (50-100)	75.8	
• Acetate Buffer (pH 4.5)	15	38.11	37.40
	30	43.81	47.44
	45	47.38	49.04
	60	51.39	52.15
	F1 (0-15)	2.8	
	F2 (50-100)	81.9	

	Provide the source of magnesium stearate. In case of human or animal origin, a certificate shall be provided, confirms that the excipient(s) are free from BSE and TSE	Magnesium stearate certificate of BSE and TSE attached
3.2.P.5.3	The firm has performed impurity testing by simultaneous method in the drug Product. The firm did not perform the method validation for the same	We had already performed impurity method validation but submitted only assay method validation as per requirement. Impurity method validation protocol and reports not submitted. • The firm did not perform analytical method validation by simultaneous method. • The firm did not perform the specificity test in the presence of impurities.
3.2.P.5.4	The European public assessment report has specified water content tests, which has not been performed by the drug product manufacturer. Justification is required	We developed the product as per FDA . In FDA Chemistry review the test for water content is not mentioned. However on your suggestion, we have included the test in our stability protocol and committed to perform the same on upcoming stability time points. Revised protocol is attached for your kind perusal.
3.2.P.6	In the COA of the working standard, you have mentioned precaution" once vial is opened it should be used within three months". Provide the rationale behind such precaution. Furthermore, the same working standard has been even used at 6-month stability data. justify its use beyond three months	The rationale behind the precautions is just to ensure the quality and potency of working standard Multiple vials are prepared after standardization of working standard against reference standard, and validity of each vial is 03 months. After 03 months, the vial is discarded and next vial is used
3.2.P.8.3	The European public assessment report specifies that the samples in stability studies were tested for water content, which has not been tested in the applied product. Clarification is required	We developed the product as per FDA. In FDA Chemistry review the test for water content is not mentioned. However on your suggestion, we have included the test in our stability protocol and committed to perform the same on upcoming stability time points. Revised protocol is attached under annexure- 10 for your kind perusal.

Decision: The Board deferred the application for submission of:

- **Analytical method validation by simultaneous method.**
- **Specificty test in the presence of impurities.**
- **Justification for not performing CDP as per WHO guideline.**

227.	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. 8047 : dated 11.03.2021
	Details of fee submitted	PKR 50,000/-: dated 01.02.2021

	proposed proprietary name / brand name	OBTIX 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Obeticholic acid …..10mg
	Pharmaceutical form of applied drug	Light green to green colored, round shape film coated tablets plain from both side Immediate release
	Pharmacotherapeutic Group of (API)	Bile and liver therapy
	Reference to Finished product specification	Innovator's Specification
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	OCALIVA 5mg Tablets by M/s. Intercept Pharma UK & Ireland, EMA Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	VIRUPAKSHA ORGANICS LIMITED Survey No. 10, Gaddapotharam Village, Jinnaram Mandal,Sangareddy District – 502319,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 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, tests for impurities & related substances, 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 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: AOBTC0217001,AOBTC0217002,AOBTC0217003
	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 OCALIVA 10mg Tablets by M/s. Intercept Pharma UK & Ireland by performing quality tests (Identification, Assay, Dissolution etc). CDP has been performed against the same brand that is OCALIVA 10mg Tablets by M/s. Intercept Pharma UK & Ireland in Acid media (pH 1.2), Phosphate Buffer (pH 6.8) & acetate buffer(pH 4.5). 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, robustness, specificity.	
STABILITY STUDY DATA			
Manufacturer of API	VIRUPAKSHA ORGANICS LIMITED Survey No. 10, Gaddapotharam Village, Jinnaram Mandal,Sangareddy District – 502319,Telangana, India.		
API Lot No.	AOBTC0118001		
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, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	02.04.2020	02.04.2020	02.04.2020
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. 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. • 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 GMP certificate No. 5884/E1/2018 issued by FAC valid till 27/03/2023 in respect of nine drugs (not containing obeticholic acid).	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice (Invoice# AEX/052/2019-20 Sep 25 2019 with received quantity i.e. 250 gm) for the purchase Obeticholic acid from VIRUPAKSHA ORGANICS LIMITED attested by AD (I&E), Karachi dated 02-10-2019	
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: As for above strength
Decision: The Board deferred the application for submission of: • **Analytical method validation by simultaneous method.** • **Specificty test in the presence of impurities.** • **Justification for not performing CDP as per WHO guideline.**

Case no. 07 Registration applications of import cases

a. New Cases (Human)

Agenda of Evaluator PEC-XI

Registration applications of New Section of human drugs on Form 5F

M/s Invictus Pharmaceuticals Plot No. 21 & 26, Street No. NS-2, RCCI, Industrial Estate, Rawat".

The Central Licensing Board in its 273rd meeting held on 15th January, 2020 has considered and approved the following three (03) sections of "M/s Invictus Pharmaceuticals Plot No. 21 & 26, Street No. NS-2, RCCI, Industrial Estate, Rawat" under Drug Manufacturing License No. 000892 (Formulation) vide approval letter No. F. 1-37/2016-Lic (Vol-I) dated 18th February 2020.

S No.	Section
1.	Dry Powder Injection Section (Cephalosporine)
2.	Dry Powder for suspension Section (Cephalosporine))
3.	Capsule Section (Cephalosporine)

Following applications have been submitted for registration by the firm.

228.	Name, address of Applicant / Marketing Authorization Holder	Invictus Pharmaceuticals NS2, Rawalpindi, Rawat Industrial Estate, Islamabad, Rawalpindi, Islamabad Capital Territory
	Name, address of Manufacturing site.	Invictus Pharmaceuticals NS2, Rawalpindi, Rawat Industrial Estate, Islamabad, Rawalpindi, Islamabad Capital Territory
	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. 23340 dated 26-08-2021
	Details of fee submitted	PKR 30,000/-: dated 26-07-2021
	proposed proprietary name / brand name	Cef –Vic Dry Suspension 100mg /5ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Cefixime as Trihydrate….100mg
	Pharmaceutical form of applied drug	Almost light pink color powder having Strawberry powder for Reconstitution Powder for suspension
	Pharmacotherapeutic Group of (API)	Cephalosporine
	Reference to Finished product specification	Innovator's specifications
	Proposed Pack size	30ml
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Cefixime for oral suspension 100mg/5ml by M/s BELCHER

		USFDA approved
	For generic drugs (me-too status)	Cefexol Suspension 100mg/5ml by M/s Nabiqasim Industries (Pvt) Ltd (Reg#025641)
	GMP status of the Finished product manufacturer	New section
	Name and address of API manufacturer.	Pharmagen Limited Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore. Tel: +92 (042) 5935261-68 Fax: +92 (042) 5935269 E-mail: pblbd@hotmail.com Web: www.pharmagen.com.pk
	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 ºC ± 2 º C / 65% ± 5% RH for 36 months. (Batch No. 00244/135/2010, 00243/136/2010 & 00244/137/2010)
	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	Firm has performed pharmaceutical equivalence against the product Cefspan DS 100mg/5ml by M/s Barret Hodgson (Pvt) Ltd
	Analytical method validation / verification of product	The firm have submitted method verification studies for applied product
STABILITY STUDY DATA		
Manufacturer of API	Pharmagen Limited Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore. Tel: +92 (042) 5935261-68	

	Fax: +92 (042) 5935269 E-mail: pblbd@hotmail.com Web: www.pharmagen.com.pk		
API Lot No.	00243/078/2020		
Description of Pack (Container closure system)	Powder Filled in Amber colored 30ml glass bottle USP Type III with 25 mm PP Alu caps with conical cups.		
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 & 24 (Months)		
Batch No.	TDS-001	TDS-002	TDS-003
Batch Size	1000 packs	1000 packs	1000 packs
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	13-05-20	13-05-20	13-05-20
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 Pharmagen Limited, valid Up to 8-1-2022.
3	Documents for the procurement of API with approval from DRAP (in case of import).	Not Applicable
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)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC [XI]:

Section	Observations	Response
1.3.1.-1.3.2	The address mentioned in submitted application is different from the address mentioned on DML, clarify?	The address of applicant in section 1.3.1 & 1.3.2 is updated as per follows: "M/s Invictus Pharmaceuticals, Plot No. 21 & 26, Street No. NS-2, RCCI, Industrial Estate, Rawat". Relevant page of module 1 Form 5F is submitted.
1.5.6	In Form 5F you have mentioned innovator's specifications for the product under section 1.5.6. while the monograph of applied product is available in USP, clarify?	We have mentioned USP specifications in section 1.5.6 and have also provided the same USP specifications for the drug product is all relevant sections of module 2 and module 3.
3.2.S.4.1.	As per the drug substance specifications of the drug substance manufacturer i.e. M/s Pharmagen Limited, the firm submitted that material complies BP, USP and in-	• The drug substance have been procured from Pharmagen Limited which have been granted approval for manufacturing of cefixime by Licensing Division DRAP and the same source have been approved by Registration Board in the cases of local manufacturing

	house specifications, justification is required as how the drug substance follow all the specifications	of cefixime for various firms on CTD after review of its complete data. • There are certain differences in the specifications of cefixime as defined in USP and BP, the drug substance manufacturer has identified all the changes and have tested its product against the BP as well as USP specifications. • The drug substance manufacturer has also performed validation / verification studies of the analytical method for assay, related substances and residual solvents for both BP as well as USP analytical procedures. As per the results of the verification studies both methods have been verified and the material complies the individual acceptance criteria for each test as specified in the monograph. • As per our vendor qualification system we have selected Pharmagen Limited based on its regulatory approval by DRAP, availability of DMF and stability study data as per zone IV-A. As per our approved SOPs after document review, we ordered small quantity of the drug substance for testing purpose and performed testing as per the USP specifications and finally selected the vendor when all tests as per USP specifications were complied. Our specifications and analytical method for in house testing of the drug substance is also based on USP method. • *It is worth mentioning that, Assay limits and type of tests are different between two monographs of USP & BP, hence compliance to both monographs has to be justified.* • Relevant documents of drug substance validation report and API specifications and analytical method of drug product manufacturer is submitted
3.2.S.4.1. - 3.2.S.4.2	Copies of Drug substance specification and analytical procedures used for routine testing of Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.	Drug substance specification and analytical procedure of Invictus Pharmaceuticals is provided
3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer of drug substance(s) shall be submitted.	Analytical method verification studies (including specificity, accuracy, repeatability) performed by drug product manufacturer is provided
3.2.P.1	• The composition of applied product is not as per innovator's product, clarify • Quantity of cefixime per unit dose shall be justified with equivalency factor for cefixime trihydrate.	• The qualitative composition of our product is based upon the USFDA approved reference product i.e. Cefixime suspension by Belcher Pharmaceuticals, LLC. Furthermore, all the excipients used in our formulation are commonly used excipients and no incompatibility among any excipient has been reported in handbook of pharmaceutical excipients. All excipients are also recommended for use in similar formulations in the FDA excipients database as well. We have also performed pharmaceutical equivalence studies with the innovator product and also completed the

<table>
<tr><td></td><td></td><td>accelerated stability studies and real time stability studies till 6 months, and the results within acceptable limit also support that the formulation is compatible and stable. However, the composition of applied product is different from the innovator product as mentioned below
<table>
<tr><td>Applied product</td><td>Suprax 100mg/5ml DS</td></tr>
<tr><td>Cefixime trihydrate (micronized)</td><td>Cefixime trihydrate</td></tr>
<tr><td>CMC Sodium</td><td>Xanthan gum</td></tr>
<tr><td>Sodium benzoate</td><td>Sodium benzoate</td></tr>
<tr><td>Sugar Fine</td><td>Sucralose</td></tr>
<tr><td>Colloidal silicon dioxide</td><td>Colloidal silicon dioxide</td></tr>
<tr><td>Strawberry flavor</td><td>Strawberry flavor</td></tr>
<tr><td></td><td>Sucrose</td></tr>
</table>
• Quantity of cefixime per unit dose and per batch have been explained and justified based upon the salt factor calculation and assay results. The justification is submitted.
• Firm has used the theoretical factor for adjustment of water content while dispensing, instead of the actual results of “water content test” reported in the drug substance analysis.</td></tr>
<tr><td>3.2.P.2.1.1</td><td>Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.</td><td>Compatibility studies of the drug substance with excipients is not required to be performed since the qualitative composition of our product is based upon the USFDA approved reference product i.e. Cefixime suspension by Belcher Pharmaceuticals, LLC. Furthermore, all the excipients used in our formulation are commonly used excipients and no incompatibility among any excipient has been reported in handbook of pharmaceutical excipients. All excipients are also recommended for use in similar formulations in the FDA excipients database as well. We have also performed pharmaceutical equivalence studies with the innovator product and also completed the accelerated stability studies and real time stability studies till 6 months, and the results within acceptable limit also support that the formulation is compatible and stable. However, Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.</td></tr>
<tr><td>3.2.P.3.3</td><td>In Description of manufacturing process and process controls, you have submitted manufacturing outline mentioning different composition of formulation than applied formulation</td><td>We have used the same composition of the formulation for the product development and stability studies and have provided the same formulation in all sections of our CTD application. However, any difference in the formulation in section 3.2.P.3.3 may be considered as a typographical mistake. However we assure that we have used only one composition throughout the studies which have already been provided in section 3.2.P.1.</td></tr>
<tr><td>3.2.P.4.1</td><td>The specifications for all the excipients used in formulation of applied product is not provided</td><td>We have provided specifications and procedures for all excipients in section 3.2.P.4.1 and 3.2.P.4.2 as per the CTD guidance document approved by Registration Board. However, we are again submitting the same for</td></tr>
</table>

		your consideration. All excipients used in our formulation are well studied and all excipients except strawberry flavor are pharmacopoeial. The specifications and analytical procedures are submitted**.** Specifications for *CMC Sodium, is not submitted*
3.2.P.5.1	Justification for finished product specifications of USP is required as the drug substance manufacturer have claimed BP specifications as per section 3.2.S.4.4 Batch Analyses?	• The drug substance have been procured from Pharmagen Limited which have been granted approval for manufacturing of cefixime by Licensing Division DRAP and the same source have been approved by Registration Board in the cases of local manufacturing of cefixime for various firms on CTD after review of its complete data. • There are certain differences in the specifications of cefixime as defined in USP and BP, the drug substance manufacturer has identified all the changes and have tested its product against the BP as well as USP specifications. • The drug substance manufacturer has also performed validation / verification studies of the analytical method for assay, related substances and residual solvents for both BP as well as USP analytical procedures. As per the results of the verification studies both methods have been verified and the material complies the individual acceptance criteria for each test as specified in the monograph. • As per our vendor qualification system we have selected Pharmagen Limited based on its regulatory approval by DRAP, availability of DMF and stability study data as per zone IV-A. As per our approved SOPs after document review, we ordered small quantity of the drug substance for testing purpose and performed testing as per the USP specifications and finally selected the vendor when all tests as per USP specifications were complied. Our specifications and analytical method for in house testing of the drug substance is also based on USP method. We have developed the drug product as per USP specifications after thorough analysis of the drug substance as per USP specifications.
3.2.P.5.2	Provide signed copy of analytical methods used for applied product	We are submitting the analytical procedure of the drug product as per the CTD guidance document approved by Registration Board.
3.2.P.5.3	Submitted method verification report does not describe the sample preparation/standard preparation for various performance parameters.	Protocols and report for method verification studies are again submitted for your review and consideration. We would also like to inform that the sample and standard preparation method are defined in the analytical procedure of drug product in section 3.2.P.5.2. The verification protocols and report are submitted. *The sample preparation procedure for different concentrations in the parameter of accuracy shall be submitted.*
3.2.P.8	• Submit Raw data sheets and COA containing detail of sample preparation, standard preparation for various performance parameters. • Preservative content and efficacy test	• The details of sample preparation and standard preparation is the same throughout the stability studies as mentioned in section 3.2.P.5.2. We have used the USP method for sample and standard preparation throughout the stability studies. However Raw data

	not performed during stability study, clarify? • In use stability study of reconstitution suspension shall be submitted • The applied pack size is 30ml while the pack size mentioned in two batches of stability study is 60ml and one batch is 30ml, clarify	sheets are submitted. • Preservative content and effectiveness is not the part of stability specifications nor recommended in USP monograph or ICH Q1 guidelines, therefore this test was not performed. Furthermore, the acceptable results of all the tests like physical appearance, taste, flavor, moisture, pH and assay depicts the effectiveness of preservative content in the formulation. • *However, tests for antimicrobial preservative content and efficacy of preservative as recommended by ICH Q1 (R2) guidelines and USP chapter <51> should be performed for finished product* • We are submitting the in-use stability study results. *The submitted pack size in the in-use stability study is also 60ml* • There is a typographic mistake, the applied product is 30mL suspension. • *Raw data sheets, including actual details of sample solution preparation & standard preparation, weight of standard, potency of standard & calculation formula applied, shall be submitted.*

Decision: Deferred for following:

- **Justification for use of CMC sodium as an excipient, since innovator's formulation does not include it.**
- **The specifications for CMC sodium used in formulation of applied product is not provided**
- **The sample preparation procedure for different concentrations in the parameter of accuracy shall be submitted.**
- **Clarification since the submitted COA of relevant batch of drug substance used for development studies is according to B.P while the specifications submitted for drug substance are USP.**
- **Tests for antimicrobial preservative content and efficacy of preservative as recommended by ICH Q1 (R2) guidelines and USP chapter <51> should be performed for finished product**
- **Raw data sheets, including actual details of sample solution preparation & standard preparation, weight of standard, potency of standard & calculation formula applied, shall be submitted.**

229.	Name, address of Applicant / Marketing Authorization Holder	Invictus Pharmaceuticals, NS2, Rawalpindi, Rawat Industrial Estate, Islamabad, Rawalpindi, Islamabad Capital Territory
	Name, address of Manufacturing site.	Invictus Pharmaceuticals, NS2, Rawalpindi, Rawat Industrial Estate, Islamabad, Rawalpindi, Islamabad Capital Territory
	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. 21323 dated 04-08-2021
	Details of fee submitted	PKR 30,000/-: dated 26-07-2021
	proposed proprietary name / brand name	Cef –Vic Dry Suspension 200mg /5ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Cefixime as Trihydrate….200mg
	Pharmaceutical form of applied drug	Almost light pink color powder having Strawberry powder for

		Reconstitution Powder for suspension
	Pharmacotherapeutic Group of (API)	Cephalosporine
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	30ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefixime for oral suspension 200mg/5ml by M/s BELCHER USFDA approved
	For generic drugs (me-too status)	Megnett DS Oral Suspension 200mg/5ml by M/s SJ & G Fazul Ellahie (Pvt) Ltd (Reg#024000)
	GMP status of the Finished product manufacturer	New section
	Name and address of API manufacturer.	Pharmagen Limited Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore. Tel: +92 (042) 5935261-68 Fax: +92 (042) 5935269 E-mail: pblbd@hotmail.com Web: www.pharmagen.com.pk
	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 ºC ± 2 º C / 65% ± 5% RH for 36 months. (Batch No. 00244/135/2010, 00243/136/2010 & 00244/137/2010)
	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	Firm has performed pharmaceutical equivalence against the product Cefspan DS 200mg/5ml by M/s Barret Hodgson Pakistan (Pvt) Ltd
	Analytical method validation / verification of product	The firm have submitted method verification studies for applied product

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore. Tel: +92 (042) 5935261-68 Fax: +92 (042) 5935269 E-mail: pblbd@hotmail.com Web: www.pharmagen.com.pk		
API Lot No.	00243/078/2020		
Description of Pack (Container closure system)	Powder Filled in Amber colored 30ml glass bottle USP Type III with 25 mm PP Alu caps with conical cups.		
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 & 24 (Months)		
Batch No.	TDS-001	TDS-002	TDS-003
Batch Size	1000 packs	1000 packs	1000 packs
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	13-05-20	13-05-20	13-05-20
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 Pharmagen Limited, valid Up to 8-1-2022.
3	Documents for the procurement of API with approval from DRAP (in case of import).	Not Applicable
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)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC [XI]:

Section	Observations	Response
1.3.1.-1.3.2	The address mentioned in submitted application is different from the address mentioned on DML, clarify?	The address of applicant in section 1.3.1 & 1.3.2 is updated as per follows: "M/s Invictus Pharmaceuticals, Plot No. 21 & 26, Street No. NS-2, RCCI, Industrial Estate, Rawat". Relevant page of module 1 Form 5F is submitted.

1.5.6	In Form 5F you have mentioned innovator's specifications for the product under section 1.5.6. while the monograph of applied product is available in USP, clarify?	We have mentioned USP specifications in section 1.5.6 and have also provided the same USP specifications for the drug product is all relevant sections of module 2 and module 3.
3.2.S.4.1.	As per the drug substance specifications of the drug substance manufacturer i.e. M/s Pharmagen Limited, the firm submitted that material complies BP, USP and in-house specifications, justification is required as how the drug substance follow all the specifications	• The drug substance have been procured from Pharmagen Limited which have been granted approval for manufacturing of cefixime by Licensing Division DRAP and the same source have been approved by Registration Board in the cases of local manufacturing of cefixime for various firms on CTD after review of its complete data. • There are certain differences in the specifications of cefixime as defined in USP and BP, the drug substance manufacturer has identified all the changes and have tested its product against the BP as well as USP specifications. • The drug substance manufacturer has also performed validation / verification studies of the analytical method for assay, related substances and residual solvents for both BP as well as USP analytical procedures. As per the results of the verification studies both methods have been verified and the material complies the individual acceptance criteria for each test as specified in the monograph. • As per our vendor qualification system we have selected Pharmagen Limited based on its regulatory approval by DRAP, availability of DMF and stability study data as per zone IV-A. As per our approved SOPs after document review, we ordered small quantity of the drug substance for testing purpose and performed testing as per the USP specifications and finally selected the vendor when all tests as per USP specifications were complied. Our specifications and analytical method for in house testing of the drug substance is also based on USP method. • *It is worth mentioning that, Assay limits and type of tests are different between two monographs of USP & BP, hence compliance to both monographs has to be justified.* • Relevant documents of drug substance validation report and API specifications and analytical method of drug product manufacturer is submitted.
3.2.S.4.1. - 3.2.S.4.2	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.	Drug substance specification and analytical procedure of Invictus Pharmaceuticals is submitted.
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.	Analytical method verification studies (including specificity, accuracy, repeatability) performed by drug product manufacturer is submitted.
3.2.P.1	• The composition of applied product is not as per innovator's product, clarify • Quantity of cefixime per unit dose shall be justified with equivalency factor for cefixime trihydrate.	• The qualitative composition of our product is based upon the USFDA approved reference product i.e. Cefixime suspension by Belcher Pharmaceuticals, LLC. Furthermore, all the excipients used in our formulation are commonly used excipients and no incompatibility among any excipient has been reported in

<table>
<tr><td></td><td></td><td>handbook of pharmaceutical excipients. All excipients are also recommended for use in similar formulations in the FDA excipients database as well. We have also performed pharmaceutical equivalence studies with the innovator product and also completed the accelerated stability studies and real time stability studies till 6 months, and the results within acceptable limit also support that the formulation is compatible and stable. However, the composition of applied product is different from the innovator product as mentioned below
<table>
<tr><td>Applied product</td><td>Suprax 100mg/5ml DS</td></tr>
<tr><td>Cefixime trihydrate (micronized)</td><td>Cefixime trihydrate</td></tr>
<tr><td>CMC Sodium</td><td>Xanthan gum</td></tr>
<tr><td>Sodium benzoate</td><td>Sodium benzoate</td></tr>
<tr><td>Sugar Fine</td><td>Sucralose</td></tr>
<tr><td>Colloidal silicon dioxide</td><td>Colloidal silicon dioxide</td></tr>
<tr><td>Strawberry flavor</td><td>Strawberry flavor</td></tr>
<tr><td></td><td>Sucrose</td></tr>
</table>
• Quantity of cefixime per unit dose and per batch have been explained and justified based upon the salt factor calculation and assay results. The justification is submitted.
• Firm has used the theoretical factor for adjustment of water content while dispensing, instead of the actual results of “water content test” reported in the drug substance analysis.</td></tr>
<tr><td>3.2.P.2.1.1</td><td>Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.</td><td>Compatibility studies of the drug substance with excipients is not required to be performed since the qualitative composition of our product is based upon the USFDA approved reference product i.e. Cefixime suspension by Belcher Pharmaceuticals, LLC. Furthermore, all the excipients used in our formulation are commonly used excipients and no incompatibility among any excipient has been reported in handbook of pharmaceutical excipients. All excipients are also recommended for use in similar formulations in the FDA excipients database as well. We have also performed pharmaceutical equivalence studies with the innovator product and also completed the accelerated stability studies and real time stability studies till 6 months, and the results within acceptable limit also support that the formulation is compatible and stable.
However, Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.</td></tr>
<tr><td>3.2.P.2.6</td><td>The results of pH (5.08) mentioned in compatibility study is out of specifications, clarify? (Limit 2.5-4.5)</td><td>There was a typographical mistake in the results of pH during the compatibility studies. We have rechecked the results and found the typographical mistake. We are submitting the actual results of compatibility studies
The submitted results were within the limits (pH-2.82)</td></tr>
<tr><td>3.2.P.3.3</td><td>In Description of manufacturing process and process controls, you have submitted manufacturing outline mentioning different composition of formulation than</td><td>We have used the same composition of the formulation for the product development and stability studies and have provided the same formulation in all sections of our CTD application. However, any difference in the formulation in section 3.2.P.3.3 may be considered as a typographical</td></tr>
</table>

	applied formulation	mistake. However we assure that we have used only one composition throughout the studies which have already been provided in section 3.2.P.1.
3.2.P.4.1	The specifications for all the excipients used in formulation of applied product is not provided	We have provided specifications and procedures for all excipients in section 3.2.P.4.1 and 3.2.P.4.2 as per the CTD guidance document approved by Registration Board. However, we are again submitting the same for your consideration. All excipients used in our formulation are well studied and all excipients except strawberry flavor are pharmacopoeial. The specifications and analytical procedures are submitted. *Specifications for CMC Sodium, is not submitted*
3.2.P.5.1	Justification for finished product specifications of USP is required as the drug substance manufacturer have claimed BP specifications as per section 3.2.S.4.4 Batch Analyses?	• The drug substance have been procured from Pharmagen Limited which have been granted approval for manufacturing of cefixime by Licensing Division DRAP and the same source have been approved by Registration Board in the cases of local manufacturing of cefixime for various firms on CTD after review of its complete data. • There are certain differences in the specifications of cefixime as defined in USP and BP, the drug substance manufacturer has identified all the changes and have tested its product against the BP as well as USP specifications. • The drug substance manufacturer has also performed validation / verification studies of the analytical method for assay, related substances and residual solvents for both BP as well as USP analytical procedures. As per the results of the verification studies both methods have been verified and the material complies the individual acceptance criteria for each test as specified in the monograph. • As per our vendor qualification system we have selected Pharmagen Limited based on its regulatory approval by DRAP, availability of DMF and stability study data as per zone IV-A. As per our approved SOPs after document review, we ordered small quantity of the drug substance for testing purpose and performed testing as per the USP specifications and finally selected the vendor when all tests as per USP specifications were complied. Our specifications and analytical method for in house testing of the drug substance is also based on USP method. We have developed the drug product as per USP specifications after thorough analysis of the drug substance as per USP specifications.
3.2.P.5.2	Provide signed copy of analytical methods used for applied product	We are submitting the analytical procedure of the drug product as per the CTD guidance document approved by Registration Board.
3.2.P.5.3	Submitted method verification report does not describe the sample preparation/standard preparation for various performance parameters.	Protocols and report for method verification studies are again submitted for your review and consideration. We would also like to inform that the sample and standard preparation method are defined in the analytical procedure of drug product in section 3.2.P.5.2. The verification protocols and report is submitted. *The sample preparation procedure for different concentrations in the parameter of accuracy shall be submitted.*
3.2.P.5.4	In section 3.2.P.1, under description you have mentioned "almost light	*No reply submitted*

	pink colour powder having strawberry powder for reconstitution" while in batch analysis and stability study you have mentioned "off white to light yellow colour powder having strawberry powder for reconstitution", clarify?	
3.2.P.8	• Submit Raw data sheets and COA containing detail of sample preparation, standard preparation for various performance parameters. • Preservative content and efficacy test not performed during stability study, clarify? • In use stability study of reconstitution suspension shall be submitted • The applied pack size is 30ml while the pack size mentioned in stability study summary & in two batches of stability study is 60ml and one batch is 30ml, clarify • The date of initiation mentioned in stability study is 12.05.2020 while the date of manufacturing mentioned in BMR is 13.05.2021. Clarify how stability study started before the manufacturing of batch.	• The details of sample preparation and standard preparation is the same throughout the stability studies as mentioned in section 3.2.P.5.2. We have used the USP method for sample and standard preparation throughout the stability studies. However Raw data sheets are submitted. • Preservative content and effectiveness is not the part of stability specifications nor recommended in USP monograph or ICH Q1 guidelines, therefore this test was not performed. Furthermore, the acceptable results of all the tests like physical appearance, taste, flavor, moisture, pH and assay depicts the effectiveness of preservative content in the formulation. • *However, tests for antimicrobial preservative content and efficacy of preservative as recommended by ICH Q1 (R2) guidelines and USP chapter <51> should be performed for finished product* • *No reply submitted for in use stability study* • *No reply submitted for different pack size* • *No reply submitted for date of initiation of stability study and date of manufacturing* • *Raw data sheets, including actual details of sample solution preparation & standard preparation, weight of standard, potency of standard & calculation formula applied, shall be submitted.*

Decision: Deferred for following:

- **Justification for use of CMC sodium as an excipient, since innovator's formulation does not include it.**
- **The specifications for CMC sodium used in formulation of applied product is not provided**
- **The sample preparation procedure for different concentrations in the parameter of accuracy shall be submitted.**
- **Clarification since the submitted COA of relevant batch of drug substance used for development studies is according to B.P while the specifications submitted for drug substance are USP.**
- **Tests for antimicrobial preservative content and efficacy of preservative as recommended by ICH Q1 (R2) guidelines and USP chapter <51> should be performed for finished product**
- **In use stability study of reconstitution suspension is not submitted**
- **Raw data sheets, including actual details of sample solution preparation & standard preparation, weight of standard, potency of standard & calculation formula applied, shall be submitted.**

Deferred cases of Human drugs (Exemption from onsite verification of stability data)

230.	Name and address of manufacturer / Applicant	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
	Brand Name +Dosage Form + Strength	Paglif-M 5/1000 mg Tablet
	Composition	Each film coated Tablet Contains: Empagliflozin ……5mg Metformin HCl ……1000mg
	Diary No. Date of R& I & fee	Dy. No. 5195 dated 13-02-2018, Rs: 50,000/- dated 13-02-2018
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5D

	Finished product Specifications	Innovator's specifications
	Pack size & Demanded Price	10's, 14's, 30's; As per SRO
	Approval status of product in Reference Regulator Authorities	SYNJARDY (5mg/500mg, 5mg/1000mg, 12.5mg/500mg, 12.5 mg/1000 mg) film-coated tablet USFDA approved
	Me-too status	Xenglu-Met 5/1000mg Tablets by M/s Hilton Pharma (Reg#093102)
	GMP status	The firm was inspected on 05-08-2019 and conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Nabi Qasim Karachi is considered to be operating at an acceptable level of compliance of GMP requirements.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug			
Name of Manufacturer	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan		
Manufacturer of API	**Empagliflozin:** Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China **Metformin HCl:** Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam- 396155 Dist. Valsad Gujarat State, India		
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin HCl:** MEF/19081807		
Description of Pack (Container closure system)	Alu-Alu; As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (month) Real Time: 0, 3, 6 (month)		
Batch No.	363DS01	363DS02	363DS03
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	10-08-2020	10-08-2020	10-08-2020
No. of Batches	03		
Date of Submission	26-03-2021 (9443)		

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	A Panel Inspection for the verification of authenticity of Stability Data of applied product on Form-5D "Sovir-C (Sofosbuvir) 400mg tablet" for Tablet Section has been conducted on 01st April, 2017. (Afternoon) and 27th October, 2020 and the Inspection Report included in the 297th DRB meeting held on 12-15th January, 2021. On the basis of Panel Inspection Report the applied product "Sofosbuvir 400mg Tablet" has been registered.

<table>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Empagliflozin: Copy of COA (Batch# EPG20190101) of API from Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China. and M/s Nabiqasim Industries is submitted
Metformin HCl: Copy of COA (Batch# MEF/19081807) of API from Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam-396155 Dist. Valsad Gujarat State, India and M/s Nabiqasim Industries is submitted</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer</td><td>Method used for analysis of Empagliflozin from API Manufacturer and Finished Product Manufacturer is provided by the firm.
Method used for analysis of Metformin from Finished Product Manufacturer is provided by the firm. Howevere Method used for analysis of Metformin by API Manufacturer is not provided</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Incompletely submitted (accelerated stability study data of empgliflozin submitted and only six month real time stability study submitted while stability study data of metformin not submitted)</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>Copy of certificate of GMP for Empagliflozin issued by Taizhou Drug Administration, is submitted. However, the GMP certificate could not be verified from China Food and Drug Administration (sfda) website.
Copy of GMP certificate for Metformin HCl is submitted</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Commercial invoice for empafliflozin batch# EPG20190101 from Zhejiang Materials Industry Chemical Group Co., Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted
<table>
<tr><th>Invoice No</th><th>Quantity Imported</th><th>Date of attestation by DRAP</th></tr>
<tr><td>30207132</td><td>0.5kg</td><td>09.07.2019</td></tr>
</table>
Commercial invoice for Metformin HCl from Aarti Drugs Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted
<table>
<tr><th>Invoice No</th><th>Quantity Imported</th><th>Date of attestation by DRAP</th></tr>
<tr><td>1907074</td><td>1000kg</td><td>08.11.2019</td></tr>
</table>
However, Batch No. is not mentioned on invoice.</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>NA
(The firm submitted that they have developed their product as per reference product Synjardy 12.5mg/1000mg. Formulation of applied drug product is qualitatively similar to that of innovator Brand Synjardy 12.5mg/1000mg tablet). However, firm have used povidone in formulation instead of copovidone as used by the innovator product</td></tr>
</table>

10.	Complete batch manufacturing record of three stability batches.	The firm has submitted Batch Manufacturing record of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** 363DS01 / 1500 tablets / 07-2020 363DS02 / 1500 tablets / 07-2020 363DS03 / 1500 tablets / 07-2020
11.	Record of comparative dissolution data (where applicable)	The firm submitted that empagliflozin/metformin Hcl 5/500mg is dose proportional of higher strength i.e empagliflozin/metformin 12.5/1000 mg and that they have perfomrd the test against the higher strength.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Incomplete Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

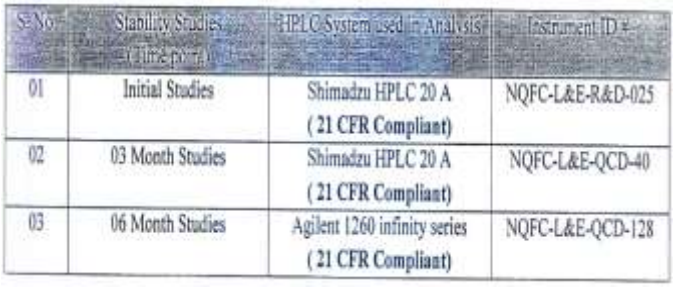
REMARKS OF EVALUATOR [XI]

S. No.	Observations/ Deficiencies/ Short-Comings	*Remarks/Justifications*

01	The registration board in its 293rd meeting decided as "Subsequent exemption will be considered after verification of CFR compliant status audit trail report on the testing of any product inspected either within three years", while the exemption report on the basis of which exemption is requested states that " Audit trail on the testing reports cannot be made as audit trail was not activated". Justification for your request for exemption is required as per above stated decision of registration board.	• Reference to the meeting minutes of 269th meeting held on 27-28th April 2017 deficiencies as pointed by panel of inspectors we have taken corrective action and removed all the deficiencies as pointed out by panel of inspectors and again panel inspection of Sofosbuvir 400mg Tablet conducted on 26th October 2020 and approved in 297th meeting with our product Navospet Gel 7.1%.
		• Reference to the Minutes of 297th Meeting of Registration Board, Report on investigation of Authenticity/ Genuineness of data submitted for registration of Navospet Gel 7.1% (Chlorhexidine digluconate) by M/s. Nabiqasim Industries, (Pvt). Ltd. Report mentioning as observed by panel against Q.No. 30 and 31
		  ◦ The HPLC Software is 21CFR Complaint as per record of the firm.
		  ◦ Audit trail was active on all HPLC systems used throughout stability study. Individual user login and IDs were available.
		• Audit trail reports were available and randomly checked.

02	Method used for analysis of Metformin API by API manufacturer is not submitted?	Method used for analysis of Metformin API by API manufacturer is submitted.
03	API manufacturer of Empagliflozin submitted only six months accelerated and real time stability study data while stability data of Metformin (both real time and accelerated) is not submitted by the API manufacturer.	Real Time Stability Data of API Manufacturers of Empagliflozin and Metformin HCl with full shelf life and Six Months Accelerated Stability Study Data by the API manufacturer as per zone IV-A are provided.
04	Submit GMP certificate of the Empagliflozin manufacturer, from the relevant (Federal or provincial) regulatory authority of China, since the submitted	Firm has submitted copy of GMP certificate (No. ZJ20180032) of Zhejiang Hongyuan Pharmaceutical co. Ltd issued by China Food and Drug Administration. The certificate is valid till 14-03-2023.

	GMP certificate is issued by city drug administration.	
05	Submit analytical record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA.	Analytical Record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA are provided by the firm**.**
06	Batch size for each three trial is 1500 tablets as per your formulation; out of which 350 tablets for each batch were kept on real time stability while 150 tablets are sufficient for test/analysis of each of the trials at all time points up till proposed shelf life.	Firm has submitted calculation justifying that the batch size was sufficient enough to perform stability studies till shelf life.
07	You have not performed tests for heavy metals, residual solvents and chiral purity of Empagliflozin as mentioned in COA of drug substance, clarify?	Test for heavy metals, residual solvents and R-isomer has not been performed due to unavailability of testing supplies. These tests will be performed on commercial consignment. Revised specification is attached to be followed for commercial QC release.
08	You have mentioned dissolution specifications NLT 85%(Q+5) after 30 minutes in COA and in protocols, however , the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT(Q) in 20 minutes, Justify or revise your dissolution specifications as per innovator's product along with submission of applicable fee?	As per CDP report the dissolution of our product is more than 85% within 20 minutes for Metformin HCl and Empagliflozin. As your goodself informed us, the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT(Q) in 20 minutes, we have revised our FP specifications for Paglif-M Tablet 12.5/500mg (Dissolution test interval from 30 minutes to 20 minutes).
09	You have not performed comparative dissolution studies for the applied product, Justify?	Justification Letter not performed comparative dissolution studies is enclosed that the study has been done on higher strength e.g. Empaglifozin 12.5mg & Metformin HCl 1000mg.
10	Justification for using Povidone in formulation instead of Copovidone.	Co povidone is also a binder and is analogue of povidone.
11	Test for impurity C of Empagliflozin not performed, clarify.	Impurity C of Eempagliflozin is a process related impurity not a degradant that's why its quantification is not required for Finished Product Testing.
12	Submit data of tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheet.	Tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheets Of Paglif-M Tablet 5/1000 mg, chromatograms are provided
13	Submit readable copy of invoice mentioning the Batch No. of metformin HCl used in formulation. Submit form 5, form 3, form 7 of metformin HCl.	Clear copy of Metformin Invoice is provided
14	Submit COA of working standard and related substances/ impurity standards.	COA of working standard and related substances/ impurity standards is provided
15	You have performed stability study at initial time point 10.08.2020 and at six months time point 6.02.2021, five days before the completion of six months. Justification is required.	To conduct stability studies of products, we have monthly stability plan for that. As product appears in our monthly stability schedule/plan we have initiated its analytical testing.
16	The diluent used for analysis of metformin	As per USP General Chapter <1092> the dissolution

	in dissolution make some disturbance of the baseline at the time at which metformin is detected. Justify that the interference due to diluent does not effect the peak area of metformin.	medium blank may not exceed 1% of the standard solution at the concentration used for analysis. In our case the blank absorbance is about 0.8% which lies within USP limit.
17	The submitted data for dissolution and assay of metformin does not show the peak of empagliflozin, although both are quantified by the same method and under similar conditions, clarify?	Traces of empagliflozin observed in metformin HCl assay sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 1mcg/ml. Traces of empagliflozin observed in metformin HCl dissolution sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 0.6mcg/ml.
18	Raw data sheet of dissolution test of real time stability study at 3rd month time point is not submitted	Raw data sheet of dissolution test of real time stability study at 3rd month time point is submitted
19	The batch number of manufactured batches is 363DS01, 363DS02, 363DS03, while the submitted raw data sheet of dissolution data at 3rd month time point for accelerated stability study is of 361DS01, 361DS02, 361DS03, clarify?	The firm submitted raw data sheet of dissolution data at 3rd month time point for accelerated stability of manufactured batches is 363DS01, 363DS02, 363DS03
20	The submitted data shows that stability is performed on three different HPLC system. Provide tabulated details of HPLC equipment used for stability study at different time point along with record of relevant audit trails. Also evidence that which HPLC system was used in previously approved product on basis of which exemption is applied.	 Shimadzu HPLC 20A system were used in previously approved product.
21	Submit compliance record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study as per submitted chromatograms.	The Compliance Record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study is provided
22	Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The record of Digital data logger for temperature and humidity monitoring of stability chambers is provide.

S. No	Stability Studies (Time point)	HPLC System used in Analysis	Instrument ID #
01	Initial Studies	Shimadzu HPLC 20 A (21 CFR Compliant)	NQFC-L&E-R&D-025
02	03 Month Studies	Shimadzu HPLC 20 A (21 CFR Compliant)	NQFC-L&E-QCD-40
03	06 Month Studies	Agilent 1260 infinity series (21 CFR Compliant)	NQFC-L&E-QCD-128

Decision of 312th meeting of Registration Board:

Deferred for following:

- Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.
- Submission of applicable fee revision of specifications

Response by the firm:

Reason for deferment	Response by the firm
Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.	Firm has submitted Comparative dissolution study of their product with reference Brand "Diampa-M 5/1000 mg tablet" of M/s Getz Pharma (Pvt) Ltd. The details are as follows:

Feature	Reference product	Product of Nabiqasim
Brand name	Diampa-M 5/1000mg tablet	Empagliflozin/Metformin HCl tablet 5/1000 mg (Test product)
Batch No.	003FD8	363DS01

	Comparative dissolution has been performed in pH 1.2 HCl, pH 4.5 buffer solution and pH 6.8 buffer solution. More than 85% of drug "Empagliflozin" and "Metformin HCl" releases in all three media in 15 minutes. Hence the dissolution profile of test product (Empagliflozin/Metformin HCl tablet 5/1000 mg) found similar against data of reference product Diampa-M 5/1000mg Tablet
Submission of applicable fee revision of specifications	Not submitted

Decision: Approved with innovator's specifications.

- **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.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.**

231.	Name and address of manufacturer / Applicant	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
	Brand Name +Dosage Form + Strength	Paglif-M 12.5/500 mg Tablet
	Composition	Each film coated Tablet Contains: Empagliflozin ……12.5mg Metformin HCl ……500mg
	Diary No. Date of R& I & fee	Dy. No. 16130 dated 07-03-2019, Rs: 20,000/- dated 07-03-2019
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5
	Finished product Specifications	Innovator's specifications
	Pack size & Demanded Price	10's, 14's, 28's; As per SRO
	Approval status of product in Reference Regulator Authorities	SYNJARDY (5mg/500mg, 5mg/1000mg, 12.5mg/500mg, 12.5 mg/1000 mg) film-coated tablet USFDA approved
	Me-too status	Xenglu-Met 12.5/500mg Tablets by M/s Hilton Pharma (Reg#093067)
	GMP status	The firm was inspected on 05-08-2019 and conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Nabi Qasim Karachi is considered to be operating at an acceptable level of compliance of GMP requirements.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Name of Manufacturer	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
Manufacturer of API	**Empagliflozin:** Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China **Metformin HCl:** Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam- 396155 Dist. Valsad Gujarat State, India
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin HCl:** MEF/19081807
Description of Pack (Container closure system)	Alu-Alu; As per SRO

Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (month) Real Time: 0, 3, 6 (month)		
Batch No.	364DS01	364DS02	364DS03
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	07-08-2020	07-08-2020	07-08-2020
No. of Batches	03		
Date of Submission	05-03-2021 (7309)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

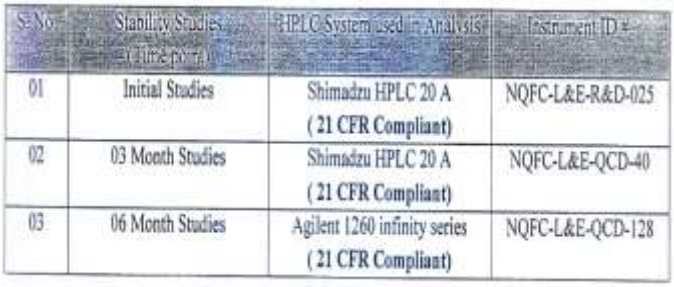
Sr.#	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	A Panel Inspection for the verification of authenticity of Stability Data of applied product on Form-5D "Sovir-C (Sofosbuvir) 400mg tablet" for Tablet Section has been conducted on 01st April, 2017. (Afternoon) and 27th October, 2020 and the Inspection Report included in the 297th DRB meeting held on 12-15th January, 2021. On the basis of Panel Inspection Report the applied product "Sofosbuvir 400mg Tablet" has been registered.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA (Batch# EPG20190101) of API from Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China. and M/s Nabiqasim Industries is submitted **Metformin HCl:** Copy of COA (Batch# MEF/19081807) of API from Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam-396155 Dist. Valsad Gujarat State, India and M/s Nabiqasim Industries is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of Empagliflozin from API Manufacturer and Finished Product Manufacturer is provided by the firm. Method used for analysis of Metformin from Finished Product Manufacturer is provided by the firm. Howevere Method used for analysis of Metformin by API Manufacturer is not provided
4.	Stability study data of API from API manufacturer	Incompletely submitted (accelerated stability study data of empgliflozin submitted and only six month real time stability study submitted while stability study data of metformin not submitted)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of certificate of GMP for Empagliflozin issued by Taizhou Drug Administration, is submitted. However, the GMP certificate could not be verified from China Food and Drug Administration (sfda) website. Copy of GMP certificate for Metformin HCl is submitted
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Commercial invoice for empafliflozin batch# EPG20190101 from Zhejiang Materials Industry Chemical Group Co., Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted

		<table><tr><th>Invoice No</th><th>Quantity Imported</th><th>Date of attestation by DRAP</th></tr><tr><td>30207132</td><td>0.5kg</td><td>09.07.2019</td></tr></table> Commercial invoice for Metformin HCl from Aarti Drugs Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted <table><tr><th>Invoice No</th><th>Quantity Imported</th><th>Date of attestation by DRAP</th></tr><tr><td>1907074</td><td>1000kg</td><td>08.11.2019</td></tr></table> However, Batch No. is not mentioned on invoice.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted
9.	Drug-excipients compatibility studies (where applicable)	NA (The firm submitted that they have developed their product as per reference product Synjardy 12.5mg/1000mg. Formulation of applied drug product is qualitatively similar to that of innovator Brand Synjardy 12.5mg/1000mg tablet). However, firm have used povidone in formulation instead of copovidone as used by the innovator product
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted Batch Manufacturing record of following 03 Batches: <table><tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr><tr><td>364DS01</td><td>1500 tablets</td><td>07-2020</td></tr><tr><td>364DS02</td><td>1500 tablets</td><td>07-2020</td></tr><tr><td>364DS03</td><td>1500 tablets</td><td>07-2020</td></tr></table>
11.	Record of comparative dissolution data (where applicable)	The firm submitted that empagliflozin/metformin Hcl 12.5/500mg is dose proportional of higher strength i.e empagliflozin/metformin 12.5/1000 mg and that they have performed the test against the higher strength.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Incomplete Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

REMARKS OF EVALUATOR [XI]

S. No.	Observations/ Deficiencies/ Short-Comings	*Remarks/Justifications*
01	The registration board in its 293rd meeting decided as "Subsequent exemption will be considered after verification of CFR compliant status audit trail report on the testing of any product inspected either within three years", while the exemption report on the basis of which exemption is requested states that " Audit trail on the testing reports cannot be made as audit trail was not activated". Justification for your request for exemption is required as per above stated decision of registration board.	• Reference to the meeting minutes of 269th meeting held on 27-28th April 2017 deficiencies as pointed by panel of inspectors we have taken corrective action and removed all the deficiencies as pointed out by panel of inspectors and again panel inspection of Sofosbuvir 400mg Tablet conducted on 26th October 2020 and approved in 297th meeting with our product Navospet Gel 7.1%. • Reference to the Minutes of 297th Meeting of Registration Board, Report on investigation of Authenticity/ Genuineness of data submitted for registration of Navospet Gel 7.1% (Chlorhexidine digluconate) by M/s. Nabiqasim Industries, (Pvt). Ltd.

		Report mentioning as observed by panel against Q.No. 30 and 31 • The HPLC Software is 21CFR Complaint as per record of the firm. • Audit trail was active on all HPLC systems used throughout stability study. Individual user login and IDs were available. • Audit trail reports were available and randomly checked.
02	Method used for analysis of Metformin API by API manufacturer is not submitted?	Method used for analysis of Metformin API by API manufacturer is submitted.
03	API manufacturer of Empagliflozin submitted only six months accelerated and real time stability study data while stability data of Metformin (both real time and accelerated) is not submitted by the API manufacturer.	Real Time Stability Data of API Manufacturers of Empagliflozin and Metformin HCl with full shelf life and Six Months Accelerated Stability Study Data by the API manufacturer as per zone IV-A are provided.
04	Submit GMP certificate of the Empagliflozin manufacturer, from the relevant (Federal or provincial) regulatory authority of China, since the submitted GMP certificate is issued by city drug administration.	Firm has submitted copy of GMP certificate (No. ZJ20180032) of Zhejiang Hongyuan Pharmaceutical co. Ltd issued by China Food and Drug Administration. The certificate is valid till 14-03-2023.
05	Submit analytical record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA.	Analytical Record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA are provided by the firm**.**
06	You have not performed tests for heavy metals, residual solvents and chiral purity of Empagliflozin as mentioned in COA of drug substance, clarify?	Test for heavy metals, residual solvents and R-isomer has not been performed due to unavailability of testing supplies. These tests will be performed on commercial consignment. Revised specification is attached to be followed for commercial QC release.
07	You have mentioned dissolution specifications NLT 85%(Q+5) after 30 minutes in COA and in protocols, however , the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT(Q) in 20 minutes, Justify or revise your dissolution specifications as per innovator's product along with submission of applicable fee?	As per CDP report the dissolution of our product is more than 85% within 20 minutes for Metformin HCl and Empagliflozin. As your goodself informed us, the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT(Q) in 20 minutes, we have revised our FP specifications for Paglif-M Tablet 12.5/500mg (Dissolution test interval from 30 minutes to 20 minutes).
08	You have not performed comparative dissolution studies for the applied product, Justify?	Justification Letter not performed comparative dissolution studies is enclosed that the study has been done on higher strength e.g. Empaglifozin 12.5mg & Metformin HCl 1000mg.
09	Justification for using Povidone in formulation instead of Copovidone.	Co povidone is also a binder and is analogue of povidone.
10	Test for impurity C of Empagliflozin not performed, clarify.	Impurity C of Eempagliflozin is a process related impurity not a degradant that's why its quantification is not required for Finished Product Testing.
11	Submit data of tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data	Tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheets Of Paglif-M Tablet 5/1000 mg, chromatograms are provided

	sheet.	
12	Submit readable copy of invoice mentioning the Batch No. of metformin HCl used in formulation. Submit form 5, form 3, form 7 of metformin HCl.	Clear copy of Metformin Invoice is provided
13	Submit COA of working standard and related substances/ impurity standards.	COA of working standard and related substances/ impurity standards is provided
14	The submitted data for dissolution and assay of metformin does not show the peak of empagliflozin, although both are quantified by the same method and under similar conditions, clarify?	Traces of empagliflozin observed in metformin HCl assay sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 1mcg/ml. Traces of empagliflozin observed in metformin HCl dissolution sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 0.6mcg/ml.
15	The submitted data shows that stability is performed on two different HPLC system. Provide tabulated details of HPLC equipment used for stability study at different time point along with record of relevant audit trails. Also evidence that which HPLC system was used in previously approved product on basis of which exemption is applied.	 Shimadzu HPLC 20A system were used in previously approved product.
16	Submit compliance record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during study as per submitted chromatograms	The Compliance Record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study is provided
17	Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time & accelerated).	The record of Digital data logger for temperature and humidity monitoring of stability chambers is provide.
18	Raw data sheets of dissolution data of B#364DS03 at 3rd month time point of real time stability studies not available?	The Raw data sheets of dissolution data of B#364DS03 at 3rd month time point of real time stability studies are attached
19	You have not performed Uniformity of Dosage Unit test,(weight variation/content uniformity) as recommended by USP General Chapter <905>for applied formulation. Justification is required in this regard.	We will perform "Uniformity of Dosage Unit test(weight variation/content uniformity) on our commercial batches.

Decision of 312th meeting of Registration Board:

Deferred for following:

- Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.
- Submission of applicable fee revision of specifications

Response by the firm:

Reason for deferment	Response by the firm
Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.	Firm has submitted Comparative dissolution study of their product with reference Brand "Diampa-M 12.5/500 mg tablet" of M/s Getz Pharma (Pvt) Ltd. The details are as follows:

Feature	Reference product	Product of Nabiqasim
Brand name	Diampa-M 12.5/500mg tablet	Empagliflozin/Metformin HCl tablet 12.5/500 mg (Test product)

	Batch No. | 003FE9 | 364DS01 Comparative dissolution has been performed in pH 1.2 HCl, pH 4.5 buffer solution and pH 6.8 buffer solution. More than 85% of drug "Empagliflozin" and "Metformin HCl" releases in all three media in 15 minutes. Hence the dissolution profile of test product (Empagliflozin/Metformin HCl tablet 12.5/500 mg) found similar against data of reference product Diampa-M 12.5/500mg Tablet	
Submission of applicable fee revision of specifications	Not submitted	

Decision: Approved with innovator's specifications.

- **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.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.**

232.	Name and address of manufacturer / Applicant	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
	Brand Name +Dosage Form + Strength	Paglif-M 5/850 mg Tablet
	Composition	Each film coated Tablet Contains: Empagliflozin ……5mg Metformin HCl ……850mg
	Diary No. Date of R& I & fee	Dy. No. 5193 dated 13-02-2018, Rs: 50,000/- dated 13-02-2018
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5D
	Finished product Specifications	Innovator's specifications
	Pack size & Demanded Price	10's, 14's, 30's; As per SRO
	Approval status of product in Reference Regulator Authorities	SYNJARDY (5mg/850mg, 12.5 mg/850 mg) film-coated tablet EMA approved
	Me-too status	Xenglu-Met 5/850mg Tablets by M/s Hilton Pharma (Reg#093104)
	GMP status	The firm was inspected on 05-08-2019 and conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Nabi Qasim Karachi is considered to be operating at an acceptable level of compliance of GMP requirements.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	
Name of Manufacturer	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
Manufacturer of API	**Empagliflozin:** Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China **Metformin HCl:** Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam- 396155 Dist. Valsad Gujarat State, India
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin HCl:** MEF/19081807

Description of Pack (Container closure system)	Alu-Alu; As per SRO		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (month) Real Time: 0, 3, 6 (month)		
Batch No.	362DS01	362DS02	362DS03
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	11-08-2020	11-08-2020	11-08-2020
No. of Batches	03		
Date of Submission	11-03-2021 (7999)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

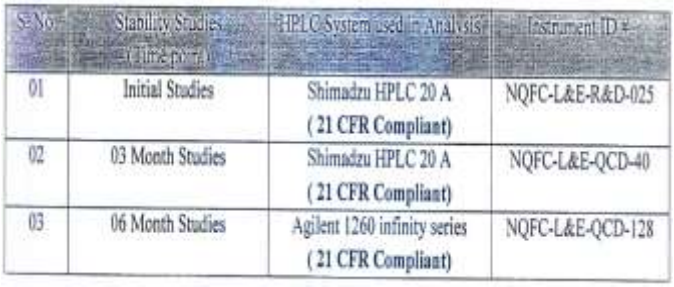
Sr.#	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	A Panel Inspection for the verification of authenticity of Stability Data of applied product on Form-5D "Sovir-C (Sofosbuvir) 400mg tablet" for Tablet Section has been conducted on 01st April, 2017. (Afternoon) and 27th October, 2020 and the Inspection Report included in the 297th DRB meeting held on 12-15th January, 2021. On the basis of Panel Inspection Report the applied product "Sofosbuvir 400mg Tablet" has been registered.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA (Batch# EPG20190101) of API from Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China. and M/s Nabiqasim Industries is submitted **Metformin HCl:** Copy of COA (Batch# MEF/19081807) of API from Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam-396155 Dist. Valsad Gujarat State, India and M/s Nabiqasim Industries is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of Empagliflozin from API Manufacturer and Finished Product Manufacturer is provided by the firm. Method used for analysis of Metformin from Finished Product Manufacturer is provided by the firm. Howevere Method used for analysis of Metformin by API Manufacturer is not provided
4.	Stability study data of API from API manufacturer	Incompletely submitted (accelerated stability study data of empgliflozin submitted and only six month real time stability study submitted while stability study data of metformin not submitted)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of certificate of GMP for Empagliflozin issued by Taizhou Drug Administration, is submitted. However, the GMP certificate could not be verified from China Food and Drug Administration (sfda) website. Copy of GMP certificate for Metformin HCl is submitted

<table>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Commercial invoice for empafliflozin batch# EPG20190101 from Zhejiang Materials Industry Chemical Group Co., Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted
<table>
<tr><th>Invoice No</th><th>Quantity Imported</th><th>Date of attestation by DRAP</th></tr>
<tr><td>30207132</td><td>0.5kg</td><td>09.07.2019</td></tr>
</table>
Commercial invoice for Metformin HCl from Aarti Drugs Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted
<table>
<tr><th>Invoice No</th><th>Quantity Imported</th><th>Date of attestation by DRAP</th></tr>
<tr><td>1907074</td><td>1000kg</td><td>08.11.2019</td></tr>
</table>
However, Batch No. is not mentioned on invoice.</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>NA
(The firm submitted that they have developed their product as per reference product Synjardy 12.5mg/1000mg. Formulation of applied drug product is qualitatively similar to that of innovator Brand Synjardy 12.5mg/1000mg tablet). However, firm have used povidone in formulation instead of copovidone as used by the innovator product</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>362DS01</td><td>1500 tablets</td><td>07-2020</td></tr>
<tr><td>362DS02</td><td>1500 tablets</td><td>07-2020</td></tr>
<tr><td>362DS03</td><td>1500 tablets</td><td>07-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>The firm submitted that empagliflozin/metformin Hcl 5/850mg is dose proportional of higher strength i.e empagliflozin/metformin 12.5/1000 mg and that they have performed the test against the higher strength.</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>Incomplete Submitted</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>Not Submitted</td></tr>
</table>

REMARKS OF EVALUATOR [XI]

S. No.	Observations/ Deficiencies/ Short-Comings	*Remarks/Justifications*
01	The registration board in its 293rd meeting decided as "Subsequent exemption will be considered after verification of CFR compliant status audit trail report on the testing of any product inspected either within three years", while the exemption report on the basis of which exemption is requested states that " Audit trail on the	• Reference to the meeting minutes of 269th meeting held on 27-28th April 2017 deficiencies as pointed by panel of inspectors we have taken corrective action and removed all the deficiencies as pointed out by panel of inspectors and again panel inspection of Sofosbuvir 400mg Tablet conducted on 26th October 2020 and approved in 297th meeting with our product Navospet Gel 7.1%. • Reference to the Minutes of 297th Meeting of

	testing reports cannot be made as audit trail was not activated". Justification for your request for exemption is required as per above stated decision of registration board.	Registration Board, Report on investigation of Authenticity/ Genuineness of data submitted for registration of Navospet Gel 7.1% (Chlorhexidine digluconate) by M/s. Nabiqasim Industries, (Pvt). Ltd. Report mentioning as observed by panel against Q.No. 30 & 31 • The HPLC Software is 21CFR Complaint as per record of the firm. • Audit trail was active on all HPLC systems used throughout stability study. Individual user login and IDs were available. • Audit trail reports were available and randomly checked.
02	Method used for analysis of Metformin API by API manufacturer is not submitted?	Method used for analysis of Metformin API by API manufacturer is submitted.
03	API manufacturer of Empagliflozin submitted only six months accelerated and real time stability study data while stability data of Metformin (both real time and accelerated) is not submitted by the API manufacturer.	Real Time Stability Data of API Manufacturers of Empagliflozin and Metformin HCl with full shelf life and Six Months Accelerated Stability Study Data by the API manufacturer as per zone IV-A are provided.
04	Submit GMP certificate of the Empagliflozin manufacturer, from the relevant (Federal or provincial) regulatory authority of China, since the submitted GMP certificate is issued by city drug administration.	Firm has submitted copy of GMP certificate (No. ZJ20180032) of Zhejiang Hongyuan Pharmaceutical co. Ltd issued by China Food and Drug Administration. The certificate is valid till 14-03-2023.
05	Submit analytical record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA.	Analytical Record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA are provided by the firm**.**
06	You have not performed tests for heavy metals, residual solvents and chiral purity of Empagliflozin as mentioned in COA of drug substance, clarify?	Test for heavy metals, residual solvents and R-isomer has not been performed due to unavailability of testing supplies. These tests will be performed on commercial consignment. Revised specification is attached to be followed for commercial QC release.
07	You have not performed comparative dissolution studies for the applied product, Justify?	Justification Letter not performed comparative dissolution studies is enclosed that the study has been done on higher strength e.g. Empaglifozin 12.5mg & Metformin HCl 1000mg.
08	Justification for using Povidone in formulation instead of Copovidone.	Co povidone is also a binder and is analogue of povidone.
09	Test for impurity C of Empagliflozin not performed, clarify.	Impurity C of Eempagliflozin is a process related impurity not a degradant that's why its quantification is not required for Finished Product Testing.
10	Submit data of tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheet.	Tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheets Of Paglif-M Tablet 5/1000 mg, chromatograms are provided
11	Submit readable copy of invoice mentioning the Batch No. of metformin HCl used in formulation. Submit form 5, form 3, form 7 of metformin HCl.	Clear copy of Metformin Invoice is provided

12	Submit COA of working standard and related substances/ impurity standards.	COA of working standard and related substances/ impurity standards is provided
13	The submitted data for dissolution and assay of metformin does not show the peak of empagliflozin, although both are quantified by the same method and under similar conditions, clarify?	Traces of empagliflozin observed in metformin HCl assay sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 1mcg/ml. Traces of empagliflozin observed in metformin HCl dissolution sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 0.6mcg/ml.
14	The submitted data shows that stability is performed on three different HPLC system. Provide tabulated details of HPLC equipment used for stability study at different time point along with record of relevant audit trails. Also evidence that which HPLC system was used in previously approved product on basis of which exemption is applied.	 Shimadzu HPLC 20A system were used in previously approved product.
15	Submit compliance record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study as per submitted chromatograms.	The Compliance Record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study is provided
16	Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time & accelerated).	The record of Digital data logger for temperature and humidity monitoring of stability chambers is provide.

Decision of 312th meeting of Registration Board: Deferred for Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.

Response by the firm:

Reason for deferment	**Response by the firm**
Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.	Firm has submitted Comparative dissolution study of their product with reference Brand "Diampa-M 5/850 mg tablet" of M/s Getz Pharma (Pvt) Ltd. The details are as follows: Feature / Reference product / Product of Nabiqasim Brand name / Diampa-M 5/850mg tablet / Empagliflozin/Metformin HCl tablet 5/850 mg (Test product) Batch No. / 006FD7 / 362DS01 Comparative dissolution has been performed in pH 1.2 HCl, pH 4.5 buffer solution and pH 6.8 buffer solution. More than 85% of drug "Empagliflozin" and "Metformin HCl" releases in all three media in 15 minutes. Hence the dissolution profile of test product (Empagliflozin/Metformin HCl tablet 5/850 mg) found similar against data of reference product Diampa-M 5/850mg Tablet

Decision: Registration Board decided to accept the stability study data as the dissolution specifications falls within the definition of immediate release drug product and approved registration with innovator's specification.

- **Manufacturer shall revise the dissolution specifications as per the innovator's product i.e. NLT Q at 20 minutes along with submission of fee for revision of dissolution specification 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.		
233.	Name and address of manufacturer / Applicant	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
	Brand Name +Dosage Form + Strength	Paglif-M 12.5/850 mg Tablet
	Composition	Each film coated Tablet Contains: Empagliflozin ……12.5mg Metformin HCl ……850mg
	Diary No. Date of R& I & fee	Dy. No. 5191 dated 13-02-2018, Rs: 50,000/- dated 13-02-2018
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5D
	Finished product Specifications	Innovator's specifications
	Pack size & Demanded Price	10's, 14's, 30's; As per SRO
	Approval status of product in Reference Regulator Authorities	SYNJARDY (5mg/850mg, 12.5 mg/850 mg) film-coated tablet EMA approved
	Me-too status	Xenglu-Met 12.5/850mg Tablets by M/s Hilton Pharma (Reg#093103)
	GMP status	The firm was inspected on 05-08-2019 and conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Nabi Qasim Karachi is considered to be operating at an acceptable level of compliance of GMP requirements.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug			
Name of Manufacturer	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan		
Manufacturer of API	**Empagliflozin:** Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China **Metformin HCl:** Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam- 396155 Dist. Valsad Gujarat State, India		
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin HCl:** MEF/19081807		
Description of Pack (Container closure system)	Alu-Alu; As per SRO		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (month) Real Time: 0, 3, 6 (month)		
Batch No.	366DS01	366DS02	366DS03
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	05-08-2020	05-08-2020	05-08-2020
No. of Batches	03		

Date of Submission	11-03-2021 (8000)

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

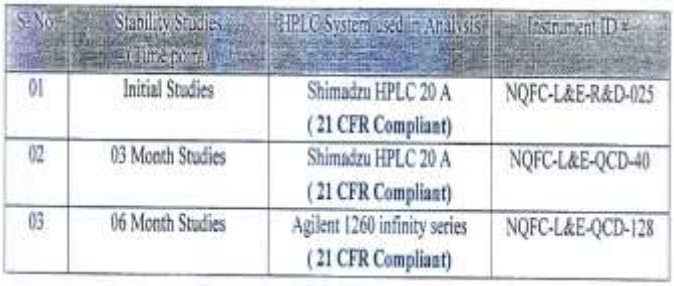
Sr.#	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	A Panel Inspection for the verification of authenticity of Stability Data of applied product on Form-5D "Sovir-C (Sofosbuvir) 400mg tablet" for Tablet Section has been conducted on 01st April, 2017. (Afternoon) and 27th October, 2020 and the Inspection Report included in the 297th DRB meeting held on 12-15th January, 2021. On the basis of Panel Inspection Report the applied product "Sofosbuvir 400mg Tablet" has been registered.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA (Batch# EPG20190101) of API from Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China. and M/s Nabiqasim Industries is submitted **Metformin HCl:** Copy of COA (Batch# MEF/19081807) of API from Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam-396155 Dist. Valsad Gujarat State, India and M/s Nabiqasim Industries is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of Empagliflozin from API Manufacturer and Finished Product Manufacturer is provided by the firm. Method used for analysis of Metformin from Finished Product Manufacturer is provided by the firm. Howevere Method used for analysis of Metformin by API Manufacturer is not provided
4.	Stability study data of API from API manufacturer	Incompletely submitted (accelerated stability study data of empgliflozin submitted and only six month real time stability study submitted while stability study data of metformin not submitted)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of certificate of GMP for Empagliflozin issued by Taizhou Drug Administration, is submitted. However, the GMP certificate could not be verified from China Food and Drug Administration (sfda) website. Copy of GMP certificate for Metformin HCl is submitted
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Commercial invoice for empafliflozin batch# EPG20190101 from Zhejiang Materials Industry Chemical Group Co., Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted **Invoice No** | **Quantity Imported** | **Date of attestation by DRAP** 30207132 | 0.5kg | 09.07.2019 Commercial invoice for Metformin HCl from Aarti Drugs Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted **Invoice No** | **Quantity Imported** | **Date of attestation by DRAP** 1907074 | 1000kg | 08.11.2019 However, Batch No. is not mentioned on invoice.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted

9.	Drug-excipients compatibility studies (where applicable)	NA (The firm submitted that they have developed their product as per reference product Synjardy 12.5mg/1000mg. Formulation of applied drug product is qualitatively similar to that of innovator Brand Synjardy 12.5mg/1000mg tablet). However, firm have used povidone in formulation instead of copovidone as used by the innovator product
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted Batch Manufacturing record of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** 366DS01 / 1500 tablets / 07-2020 366DS02 / 1500 tablets / 07-2020 366DS03 / 1500 tablets / 07-2020
11.	Record of comparative dissolution data (where applicable)	The firm submitted that empagliflozin/metformin Hcl 12.5/850mg is dose proportional of higher strength i.e empagliflozin/metformin 12.5/1000 mg and that they have performed the test against the higher strength.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

REMARKS OF EVALUATOR [XI]

S.No.	Observations/ Deficiencies/ Short-Comings	*Remarks/Justifications*
01	The registration board in its 293rd meeting decided as "Subsequent exemption will be considered after verification of CFR compliant status audit trail report on the testing of any product inspected either within three years", while the exemption report on the basis of which exemption is requested states that " Audit trail on the testing reports cannot be made as audit trail was not activated". Justification for your request for exemption is required as per above stated decision of registration board.	• Reference to the meeting minutes of 269th meeting held on 27-28th April 2017 deficiencies as pointed by panel of inspectors we have taken corrective action and removed all the deficiencies as pointed out by panel of inspectors and again panel inspection of Sofosbuvir 400mg Tablet conducted on 26th October 2020 and approved in 297th meeting with our product Navospet Gel 7.1%. • Reference to the Minutes of 297th Meeting of Registration Board, Report on investigation of Authenticity/ Genuineness of data submitted for registration of Navospet Gel 7.1% (Chlorhexidine digluconate) by M/s. Nabiqasim Industries, (Pvt). Ltd. Report mentioning as observed by panel against Q.No. 30 and 31 ◦ The HPLC Software is 21CFR Complaint as per record of the firm. ◦ Audit trail was active on all HPLC systems used throughout stability study. Individual user login and IDs were available. • Audit trail reports were available and randomly checked.
02	Method used for analysis of Metformin API by API manufacturer is not submitted?	Method used for analysis of Metformin API by API manufacturer is submitted.
03	API manufacturer of Empagliflozin submitted only six months accelerated and real time stability study data while stability data of Metformin (both real time and	Real Time Stability Data of API Manufacturers of Empagliflozin and Metformin HCl with full shelf life and Six Months Accelerated Stability Study Data by the API manufacturer as per zone IV-A are provided.

	accelerated) is not submitted by the API manufacturer.	
04	Submit GMP certificate of the Empagliflozin manufacturer, from the relevant (Federal or provincial) regulatory authority of China, since the submitted GMP certificate is issued by city drug administration.	Firm has submitted copy of GMP certificate (No. ZJ20180032) of Zhejiang Hongyuan Pharmaceutical co. Ltd issued by China Food and Drug Administration. The certificate is valid till 14-03-2023.
05	Submit analytical record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA.	Analytical Record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA are provided by the firm**.**
06	You have not performed tests for heavy metals, residual solvents and chiral purity of Empagliflozin as mentioned in COA of drug substance, clarify?	Test for heavy metals, residual solvents and R-isomer has not been performed due to unavailability of testing supplies. These tests will be performed on commercial consignment. Revised specification is attached to be followed for commercial QC release.
07	The batch No. of the manufactured batch mentioned in BMR is 366DS01, 366DS02, 366DS03 while the batch No. mentioned in protocols and stability data sheet is 365DS01, 365DS02, 365DS03, clarify.	The firm submitted that they have manufactured 03 trial batches to conduct stability study having Batch no. 366DS01, 366DS02, 366DS03 and also submitted data sheet, raw data/chromatograms, protocols of these batches. Batch No. mentioned in BMR is a typographical error.
08	You have not performed comparative dissolution studies for the applied product, Justify?	Justification Letter not performed comparative dissolution studies is enclosed that the study has been done on higher strength e.g. Empaglifozin 12.5mg & Metformin HCl 1000mg.
09	Justification for using Povidone in formulation instead of Copovidone.	Co povidone is also a binder and is analogue of povidone.
10	Test for impurity C of Empagliflozin not performed, clarify.	Impurity C of Eempagliflozin is a process related impurity not a degradant that's why its quantification is not required for Finished Product Testing.
11	Submit data of tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheet.	Tests performed for metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheets Of Paglif-M Tablet 5/1000 mg, chromatograms are provided
12	Submit readable copy of invoice mentioning the Batch No. of metformin HCl used in formulation. Submit form 5, form 3, form 7 of metformin HCl.	Clear copy of Metformin Invoice is provided
13	Submit COA of working standard and related substances/ impurity standards.	COA of working standard and related substances/ impurity standards is provided
14	The submitted data for dissolution and assay of metformin does not show the peak of empagliflozin, although both are quantified by the same method and under similar conditions, clarify?	Traces of empagliflozin observed in metformin HCl assay sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 1mcg/ml. Traces of empagliflozin observed in metformin HCl dissolution sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 0.6mcg/ml.

15	The submitted data shows that stability is performed on two different HPLC system. Provide tabulated details of HPLC equipment used for stability study at different time point along with record of relevant audit trails. Also evidence that which HPLC system was used in previously approved product on basis of which exemption is applied.	 Shimadzu HPLC 20A system were used in previously approved product.
16	Submit compliance record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study as per submitted chromatograms.	The Compliance Record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study is provided
17	Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The record of Digital data logger for temperature and humidity monitoring of stability chambers is provide.
18	You have not performed Uniformity of Dosage Unit test,(weight variation/content uniformity) as recommended by USP General Chapter <905>for applied formulation. Justification is required in this regard.	We will perform "Uniformity of Dosage Unit test(weight variation/content uniformity) on our commercial batches.

S. No	Stability Studies (Time point)	HPLC System used in Analysis	Instrument ID #
01	Initial Studies	Shimadzu HPLC 20 A (21 CFR Compliant)	NQFC-L&E-R&D-025
02	03 Month Studies	Shimadzu HPLC 20 A (21 CFR Compliant)	NQFC-L&E-QCD-40
03	06 Month Studies	Agilent 1260 infinity series (21 CFR Compliant)	NQFC-L&E-QCD-128

Decision of 312th meeting of Registration Board: Deferred for Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.

Response by the firm:

Reason for deferment	**Response by the firm**
Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.	Firm has submitted Comparative dissolution study of their product with reference Brand "Diampa-M 12.5/850 mg tablet" of M/s Getz Pharma (Pvt) Ltd. The details are as follows: Feature / Reference product / Product of Nabiqasim Brand name / Diampa-M 12.5/850mg Tablet / Empagliflozin/Metformin HCl tablet 12.5/850 mg (Test product) Batch No. / 002FFI / 365DS01 Comparative dissolution has been performed in pH 1.2 HCl, pH 4.5 buffer solution and pH 6.8 buffer solution. More than 85% of drug "Empagliflozin" and "Metformin HCl" releases in all three media in 15 minutes. Hence the dissolution profile of test product (Empagliflozin/Metformin HCl tablet 12.5/850 mg) found similar against data of reference product Diampa-M 12.5/850mg Tablet

Decision: Registration Board decided to accept the stability study data as the dissolution specifications falls within the definition of immediate release drug product and approved registration with innovator's specification.

- **Manufacturer shall revise the dissolution specifications as per the innovator's product i.e. NLT Q at 20 minutes along with submission of fee for revision of dissolution specification 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.	

Deferred cases of Human drugs (Form 5)

234.	Name and address of manufacture / Applicant	M/s Hudson Pharma Private Limited. Site-Plot No. D-93, North Western Industrial Zone, Port Qasim Authority, Pakistan
	Brand Name+Dosage Form+Strength	Recuro UD Eye Drops (solution)
	Composition	Each ml Contains: Carboxymethylcellulose Sodium…..…5mg Glycerin……10mg Polysorbate 80……...5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10357 dated 05-03-2019 Rs.20,000/- 05-03-2019
	Pharmacological Group	Lubricating and moisturizing comfort solution
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	0.4ml (30's ampoules), 0.4ml (60's ampoules); As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	
	GMP Status	Firm was inspected on 03-04-2019 and conclusion of inspection was: Overall cGMP is found at acceptable level and the management is committed for continual improvement and has assured further cGMP compliance.
	Previous Remark of Evaluator [XI]	• The firm provided evidence of RRA. Refresh Optive Advanced Lubricant Eye Drops OTC product by M/s Allergan Inc, (Daily Med) • The firm provided evidence of me-too. Recuro Drops 0.5% by M/s Hudson Pharma (Reg#091123). However, the provided me-too is not as per applied product (contain only carboxymethyl cellulose 5mg).
	Previous Decision (307-DRB)	• 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	• The firm again provided evidence of same me-too. Recuro Drops 0.5% by M/s Hudson Pharma (Reg#091123). However, the provided me-too is not as per applied product (contain only carboxymethyl cellulose 5mg). • The firm itself revised the formulation and revised the label claim along with submission of Rs 30000/- on deposit SlipNo.991599286662. The revised label claim is as under: Each ml Contains: Carboxymethylcellulose Sodium…..…5mg Evidence of RRA: Celluvisc 0.5 %w/v eye drops solution (Ireland approved) Pack size: 30's (0.4ml LDPE container), 60's (0.4ml LDPE container) • The same molecule is already registered with the firm • The firm submitted revised master formulation of already applied product containing all three APIs.
	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 OR submission of stability study data as per the guidelines approved in 293rd meeting of Registration Board.	
235.	Name and address of manufacture / Applicant	M/s Invictus Pharmaceuticals. Plot No. 21,26, Street No.NS-2, National Industrial Zone, Rawat, Rawalpindi
	Brand Name+Dosage Form+Strength	Diacet 50mg Capsule

	Composition	Each Capsule Contains: Zonisamide……50mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10102 dated 04-03-2019 Rs.20,000/- 04-03-2019
	Pharmacological Group	Other antiinflammatory and antirheumatic agents, non-steroids
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10's, 20's, 30's, 50's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ART 50mg, hard capsule ANSM France approved
	Me-too-status	Wincerin Capsule 50mg by M/s Winthrox Labs. (Reg# 098611)
	GMP Status	The firm has been granted DML on the basis of inspection conducted on 13.11.2018 & 17.12.2018.
	Previous Remark of Evaluator [XI]	Firm have corrected the label claim as per the applied product without submission of applicable fee. The revise label claim is as under: Each Capsule Contains: Diacerein ……50mg
	Previous Decision (307-DRB)	• Deferred for clarification from the firm regarding the applied composition since the label claim in Form 5 contains zonisamide 50mg capsule while the rest of the documents in Form 5 specifies that the applied product is diacerein 50mg capsule.
	Evaluation by PEC	• The firm submitted that the applied product is diacerein 50mg capsule and submitted revised form 5 of applied product as per submitted documents and submitted Rs 7500/- on deposit slip No. 23445124 for correction of label claim in enclosure of form 5. The corrected label claim is as under: Each Capsule Contains: Diacerein ……50mg
	Decision: Approved with innovator's specifications and following label claim: **Each Capsule Contains:** **Diacerein ……50mg**	
236.	Name and address of manufacture / Applicant	M/s Invictus Pharmaceuticals. Plot No. 21,26, Street No.NS-2, National Industrial Zone, Rawat, Rawalpindi
	Brand Name+Dosage Form+Strength	Esogast 10mg
	Composition	Each Tablet Contains: Domperidone……..…10mg
	Dairy No. date of R &I fee	Form-5D Dy.No 10096 dated 04-03-2019 Rs.20,000/- 04-03-2019
	Pharmacological Group	Propulsives
	Type of form	Form 5
	Finished product specifications	BP
	Pack size and Demand Price	5x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Motilium 10mg film-coated tablets MHRA Approved
	Me-too-status	CP-Lium Tablet 10mg by M/s Caliph Pharma (Reg#098812)
	GMP Status	The firm has been granted DML on the basis of inspection 13.11.2018 & 17.12.2018.
	Previous Remark of Evaluator [XI]	• Form 5 submitted without signature/in reply form 5 not submitted • The firm has mentioned the correct salt form of Domperidone in the label claim as per reference formulation without adjustment of its weight in master formulation considering the salt form and without submission of applicable fee. Furthermore, the firm have also revised the label claim from uncoated to film coated tablets. The revised label claim is as under: Each film coated Tablet Contains: Domperidone maleate eq. to Domperidone……10mg

	Previous Decision (307-DRB)	Deferred for following: • Submission of form 5 as per prescribed format duly signed by the applicant • Submission of applicable fee for correction of formulation from uncoated tablets to film coated tablets and salt form of API and in label claim • Adjustment of weight of API in master formulation considering the salt form
	Evaluation by PEC	• The firm have submitted revised form 5 as prescribed format duly signed by the applicant • The firm submitted Rs 7500/- on deposit slip No. 3214700807 for correction of formulation. • The firm submitted revised master formulation and adjusted weight of API considering the salt form
	Decision: Approved with following label claim: **Each film coated Tablet Contains:** **Domperidone maleate eq. to Domperidone……10mg**	
237.	Name and address of manufacture / Applicant	M/s Invictus Pharmaceuticals. Plot No. 21,26, Street No.NS-2, National Industrial Zone, Rawat, Rawalpindi
	Brand Name+Dosage Form+Strength	Ursan 500mg Capsule
	Composition	Each Capsule Contains: Ursodeoxycholic Acid……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10101 dated 04-03-2019 Rs.20,000/- 04-03-2019
	Pharmacological Group	Bile acids and derivatives
	Type of form	Form 5
	Finished product specifications	BP
	Pack size and Demand Price	1x6's, 1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Vdoxyl 500mg Capsule by M/s EG Pharmaceuticals (Reg#095838)
	GMP Status	The firm has been granted DML on the basis of inspection 13.11.2018 & 17.12.2018.
	Previous Remark of Evaluator [XI]	• The firm provided evidence of approval of applied formulation in RRA. "Ursochol 500mg capsule", approved by Swedish Medicine agency. However, the product is Deregistered or temporarily recalled.
	Previous Decision (307-DRB)	• 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	• The firm provided evidence of URSO FORTE tablets, by USFDA, while the applied product is capsule
	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	
238.	Name and address of manufacture / Applicant	M/s Invictus Pharmaceuticals.Plot No. 21,26, Street No.NS-2, National Industrial Zone, Rawat, Rawalpindi
	Brand Name+Dosage Form+Strength	Fungnil 200mg tablet
	Composition	Each Film Coated Tablet Contains: Voriconazole…….200mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10095 dated 04-03-2019 Rs.20,000/- 04-03-2019
	Pharmacological Group	Triazole derivatives
	Type of form	Form 5
	Finished product specifications	JP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Voriconazole Zentiva 200mg film-coated tablets MHRA approved

	Me-too-status	Tavora Tablets 200mg by M/s Macter International (Reg#096861)
	GMP Status	The firm has been granted DML on the basis of inspection 13.11.2018 & 17.12.2018.
	Previous Remark of Evaluator XI	• You have applied on form 5D. Apply on prescribed form 5 for the applied product
	Previous Decision (307-DRB)	• Deferred for submission of prescribed form 5 for the applied product
	Evaluation by PEC	• The firm submitted prescribed form 5 for the applied product
	Decision: Approved with JP's specifications	
239.	Name and address of manufacture / Applicant	M/s Kanel Pharma. Plot # 6, St # SS-3, National Industrial Zone, Rawat, Rawalpindi. ***Contract Manufactured By:*** M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore
	Brand Name+Dosage Form+Strength	Anzifur Injection 100mg/5ml
	Composition	Each 5ml contains: Iron sucrose complex eq to elemental iron……100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11459 dated 05-03-2019 Rs.50,000/- 06-03-2019
	Pharmacological Group	Anti-anaemic
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	5ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	Venofer (50mg/2.5mL, 100mg/5mL, 200mg/10mL) (20mg/mL) in single-dose vials. Injection USFDA Approved
	Me-too-status	Irofit Injection 100mg/5ml by M/s Zafa Pharma (Reg#82291)
	GMP Status	M/s Kanel Pharma was inspected on 06-03-2019 and recommendations of inspection was: Keeping in view the above stated observations during inspection, areas visited, documents reviewed it is concluded that M/s Kanel Pharma Rawat is operating in compliance to GMP guidelines as of today. However the points of improvements have been discussed and agreed by the representatives of the firm. Certificate of GMP Issued to English Pharmaceuticals on 16-1-2018.
	Previous Remark of Evaluator XI	• Form 5 has been submitted by the applicant duly signed by the signatory • The firm did not submit undertaking at the end of form 5 • A copy of contract manufacturing agreement between M/s Kanel Pharma and M/s English Pharmaceuticals Industries is submitted • The firm submitted list of 05 approved sections of applicant. i.e. M/s Kanel Pharma • The firm informed that they don't have any product registered/approved on contract manufacturing • The firm submitted list of 09 applied products for contract manufacturing • The firm mentioned the use of type II glass container as primary packaging material of applied formulation
	Previous Decision (296-DRB)	• Deferred for clarification regarding use of type of primary packaging material for applied formulation and submission of undertaking
	Evaluation by PEC	• The firm mentioned the use of type I glass container as primary packaging material of applied formulation and submitted undertaking at the end of form 5 as per prescribed format
	Previous Decision (297-DRB)	• Deferred for consideration on its turn
	Evaluation by PEC	•

	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee change of primary packaging material of applied formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
240.	Name and address of manufacture / Applicant	M/s Kanel Pharma. Plot # 6, St # SS-3, National Industrial Zone, Rawat, Rawalpindi. ***Contract Manufactured By:*** M/s English Pharmaceuticals Industries. Link Kattar Bund Road, Thokar Niaz Baig, Multan Road, Lahore
	Brand Name+Dosage Form+Strength	Anzi-Cilin 4.5g Dry Powder Injection
	Composition	Each Vial Contains: Piperacillin (as Sodium)……..4g Tazobactam (as Sodium)……..0.5g
	Dairy No. date of R &I fee	Form-5 Dy.No 11460 dated 05-03-2019 Rs.50,000/- 05-03-2019
	Pharmacological Group	Penicillin and beta-lactamase inhibitor
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	50ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZOSYN (piperacillin and tazobactam, 4gm/0.5gm) for injection, for intravenous use. USFDA approved
	Me-too-status	Tacip 4.5gm Injection by M/s Macter Int. (Reg#73632)
	GMP Status	M/s Kanel Pharma was inspected on 06-03-2019 and recommendations of inspection was: Keeping in view the above stated observations during inspection, areas visited, documents reviewed it is concluded that M/s Kanel Pharma Rawat is operating in compliance to GMP guidelines as of today. However, the points of improvements have been discussed and agreed by the representatives of the firm. Certificate of GMP Issued to English Pharmaceuticals on 16-1-2018.
	Previous Remark of Evaluator [XI]	• Form 5 has been submitted by the applicant duly signed by the signatory • The firm did not submit undertaking at the end of form 5 • A copy of contract manufacturing agreement between M/s Kanel Pharma and M/s English Pharmaceuticals Industries is submitted • The firm submitted list of 05 approved sections of applicant. i.e. M/s Kanel Pharma • The firm informed that they don't have any product registered/approved on contract manufacturing • Firm submitted list of 09 applied products for contract manufacturing • The firm mentioned the use of type II glass container as primary packaging material of applied formulation
	Previous Decision (296-DRB)	• Deferred for clarification regarding type of primary packaging material for applied formulation and submission of undertaking
	Evaluation by PEC	• The firm mentioned the use of type I glass container as primary packaging material of applied formulation and submitted undertaking at the end of form 5 as per prescribed format
	Previous Decision (297-DRB)	• Deferred for consideration on its turn
	Evaluation by PEC	•
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee change of primary packaging material of applied formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
241.	Name and address of manufacture / Applicant	M/s EG Pharmaceuticals. Plot. No. 13-A, Industrial Triangle, Kahuta Road, Islamabad *Contract Manufactured By:* M/s Nimrall Laboratories Plot 24, Street SS-3, Rawat, Industrial Area, Islamabad

	Brand Name+Dosage Form+Strength	Doxfree Syrup 100mg/5ml
	Composition	Each 5ml Contains: Doxofylline……100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 12982 dated 05-03-2019 Rs.50,000/- 05-03-2019
	Pharmacological Group	Xanthines
	Type of form	Form 5
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	60ml, 120ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	DOXOFILLINA ABC "200 mg/10 ml syrup" (200ml bottle) AIFA Italy approved
	Me-too-status	Fylod Syrup 100mg/5ml by M/s Sami Pharma (Reg#092698)
	GMP Status	The firm M/s EG Pharmaceuticals was inspected on 13-02-2019 and recommendations of inspection was: Keeping in view the above facts on record, the panel unanimously recommended the renewal of DML no 000752 by way of formulation to M/s EG Pharma Islamabad. The firm M/s Nimrall Laboratories has been granted GMP certificate for export dated 27-12-2019 based on the inspection dated 24-7-2019.
	Previous Remark of Evaluator [XI]	• Form 5 is submitted by applicant i.e. M/s EG Pharmaceuticals and name of manufacturer and applicant is mentioned on enclosure in form 5 • The firm did not submit manufacturing outline for the applied product • The firm submitted a list of 07 approved sections. • The firm submitted that none of their product is already registered/approved on contract manufacturing • The firm submitted list of 08 product applied for contract manufacturing • The firm submitted copy of contract manufacturing agreement between M/s EG Pharmaceuticals and M/s Nimrall Laboratories
	Previous Decision (307-DRB)	• Deferred for submission of manufacturing outline for the applied product.
	Evaluation by PEC	• The firm submitted manufacturing outline for the applied product.
	Decision: Approved with innovator's specifications	
242.	Name and address of manufacture / Applicant	M/s EG Pharmaceuticals. Plot. No. 13-A, Industrial Triangle, Kahuta Road, Islamabad *Contract Manufactured By:* M/s Nimrall Laboratories Plot 24, Street SS-3, Rawat, Industrial Area, Islamabad
	Brand Name+Dosage Form+Strength	Avelon Eye Drops 5mg/ml (0.5% w/v)
	Composition	Each ml Contains: Moxifloxacin HCl eq. to Moxifloxacin……..…5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 12979 dated 05-03-2019 Rs.50,000/- 05-03-2019
	Pharmacological Group	Fluoroquinolones
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	5ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	VIGAMOX 0.5% (5mg/ml) ophthalmic solution USFDA approved
	Me-too-status	Xomelox Eye Drops 5mg/ml by M/s Pakistan Pharma (Reg#089019)
	GMP Status	The firm M/s EG Pharmaceuticals was inspected on 13-02-2019 and recommendations of inspection was: Keeping in view the above facts on record, the panel unanimously

		recommended the renewal of DML no 000752 by way of formulation to M/s EG Pharma Islamabad. The firm M/s Nimrall Laboratories has been granted GMP certificate for export dated 27-12-2019 based on the inspection dated 24-7-2019.
	Previous Remark of Evaluator XI	• The firm submitted letter No. F. 1-21/2003-Lic (M-227) dated 11th June 2011 issued by Secretary Central Licensing Board confirming the presence of Eye Drops (General) section to M/s Nimral Laboratories • Form 5 is submitted by applicant i.e. M/s EG Pharmaceuticals and name of manufacturer and applicant is mentioned on enclosure in form 5 • The firm submitted a list of 07 approved sections. • The firm submitted that none of their product is already registered/approved on contract manufacturing • The firm submitted list of 08 product applied for contract manufacturing • The firm submitted that product is terminally sterilization by gamma radiation • The firm submitted copy of contract manufacturing agreement between M/s EG Pharmaceuticals and M/s Nimrall Laboratories
	Previous Decision (307-DRB)	• Deferred for clarification regarding source of gamma radiation for terminal sterilization
	Evaluation by PEC	• The firm submitted that bottles, nozzles and caps must be sterilized by Gamma radiation before filling from PARAS Lahore and filling must be done by aseptic filling under the laminar
	Decision: The Board deliberated the case in detail and decided to refer the case to Licensing division for clairifcation of legal standing of M/s PARAS, Lahore for performing the said activity.	
243.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road, Lahore
	Brand Name+Dosage Form+Strength	Mentin 10mg Tablet
	Composition	Each film coated tablet contains: Memantine as (HCl)……10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 9523 dated 01-03-2019 Rs.20,000/- 01-03-2019
	Pharmacological Group	Anti- Dementia Drug
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	28, 30, 42, 50, 56, 60, 98, 100; As per SRO
	Approval status of product in Reference Regulatory Authorities	NAMENDA (5mg, 10 mg) film coated tablets USFDA Approved
	Me-too-status	Memlip 10mg Tablets by M/s WnsFeild Pharma (Reg. # 84222)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Previous Remark of Evaluator XI	• Letter of deficiencies sent on 15-07-2020 and reminder on 27-01-2021 but no reply received yet • You have applied as Each film coated tablet contains: Memantine as (HCl) while the reference formulation contains Memantine HCl not considering the salt factor in the label claim. Revise the label claim as per reference formulation along with submission of applicable fee. Furthermore, revise master formulation adjusting the weight of API not

		considering the salt factor • The applicant has claimed manufacturer's specifications and the official monograph is available in USP.
	Previous Decision (307-DRB)	• Deferred for revision of the label claim and master formulation adjusting the weight of API not considering the salt factor as per reference formulation along with submission of applicable fee.
	Evaluation by PEC	• The firm revised the label claim and master formulation as per reference formulation along with submission of Rs. 7500/- on deposit slip No#456066693867. The revised label claim is as under: Each film coated tablet contains: Memantine HCl……10mg equivalent to 8.31 mg memantine.
	Decision: Approved with USP specifications and following label claim: **Each film coated tablet contains:** **Memantine HCl……10mg equivalent to 8.31 mg memantine.**	
244.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road,Lahore
	Brand Name + Dosage Form+Strength	Cabriz Suspension 100mg/5ml
	Composition	Each 5ml Contains: Carbamazepine……100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11328 dated 05-03-2019 Rs.20,000/- 04-03-2019
	Pharmacological Group	Antiepileptics
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	120ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	Tegretol 100mg/5ml Liquid (Oral suspension) MHRA Approved
	Me-too-status	Tegral 100mg/5ml suspension by M/s Novartis Pharma (Reg#70803)
	GMP Status	Certificate of GMP issued to Neutro Pharma on 11.07.2019 based on inspection conducted on 28.02.2019
	Previous Remark of Evaluator [XI]	• The firm have submitted Rs. 7500/- on deposit slip No# 3753638206 for revision of formulation from dry powder suspension to liquid suspension. However, the firm did not revise the formulation and did not submit requisite documents.
	Previous Decision (308-DRB)	• Deferred for revision of formulation and submission of requisite documents along with submission of full fee for revision of formulation
	Evaluation by PEC	• The firm have revised the formulation from dry powder suspension to liquid suspension and submitted revised form 5, master formulation and manufacturing outline. However, the firm did not submit full fee for revision of formulation
	Decision: Approved. Registration Board further decided that registration letter will be issued after submission of applicable fee as per No.F.7-11/2012-B&A/DRAP dated 07-05-2021 for revision of formulation from dry powder suspension to liquid suspension	
245.	Name and address of manufacture / Applicant	M/s Hiranis Pharmaceuticals Pvt Ltd. Plot No. E-145 to E-149, North Western Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name+Dosage Form+Strength	Ultradol SR Tablet 100mg
	Composition	Each film coated sustained release Tablet Contains: Tramadol HCl…….100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10818 dated 05-03-2019 Rs.20,000/- 01-3-2019
	Pharmacological Group	Opioid analgesic
	Type of form	Form-5
	Finished product specifications	USP

	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Brimisol PR 100mg prolonged release tablets MHRA Approved
	Me-too-status	Zultra SR 100mg tablet by M/s Wilshire Laboratories (Reg#80713)
	GMP Status	The firm was inspected on 29-01-2019 and was overall GMP compliant
	Previous Remark of Evaluator [XI]	• The firm did not revised the 1st page of form 5 as per prescribed format and also submitted without applicant signature. • The firm submitted revised form 5 and revised the label claim from immediate release tablet to film coated sustained release tablet along with submission of Rs. 5000/- on deposit slip No. 2048069 dated 29.07.2020. The also submitted revised master formulation and manufacturing outline.
	Previous Decision (296-DRB)	• Deferred for submission of differential fee of Rs. 15,000 for revision of formulation.
	Evaluation by PEC	• The firm submitted differential fee of Rs 15000/- on deposit slip No. 2027790 dated 20.11.2020 for revision of formulation.
	Previous Decision (297-DRB)	• Deferred for consideration on its turn.
	Evaluation by PEC	•
	Decision: Approved.	
246.	Name and address of manufacture / Applicant	M/s Hiranis Pharmaceuticals Pvt Ltd.Plot No. E-145 to E-149, North Western Industrial Zone, Port Qasim, Karachi, Pakistan
	Brand Name+Dosage Form+Strength	Alavert-D Tablet 5/120mg
	Composition	Each film coated extended-release tablet contains: Loratadine …….....5mg Pseudoephedrine Sulfate ……....120mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10936 dated 05-03-2019 Rs.20,000/- 01-03-2019
	Pharmacological Group	Sympathomimetics (Nasal Decongestants)
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Claritin-D (5mg;120mg) Extended Release tablets USFDA Approved
	Me-too-status	Softin- P tablet of M/s Werrick Pharma (Reg. # 060094) Could not be confirmed as extended- release tablet
	GMP Status	The firm was inspected on 29-01-2019 and was overall GMP compliant
	Previous Remark of Evaluator [XI]	• The firm revised the 1st page of form 5 as per prescribed format but submitted without applicant signature. • The firm submitted revised form 5 and revised the label claim from bilayered tablet to film coated extended release tablet along with submission of Rs. 5000/- on deposit slip No. 2048070 dated 29.07.2020. The also submitted revised master formulation and manufacturing outline. • However, the reference formulation contains contains 5 mg loratadine in the tablet coating (immediate release) and 120mg pseudoephedrine sulfate equally distributed between the tablet coating (immediate release) and the barrier-coated core (extended release). The two active components in the coating are quickly liberated; release of the decongestant in the core is delayed for several hours. • The manufacturing method of the applied product is not as per reference formulation
	Previous Decision (296-DRB)	• Deferred for submission of manufacturing outline as per reference formulation

	Evaluation by PEC	• The firm submitted manufacturing outline as per reference formulation
	Previous Decision (297-DRB)	• Deferred for consideration on its turn
	Evaluation by PEC	•
	Decision: Approved with innovator's specifications. 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.	

247.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Drema Tablet 50mg
	Composition	Each Film Coated Tablet Contains: Clomiphene Citrate…….50mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11310 dated 05-03-2019 Rs.20,000/- 04-3-2019
	Pharmacological Group	Ovulation stimulants
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Clomid 50mg Tablets MHRA Approved
	Me-too-status	Clomidex Tablets 50mg by CSH Pharmaceuticals-North (Reg#078433)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not revise the label claim from film coated to uncoated tablets as per reference formulation. • The firm did not submit enclosure of form 5 as per prescribed format • The firm did not submit undertaking at the end of form 5 • The firm submitted complete manufacturing outline for the applied product
	Previous Decision (307-DRB)	Deferred for following: • Revise the label claim from film coated to uncoated tablets as per reference formulation along with submission of applicable fee • Submit enclosure of form 5 as per prescribed format • Submit undertaking at the end of form 5
	Evaluation by PEC	• The firm have revised the label claim from film coated to uncoated tablets along with submission of Rs. 7500/- on deposit slip#920017445559. The revised label claim is as under: Each Uncoated Tablet Contains: Clomiphene Citrate…….50mg • The firm submitted enclosure of form 5 and undertaking at the end of form 5
	Decision: Approved with following label claim: **Each Uncoated Tablet Contains:** **Clomiphene Citrate…….50mg**	
248.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Gildin 5mg Tablet
	Composition	Each Film Coated Tablet Contains: Desloratadine……..…5mg

	Dairy No. date of R &I fee	Form-5 Dy.No 11307 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antihistamine
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Clarinex 5mg film coated tablet USFDA Approved.
	Me-too-status	Desatil Tablets 5mg by Aries Pharmaceuticals (Reg#84270)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not submit enclosure of form 5 as per prescribed format • The firm did not submit undertaking at the end of form 5 • The firm submitted complete manufacturing outline for the applied product • The firm have claimed for manufacturer's specifications while the official monograph is available in USP
	Previous Decision (307-DRB)	Deferred for following: • Submit enclosure of form 5 as per prescribed format • Submit undertaking at the end of form 5
	Evaluation by PEC	• The firm submitted enclosure of form 5 and undertaking at the end of form 5 • Submission of applicable fee for revision of specifications
	Decision: Approved. 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.	
249.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Setron 8mg Tablet
	Composition	Each Film Coated Tablet Contains: Ondansetron as HCl……..…8mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11305 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antiemetics and Antinauseants
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's; 2x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Ondansetron 8mg film coated Tablets MHRA approved
	Me-too-status	Curaon 8mg Tablet by M/s Curatech Pharma (Reg# 101662)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm have not mentioned the hydrated form of ondansetron in label claim and did not adjust its weight considering the salt and hydrated form in master formulation. • The firm did not submit enclosure of form 5 as per prescribed format • The firm submitted complete manufacturing outline for the applied product • The firm have claimed for manufacturer's specifications while

		the official monograph is available in USP
	Previous Decision (307-DRB)	• Deferred for following: • Mention the hydrated form of ondansetron in label claim and adjust its weight in master formulation considering the salt and hydrated form • Submit enclosure of form 5 as per prescribed format
	Evaluation by PEC	• The firm have mentioned the hydrated form of ondansetron in label claim as per reference formulation. The revised label claim is as under: Each Film Coated Tablet Contains: Ondansetron HCl dihydrate eq. to Ondansetron……8mg However, the firm did not submit revised master formulation and adjusted its weight considering the salt and hydrated form • The firm submitted enclosure of form 5 as per prescribed format • Submission of applicable fee for revision of specifications
	Decision: Deferred for revision of master formulation and adjustment of weight of API considering the salt and hydrated form	
250.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Sogil 5mg Tablet
	Composition	Each Film Coated Tablet Contains: Solifenacin Succinate……..…5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11309 dated 05-03-2019 Rs.20,000/- 4-3-2019
	Pharmacological Group	Drugs for urinary frequency and incontinence
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	1x10's, 2x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Solifenacin succinate 5mg film-coated tablets MHRA Approved
	Me-too-status	Enablex Tablet 5mg by M/s Regal Pharma (Reg#81958)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not submit enclosure of form 5 as per prescribed format • The firm submitted complete manufacturing outline for the applied product
	Previous Decision (307-DRB)	• Deferred for submission of enclosure of form 5 as per prescribed format
	Evaluation by PEC	• The firm submitted enclosure of form 5 as per prescribed format
	Decision: Approved with innovator's specifications. 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.	
251.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Linzogil 600mg Tablet
	Composition	Each Film Coated Tablet Contains: Linezolid……600mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11306 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Oxazolidinone Antibacterial
	Type of form	Form 5
	Finished product specifications	USP

	Pack size and Demand Price	2x6's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZYVOX 600mg film coated Tablets USFDA Approved.
	Me-too-status	Novozid 600mg Tablet by M/s Wenovo Pharmaceuticals (Reg#098240)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not submit enclosure of form 5 as per prescribed format • The firm did not submit undertaking at the end of form 5 • The firm submitted complete manufacturing outline for the applied product • The firm have claimed for USP specifications while the official monograph is not available in any pharmacopeia
	Previous Decision (307-DRB)	Deferred for following: • Submit enclosure of form 5 as per prescribed format • Submit undertaking at the end of form 5.
	Evaluation by PEC	• The firm submitted enclosure of form 5 and undertaking at the end of form 5 • Submission of applicable fee for revision of specifications
	Decision: Approved with innovator's specifications. 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.	
252.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Letra 2.5mg Tablets
	Composition	Each Film Coated Tablet Contains: Letrozole ……2.5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11312 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Aromatase inhibitor
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's, 3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	FEMARA 2.5mg film coated tablet USFDA Approved
	Me-too-status	Letzole 2.5mg Tablet by M/s Opal Labs (Reg#075805)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not submit enclosure of form 5 as per prescribed format • The firm submitted complete manufacturing outline for the applied product
	Previous Decision (307-DRB)	• Deferred for submission of enclosure of form 5 as per prescribed format
	Evaluation by PEC	• The firm submitted enclosure of form 5 as per prescribed format
	Decision: Approved.	
253.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Sogil 10mg Tablet

	Composition	Each Film Coated Tablet Contains: Solifenacin Succinate……10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11308 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Drugs for urinary frequency and incontinence
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	1x10's, 2x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Solifenacin succinate 10mg film-coated tablets MHRA Approved
	Me-too-status	Enablex Tablet 10mg by M/s Regal Pharma (Reg#81959)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not submit enclosure of form 5 as per prescribed format • The firm submitted complete manufacturing outline for the applied product
	Previous Decision (307-DRB)	• Deferred for submission of enclosure of form 5 as per prescribed format
	Evaluation by PEC	• The firm submitted enclosure of form 5 as per prescribed format
	Decision: Approved with innovator's specifications. 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.	
254.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Terbina 250mg Tablet
	Composition	Each Film Coated Tablet Contains: Terbinafine (as HCl)……250mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11311 dated 05-03-2019 Rs.20,000/- 4-03-2019
	Pharmacological Group	Antifungal
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's, 3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Lamisil Tablets 250mg MHRA Approved
	Me-too-status	Fibet Tablet 250mg by M/s Bio-Mark Pharma (Reg#85717)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not revise the label claim from film coated tablets to uncoated tablets as per reference formulation. • The firm did not submit enclosure of form 5 as per prescribed format • The firm did not submit undertaking at the end of form 5 • The firm submitted complete manufacturing outline for the applied product
	Previous Decision (307-DRB)	Deferred for following: • Revise the label claim from film coated to uncoated tablets as per reference formulation along with submission of applicable fee • Submit enclosure of form 5 as per prescribed format

		• Submit undertaking at the end of form 5
	Evaluation by PEC	• The firm have revised the label claim from film coated to uncoated tablets as per reference formulation along with submission of Rs. 7500/- on deposit slip No#58034598072. The revised label claim is as under: Each Uncoated Tablet Contains: Terbinafine (as HCl)……250mg • The firm submitted enclosure of form 5 and undertaking at the end of form 5
	Decision: Approved with following label claim: Each Uncoated Tablet Contains: Terbinafine (as HCl)……250mg	
255.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals. 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan
	Brand Name+Dosage Form+Strength	Transagil 500mg Capsule
	Composition	Each Capsule Contains: Tranexamic Acid……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11304 dated 05-03-2019 Rs.20,000/- 04-3-2019
	Pharmacological Group	Antifibrinolytics
	Type of form	Form 5
	Finished product specifications	JP
	Pack size and Demand Price	3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	TRANEX 500mg capsule. AIFA approved
	Me-too-status	Tenamic 500mg Capsule by M/s Rotex Pharma (Reg#097425)
	GMP Status	The firm was inspected on 18.07.2019 and conclusion of inspection was: The overall GMP compliance status of the firm may be considered as satisfactory
	Previous Remark of Evaluator [XI]	• The firm did not submit enclosure of form 5 as per prescribed format • The firm submitted complete manufacturing outline for the applied product • The firm have claimed for USP specifications while the official monograph is available in JP
	Previous Decision (307-DRB)	• Deferred for submission of enclosure of form 5 as per prescribed format
	Evaluation by PEC	• The firm submitted enclosure of form 5 as per prescribed format • Submission of applicable fee for revision of specifications
	Decision: Approved with JP specifications. 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.	
256.	Name and address of manufacture / Applicant	M/s Medisure Laboratories Pakistan Pvt Ltd. A-115, S.I.T.E, Super Highway, Karachi, Pakistan
	Brand Name+Dosage Form+Strength	Discium Tablet 50mg
	Composition	Each enteric coated tablet contains: Rabeprazole sodium…….10mg
	Dairy No. date of R &I fee	Form-5 Dy.No.44 Dated 08-02-2011 Rs.8,000 Dated 08-02-2011, Rs.12,000 Dated 08-04-2016, *Duplicate Dossier, R&I Verified*
	Pharmacological Group	NSAIDS
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in	Diclofenac potassium 50mg Film Coated Tablets MHRA

	Reference Regulatory Authorities	Approved.
	Me-too-status	Kalfen 50mg tablets by M/s Candid Pharma (Reg#100912)
	GMP Status	Certificate of GMP Issued on 02-10-2019
	Previous Remark of Evaluator [XI]	• Initially the firm have submitted Rs 8000/- dated 08.02.2011 for the applied product. Later on, firm submitted differential fee Rs 12000/- on deposit slip No. 0533318 dated 08.04.2016. Firm submitted copy of fee challan • The firm submitted the 1st page of form 5 as per prescribed format • The firm have revised the label claim as under: Each coated tablet contains: Diclofenac potassium …….50mg However, the firm did not mention the type of coating and without submission of applicable fee. • The firm submitted manufacturing method of the applied product
	Previous Decision (297-DRB)	• Deferred for revision of label claim along with submission of applicable fee.
	Evaluation by PEC	• The firm have mentioned diclofenac potassium. The firm have revised the label claim and mentioned the type of coating along with submission of Rs.5000/- on deposit slip No#1985397 dated 03.02.2021. The revised label claim is as under: Each film coated tablet contains: Diclofenac potassium …….50mg
	Previous Decision (307-DRB)	• Deferred for clarification from the firm regarding the applied composition since the label claim in Form 5 contains rabeprazole 10mg tablet while the rest of the documents in Form 5 specifies that the applied product is diclofenac potassium 50mg tablet.
	Evaluation by PEC	• The firm submitted that the applied product is Diclofenac potassium 50mg tablet and submitted revised form 5 and all other relevant documents of applied product as per submitted documents and corrected the label claim in enclosure of form 5. The corrected label claim is as under: Each film coated tablet contains: Diclofenac potassium …….50mg
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Diclofenac potassium …….50mg** **Registration Board further decided that registration letter will be issued after submission of applicable fee for correction of label claim in enclosure of form 5 as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

Deferred cases of priority approval of Azithromycin (Human-Covid):

Sr. No.	Name of applicant	Brand Name	Composition	Diary no. / Date / fee / form	Pack Size / Price	Remarks/ GMP status
257.	M/s Lawari International Pharmaceuticals Valley Road, Gul KADU Saidu Sharif Swat, KPK	Azor 250mg film coated Tablet	Each film coated Tablet Contains: Azithromycin as dihydrate …250mg	Form-5 Dy.No 11427 dated 05-03-2019 Rs.20,000/- Dated 05-03-2019	1x10's As per SRO	The firm applied on prescribed form 5 for the product along with undertaking at the end of form 5. The firm revised the label claim from uncoated to film coated tablets without submission of applicable fee. Latest GMP inspection report not submitted Justification for addition of 2% overage
	Previous Decision (296-DRB)	• Deferred for submission of justification for addition of 2% overage, GMP status, fee for revision of formulation				
	Evaluation by PEC	• The firm submitted Rs 5000/- on deposit slip# 2030392 for revision of formulation. • The firm also submitted panel inspection report conducted on 05.09.2020 for renewal of DML and conclusion of inspection was: Keeping in view the above the panel unanimously recommends the grant of renewal of DML No. 000658 by way of formulation to M/s Lawari International swat and resumption of production in the manufacturing facility • The firm submitted that as per the official monograph the limit of raw material is 98% to 102%, therefore we add 2% overages in our formulation for safety of our product.				
	Previous Decision (307-DRB)	• Deferred for scientific justification for addition of overage				
	Evaluation by PEC	• The firm submitted revised master formulation and removed addition of overage along with submission of Rs. 7500/- on deposit slip No. 05772669.				
Decision: Approved.						
258.	M/s Lawari International Pharmaceuticals Valley Road, Gul KADU Saidu Sharif Swat, KPK	Azor 500mg film coated Tablet	Each film coated Tablet Contains: Azithromycin as dihydrate.…500mg	Form-5 Dy.No 11426 dated 05-03-2019 Rs.20,000/- Dated 05-03-2019	1x6's; As per SRO	The firm applied on prescribed form 5 for the product along with undertaking at the end of form 5. The firm revised the label claim from uncoated to film coated tablets without submission of applicable fee.

						Latest GMP inspection report not submitted Justification for addition of 2% overage
	Previous Decision (296-DRB)	• Deferred for revision of formulation as per reference product. Submission of applicable fee, GMP status during last 3 years and justification of using overage.				
	Evaluation by PEC	• The firm submitted Rs 5000/- on deposit slip# 2030393 for revision of formulation. • The firm also submitted panel inspection report conducted on 05.09.2020 for renewal of DML and conclusion of inspection was: Keeping in view the above the panel unanimously recommends the grant of renewal of DML No. 000658 by way of formulation to M/s Lawari International swat and resumption of production in the manufacturing facility • The firm submitted that as per the official monograph the limit of raw material is 98% to 102%, therefore we add 2% overages in our formulation for safety of our product.				
	Previous Decision (307-DRB)	• Deferred for scientific justification for addition of overage				
	Evaluation by PEC	• The firm submitted revised master formulation and removed addition of overage along with submission of Rs. 7500/- on deposit slip No. 4058108680.				
Decision: Approved.						

Deferred cases of veterinary drugs import:

259.	Name and address of Applicant	M/s Meezab Z.International Fareed Abad Near Bilal Mosque, Jahanian, Punjab
	Detail of Drug Sale License	Name: M/s Meezab Z International Address: Fareed Abad, Jahanian District khanewal Validity: 05th October 2021 Status: License to sell drugs as a distributor
	Name and address of manufacturer	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,(REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name and address of marketing authorization holder	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,(REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 9723 dated 04-03-2019
	Fee including differential fee	Rs100,000/- dated 28-02-2019
	Brand Name+Dosage Form+ Strength	Reefmox Plus Powder
	Composition	Each 1gm Contains: Amoxicillin Trihydrate……200mg Colistin Sulphate……...600,000 IU
	Finished Product Specification	Manufacturer's specifications
	Pharmacological Group	Broad spectrum antibiotic
	Shelf life	36 months
	Demanded Price	Decontrolled
	Pack size	100gm, 250gm, 500gm, 1kg, 5kg, 10kg HDPE Jar
	International availability	N/A
	Me-too status	
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and 65 ± 5%RH of three batches for 36 months and accelerated stability data sheet conducted at 40 ± 2 ºC and 75 ± 5%RH of three batches for six months
	Detail of certificates attached	Original legalized GMP certificate

		Certificate No: 5/5/10 002730 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department Date: 08-03-2021 Validity: Valid for five years GMP status: GMP certificate states that firm is subjected to inspection at adequate interval in order to verify GMP Original legalized Free sale Certificate Certificate No: 5/5/10 002719 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department Date: 08-03-2021 Validity: Valid for ten years Free Sale Certificate Confirms the free sale of the product in exporting country. Letter of Authorization Letter of authorization from M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals, (REEFCO) in the name of M/s Meezab Z.International company, Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan Date of Agreement: 04.03.2021 Validity: Valid until revoked by Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,
	Previous Remark of Evaluator [XI]	• The firm did not provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm **OR** evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting
	Previous Decision (308-DRB)	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 required manufacturing facility/section by regulatory authority (penicillin section)
	Evaluation by PEC	• The firm provided evidence of me-too "Cola-Moxin 200 Water Soluble Powder" by M/s Inshal Pharmaceutical (Reg#099339). However, the strength of Colistin Sulphate (60,00,000IU) in provided me-too is different from the applied product. • The firm submitted Certificate No: 5/5/10 010434 dated 14/09/2021 issued by Minister of Agriculture / Acting Director of Veterinary and Animal Health Directorate showing presence of four sections 1. Oral Liquid (General) 2. Oral Soluble powder 3. Suspension (General) 4. Penicillin (Powder)
	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	
260.	Name and address of Applicant	M/s Meezab Z.International Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan
	Detail of Drug Sale License	Name: M/s Meezab Z International Address: Fareed Abad, Jahanian District Khanewal Validity: 05th October 2021 Status: License to sell drugs as a distributor
	Name and address of manufacturer	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals, (REEFCO) Alhassan Industrial Estate-Irbid-Jordan

	Name and address of marketing authorization holder	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals, (REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 9720 dated 04-03-2019
	Fee including differential fee	Rs100,000/- dated 28-02-2019
	Brand Name+Dosage Form+ Strength	Colireef 5M Powder
	Composition	Each 1gm Contains: Colistin Sulphate……500,0000 IU
	Finished Product Specification	In House
	Pharmacological Group	Polymyxins
	Shelf life	36 months
	Demanded Price	Decontrolled
	Pack size	100gm, 250gm, 500gm, 1kg, 5kg, 10kg HDPE Jar
	International availability	N/A
	Me-too status	Bio-Col Water Soluble Powder by M/s Bio-Labs (Reg#088825)
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and 65 ± 5%RH of three batches for 36 months and accelerated stability data sheet conducted at 40 ± 2 ºC and 75 ± 5%RH of three batches for six months
	Detail of certificates attached	Original legalized GMP certificate Certificate No: 5/5/10 002372 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department date: 28-02-2021 Validity: Valid for five years GMP status: GMP certificate states that firm is subjected to inspection at adequate interval in order to verify GMP Original legalized Free sale Certificate Certificate No: 5/5/10 002368 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department Date:28-02-2021 Validity: Valid for ten years Free Sale Certificate Confirms the free sale of the product in exporting country. Letter of Authorization Letter of authorization from M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals, (REEFCO) in the name of M/s Meezab Z.International company, Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan Date of Agreement: 28.02.2021 while (stamped/sign date 03.02.2021) Validity: Valid until revoked by Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,
	Previous Remark of Evaluator [XI]	•
	Previous Decision (308-DRB)	• Deferred for evidence of approval of required manufacturing facility / section by regulatory authority i.e. penicillin and dry powder suspension sections are separate.
	Evaluation by PEC	• The firm submitted Certificate No: 5/5/10 010434 dated 14/09/2021 issued by Minister of Agriculture / Acting Director of Veterinary and Animal Health Directorate showing presence of four sections 1. Oral Liquid (General) 2. Oral Soluble powder

		3. Suspension (General) 4. Penicillin (Powder)
	Decision: Approved with innovator's specifications. 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.	
261.	Name and address of Applicant	M/s Meezab Z.International Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan
	Detail of Drug Sale License	Name: M/s Meezab Z International Address: Fareed Abad, Jahanian District khanewal Validity: 05th October 2021 Status: License to sell drugs as a distributor
	Name and address of manufacturer	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,(REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name and address of marketing authorization holder	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,(REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 9719 dated 04-03-2019
	Fee including differential fee	Rs100,000/- dated 28-02-2019
	Brand Name+Dosage Form+ Strength	Tylodoxyreef Powder
	Composition	Each 1gm Contains: Tylosin Tartrate……..…200mg Doxycycline Hyclate…….200mg
	Finished Product Specification	Manufacturer's specifications
	Pharmacological Group	Macrolide /tetracycline antibiotics
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	100gm, 250gm, 500gm, 1kg, 5kg, 10kg HDPE Jar
	International availability	N/A
	Me-too status	Doximac-Forte Water Soluble Powder by M/s Prix Pharmaceutical (Reg# 080927)
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and 65 ± 5%RH of three batches for 24 months and accelerated stability data sheet conducted at 40 ± 2 ºC and 75 ± 5%RH of three batches for six months
	Detail of certificates attached	Original legalized GMP certificate Certificate No: 5/5/10 002374 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department date: 28-02-2021 Validity: Valid for five years GMP status: GMP certificate states that firm is subjected to inspection at adequate interval in order to verify GMP Original legalized Free sale Certificate Certificate No: 5/5/10 002371 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department Date:28-02-2021 Validity: Valid for ten years Free Sale Certificate Confirms the free sale of the product in exporting country. Letter of Authorization Letter of authorization from M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals, (REEFCO) in the name of M/s Meezab Z.International company, Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan

		Date of Agreement: 28.2.2021 while (stamped/sign date 03.2.2021) Validity: Valid until revoked by Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,
	Previous Remark of Evaluator [XI]	•
	Previous Decision (308-DRB)	• Deferred for evidence of approval of required manufacturing facility / section by regulatory authority i.e. penicillin and dry powder suspension sections are separate.
	Evaluation by PEC	• The firm submitted Certificate No: 5/5/10 010434 dated 14/09/2021 issued by Minister of Agriculture / Acting Director of Veterinary and Animal Health Directorate showing presence of four sections 1. Oral Liquid (General) 2. Oral Soluble powder 3. Suspension (General) 4. Penicillin (Powder)
	Decision: Approved with innovator's specifications. 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.	
262.	Name and address of Applicant	M/s Meezab Z.International Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan
	Detail of Drug Sale License	Name: M/s Meezab Z International Address: Fareed Abad, Jahanian District khanewal Validity: 05th October 2021 Status: License to sell drugs as a distributor
	Name and address of manufacturer	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,(REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name and address of marketing authorization holder	M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,(REEFCO) Alhassan Industrial Estate-Irbid-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 9726 dated 04-03-2019
	Fee including differential fee	Rs100,000/- dated 28-02-2019
	Brand Name+Dosage Form+ Strength	Gentareef Plus Powder
	Composition	Each 1gm Contains: Gentamycin Sulphate……..100mg Doxycycline Hyclate……...100mg
	Finished Product Specification	Manufacturer's specifications
	Pharmacological Group	Aminoglycoside/ tetracycline antibiotics
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	100gm, 250gm, 500gm, 1kg, 5kg, 10kg HDPE Jar
	International availability	N/A
	Me-too status	
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and 65 ± 5%RH of three batches for 24 months and accelerated stability data sheet conducted at 40 ± 2 ºC and 75 ± 5%RH of three batches for six months
	Detail of certificates attached	Original legalized GMP certificate Certificate No: 5/5/10 002370 Certifying Authority: Minister of Agriculture and Minister of Environment date: 28-02-2021 Validity: Valid for five years GMP status: GMP certificate states that firm is subjected to inspection at adequate interval in order to verify GMP Original legalized Free sale Certificate

		Certificate No: 5/5/10 002721 Certifying Authority: Minister of Agriculture / Director of Veterinary and Animal Health Department Date:08-03-2021 Validity: Valid for ten years Free Sale Certificate Confirms the free sale of the product in exporting country. Letter of Authorization Letter of authorization from M/s Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals, (REEFCO) in the name of M/s Meezab Z.International company, Fareed Abad Near Bilal Mosque, Jahanian, Punjab Pakistan Date of Agreement: 04.03.2021 Validity: Valid until revoked by Al Reef Company for Manufacturing Veterinary Drugs & Argochemicals,
	Previous Remark of Evaluator [XI]	• The firm did not provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm **OR** evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting
	Previous Decision (308-DRB)	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 required manufacturing facility / section by regulatory authority i.e. penicillin and dry powder suspension sections are separate
	Evaluation by PEC	• The firm did not provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) • The firm submitted Certificate No: 5/5/10 010434 dated 14/09/2021 issued by Minister of Agriculture / Acting Director of Veterinary and Animal Health Directorate showing presence of four sections 1. Oral Liquid (General) 2. Oral Soluble powder 3. Suspension (General) 4. Penicillin (Powder)
	Decision: Deferred for evidence of applied formulation/drug already approved by DRAP (generic status) alongwith registration number, brand name and name of firm	

Agenda of Evaluator PEC-XIII.

Case No. 1: Registration applications of locally manufactured (Human) drugs on Form 5F. A; New cases

263.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (Pvt.) Ltd., Plot # 204-205, Industrial Triangle, Kahuta Road, 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. 11283: dated 13-04-2021.
	Details of fee submitted	PKR 20,000/-: dated 16/03/2021.
	proposed proprietary name / brand name	TICA 60mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Ticagrelor ……60mg (Innovator Specifications)
	Pharmaceutical form of applied drug	Pink color, round shaped Biconvex Film coated tablets.
	Pharmacotherapeutic Group of (API)	Platelet aggregation inhibitor excl. heparin.
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	BRILINTA 60mg film coated tablets, AstraZeneca Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Anplag 60mg Tablet, Pharma Evo (Pvt.) Ltd., R.No. 093105.
	GMP status of the Finished product manufacturer	GMP certificate issued on 24-12-2018 on the basis of inspection conducted on 24-10-2018. Not valid.
	Evidence of section approval.	Tablet section (general) vide letter No. F. 1-1/96-Lic. (Vol-II) dated 13-06-2017.
	Name and address of API manufacturer.	M/s Changzhou Pharmaceuticals Factory No. 518 Laodong East Road, Changzhou, Jiangsu Province, China, China M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, 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)	Ticagrelor is based Inhouse Specification. 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 (Drug substance.)	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: (140901, 141001 & 141101)

	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 Anplag 60mg Tablet by Pharma Evo (Pvt.) Ltd., (Batch No: 9H209 Mfg. 07-2019 & Exp. 07-2021) by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Anplag 60mg Tablet by Pharma Evo (Pvt) Ltd in in three different mediums i.e. pH 1.2 in 0.1 N HCl, pH 4.5 Acetate buffer & pH 6.8 Phosphate buffer. Both the test and comparator product releases more than 85% in 15 minutes in all the mediums. However, they have used 0.2 % polysorbate in all the three mediums.
	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 Changzhou Pharmaceuticals Factory No. 518 Laodong East Road, Changzhou, Jiangsu Province, China, China M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China.		
API Lot No.	RD-TG-202003101		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (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.	ST20J003	ST20J004	ST20J005
Batch Size	5000 tabs	5000 tabs	5000 tabs
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	20-10-2020	20-10-2020	20-10-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.

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 Promig plus tablets 375mg/20mg which was conducted on 1st, 13th & 14th March 2019 and was presented in 289th meeting of Registration Board held on 14-16th May, 2019. According to the report following points were confirmed.

		• The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. 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 GMP certificate of API Manufacturer is provided, issued by Nantong Chemical & Medical Industry association valid till 05/04/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of NOC with diary No: 1469 dated 23/06/2020 is submitted wherein the permission to import Ticagrelor for the purpose of test/analysis and stability studies is granted. • DHL No. CY120101 dated 03/23/2020
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:

Sr. No.	Section Number	Observations	Response of the firm.
1	1.3	Latest GMP certificate/inspection report conducted within last three years of drug product manufacturer shall be submitted.	Firm has provided inspection report for Renewal of DML conducted on 26-12-2018 wherein the panel unanimously recommended the renewal of DML License No. 000417 (by way of formulation) M/s Global Pharmaceuticals (Pvt.) Ltd., Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad.
2	1.6.5	Valid GMP certificate/DML of API manufacturer issued by regulatory body of country shall be submitted.	Submitted valid GMP certificate of API manufacturer valid until 05-04-2022.
3	3.2 S.4	The reference product literature specifies polymorphic form II for ticagrelor tablets whereas no such declaration has been made in the COA of drug substance	Firm has submitted that Drug Master File of Ticagrelor provided by "Nantong Chanyoo Pharmatec Co., Limited clearly specifies polymorphic form II only for Ticagrelor.
4	3.2 S.5	As per submitted raw data sheets, working standard has been standardized on 1-9-2020 whereas, drug substance analysis has been performed prior to that. Justification is required.	Firm has submitted that upon receiving ticagrelor API, its analysis has been performed using working standard that was imported along with API lot. Afterwards, due to the limited quantity of working standard i.e. 150mg, standardization of ticagrelor API was performed using remaining quantity of working standard and then it has been used since than for further studies.
5	3.2. P.2.2.1	• Justification of not performing Pharmaceutical Equivalence & CDP against innovator product shall be submitted.	Firm submitted that they were unable to procure innovator pack at that time because of COVID-19 pandemic. Therefore, comparative dissolution has been performed using comparator product already approved by DRAP i.e. Anplag 60mg tablets and Anplag 90mg tablets Reg. No. 093105 and 089382 respectively.

		• Justification of use of surfactant in comparative dissolution profile shall be submitted.	As ticagrelor is BCS Class IV molecule and surfactant addition is restricted in the bio-wavier study of BCS Class I, Class II and Class III molecules in the guidelines, but not in the case of BCS Class IV. Focusing the low solubility and permeability nature of the molecule surfactant was used. Moreover, they also provided comparative dissolution without surfactant.
6	3.2. P.5.2	One-point sampling in dissolution process is submitted while the innovator has mentioned two different time points for dissolution. Justification required.	Firm submitted that they performed the dissolution on both time points mentioned by the innovator, but the data with one time point dissolution is submitted with an understanding that: - • For IR tablet single time point, with limit is the criteria for immediate release tablet as per guidelines. • Secondly innovator did not mention the acceptance criteria for 45minute and 60minutes separately. They submitted 6-month data with inclusion of both sampling time points.
7	3.2. P.8	Stability data protocol has mentioned 5000 batch size while the stability data sheets have mentioned 2000 batch size. Also, the protocols have 007, 008 & 009 batch numbers while the stability data sheets have 006, 007 & 008 batch numbers. Justification required.	Trial batch sizes of both Tica 60mg & 90mg is 5000 tablets as stated in all three BMRs and stability study protocol as well. While preparation of 3-month stability summary sheet, batch size of 2000 tablets as typographic error was mentioned. Moreover, while submission of 6th month data prior receiving shortcoming letter by your kind office, correct batch size on stability summary sheet has been submitted.
8	3.2. P.8	Only three-month stability data is submitted by the firm. Stability study data of six months shall be submitted.	Submitted six months stability study data.
9	3.2 P.8	Reference of previous approval of applications with stability study data of the firm shall be submitted.	Firm has referred to onsite inspection report of their product Promig plus tablets 375mg/20mg which was conducted on 1st, 13th & 14th March 2019 and was presented in 289th meeting of Registration Board held on 14-16th May, 2019.

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 i.e. 7500/- for pre-registration variation 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 Global Pharmaceuticals (Pvt.) Ltd., Plot # 204-205, Industrial Triangle, Kahuta Road, 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. 13082 dated 05-05-2021.
	Details of fee submitted	PKR 20,000/-: dated 16/03/2021
	The proposed proprietary name / brand name	TICA 90mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Ticagrelor ……90mg (Innovator Specifications)
	Pharmaceutical form of applied drug	yellow color, round shaped, biconvex film coated tablets.
	Pharmacotherapeutic Group of (API)	Platelet aggregation inhibitor excl. heparin.
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	BRILINTA 90mg Tablets by M/s AstraZeneca Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Anplag 90mg Tablet, PharmEvo(Pvt) Ltd, R. No. 089382.
	GMP status of the Finished product manufacturer	GMP certificate issued on 24-12-2018 on the basis of inspection conducted on 24-10-2018. Not valid.
	Name and address of API manufacturer.	M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, 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)	Ticagrelor is based Inhouse Specification. The firm has 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 (Drug substance.)	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: (140901, 141001 & 141101)
	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 Anplag 90mg Tablet by Pharma Evo (Pvt) Ltd (Batch No: 0C 118 Mfg. 03-2020 & Exp. 03-2022) by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). Dissolution test is carried out in three different mediums i.e. pH 1.2 in 0.1 N HCl, pH 4.5 Acetate buffer & pH 6.8 Phosphate buffer. However, they have used 0.2 % polysorbate in all the three mediums.
	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 Changzhou Pharmaceuticals Factory No. 518 Laodong East Road, Changzhou, Jiangsu Province, China, China M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China.		
API Lot No.	RD-TG-202003101		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (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.	ST20J006	ST20J007	ST20J008
Batch Size	2000 tabs	2000 tabs	2000 tabs
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	20-10-2020	20-10-2020	20-10-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.

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 Promig plus tablets 375mg/20mg which was conducted on 1st, 13th & 14th March 2019 and was presented in 289th meeting of Registration Board held on 14-16th May, 2019. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software

		• The firm has audit trail reports available. 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 GMP certificate of API Manufacturer is provided, issued by Nantong Chemical & Medical Industry association valid till 05/04/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of NOC with diary No: 1469 dated 23/06/2020 is submitted wherein permission to import Ticagrelor for purpose of test/analysis and stability studies is granted. • DHL No. CY120101 dated 23/03/2020
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:

Sr. No.	Section Number	Observations	Response of the firm.
1.	1.3	Latest GMP certificate/inspection report conducted within last three years of drug product manufacturer shall be submitted.	Firm has provided inspection report for Renewal of DML conducted on 26-12-2018 wherein the panel unanimously recommended the renewal of DML License No. 000417 (by way of formulation) M/s Global Pharmaceuticals (Pvt.) Ltd., Plot # 204-205, Industrial Triangle, Kahuta Road, Islamabad.
2.	1.6.5	Valid GMP certificate/DML of API manufacturer issued by regulatory body of country shall be submitted.	Submitted valid GMP certificate of API manufacturer valid until 05-04-2022.
3.	3.2 S.4	The reference product literature specifies polymorphic form II for ticagrelor tablets whereas no such declaration has been made in the COA of drug substance	Firm has submitted that Drug Master File of Ticagrelor provided by "Nantong Chanyoo Pharmatec Co., Limited clearly specifies polymorphic form II only for Ticagrelor.
4.	3.2 S.5	As per submitted raw data sheets, working standard has been standardized on 1-9-2020 whereas, drug substance analysis has been performed prior to that. Justification is required.	Firm has submitted that upon receiving ticagrelor API, its analysis has been performed using working standard that was imported along with API lot. Afterwards, due to the limited quantity of working standard i.e. 150mg, standardization of ticagrelor API was performed using remaining quantity of working standard and then it has been used since than for further studies.
5.	3.2. P.2.2.1	• Justification of not performing Pharmaceutical Equivalence & CDP against innovator product shall be submitted. • Justification of use of surfactant in	Firm submitted that they were unable to procure innovator pack at that time because of COVID-19 pandemic. Therefore, comparative dissolution has been performed using comparator product already approved by DRAP i.e. Anplag 60mg tablets and Anplag 90mg tablets Reg. No. 093105 and 089382 respectively. As ticagrelor is BCS Class IV molecule and

		comparative dissolution profile shall be submitted.	surfactant addition is restricted in the bio-wavier study of BCS Class I, Class II and Class III molecules in the guidelines, but not in the case of BCS Class IV. Focusing the low solubility and permeability nature of the molecule surfactant was used. Moreover, they also provided comparative dissolution without surfactant.
6.	3.2. P.5.2	One-point sampling in dissolution process is submitted while the innovator has mentioned two different time points for dissolution. Justification required.	Firm submitted that they performed the dissolution on both time points mentioned by the innovator, but the data with one time point dissolution is submitted with an understanding that: - • For IR tablet single time point, with limit is the criteria for immediate release tablet as per guidelines. • Secondly innovator did not mention the acceptance criteria for 45minute and 60minutes separately. They submitted 6-month data with inclusion of both sampling time points.
7.	3.2. P.8	Stability data protocol has mentioned 5000 batch size while the stability data sheets have mentioned 2000 batch size. Also, the protocols have 007, 008 & 009 batch numbers while the stability data sheets have 006, 007 & 008 batch numbers. Justification required.	Trial batch sizes of both Tica 60mg & 90mg is 5000 tablets as stated in all three BMRs and stability study protocol as well. While preparation of 3-month stability summary sheet, batch size of 2000 tablets as typographic error was mentioned. Moreover, while submission of 6th month data prior receiving shortcoming letter by your kind office, correct batch size on stability summary sheet has been submitted.
8.	3.2. P.8	Only three-month stability data is submitted by the firm. Stability study data of six months shall be submitted.	Submitted six months stability study data.
9.	3.2 P.8	Reference of previous approval of applications with stability study data of the firm shall be submitted.	Firm has referred to onsite inspection report of their product Promig plus tablets 375mg/20mg which was conducted on 1st, 13th & 14th March 2019 and was presented in 289th meeting of Registration Board held on 14-16th May, 2019.

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 i.e. 7500/- for pre-registration variation 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 Davis Pharmaceutical Laboratories, Plot No. 121 industrial Triangle area, Kahuta Road, Islamabad.
	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)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11388; dated 14-04-2021.
	Details of fee submitted	PKR 50,000/-: dated 26-01-2021.
	The proposed proprietary name / brand name	Kerolac 30mg IV/IM Injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains: Ketorolac Tromethamine …….. 30mg
	Pharmaceutical form of applied drug	Clear colorless liquid filled in glass ampoule
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	1ml x 5's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	US FDA approved.
	For generic drugs (me-too status)	Tekac 30mg/ml Injection, Sami Pharma, R.No. 092855.
	GMP status of the Applicant.	GMP certificate issued on 08-10-2020 on the basis of inspection conduct 01-10-2019.
	GMP status of the Finished product manufacturer	GMP certificate issued on 21-05-2019 on the basis of inspection conduct 23-4-2019, valid up to 22-04-2022.
	Evidence of section approval of the Finished product manufacturer.	Liquid ampoule (from GMP certificate.) Ampoule general vide letter No. F. 1-12/89-Lic (Vol-II) dated 23-07-2012.
	Name and address of API manufacturer.	M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab 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, 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 (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 ^{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 60 months. (Batch No. KTM06130016, KTM06130017 & KTM06130018)
	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	Firm has performed pharmaceutical equivalence against the product Toradol Ampoule 30mg, B. No. C2436, Mfg. date 01, 2020 by Barrett Hodgson by performing quality tests (Description, Identification, pH, Assay, Sterility, Bacterial endotoxin.)
	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. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India		
API Lot No.	KM-0100918, KTM-180015 & KTM180015.		
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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	A-439	A-596	A-611
Batch Size	46,200 Ampoules	16,000 Ampoules	33,000 Ampoules
Manufacturing Date	05-2018	03-2019	03-2019
Date of Initiation	25-06-2018	22-04-2019	20-05-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the	NA

	firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India Valid till 25-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice# SCL2018/18-19 dated 29-01-2019.
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 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)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Sr. No.	Section Number	Observations	Firm's Response
1	1.4.3	Total number of approved registered products on contract basis could not be confirmed. Complete details of products registered on contract basis shall be submitted.	Applicant has 07 approved sections and applicant has also submitted that they no product is registered on contract manufacturing.
2	1.5.6	Official monograph is available in USP. Firm has claimed innovator's specifications in "1.5.6" section of form 5F.	Firm has provided new Form 5F wherein they have revised their specifications from innovator's specifications to USP specifications without submission of applicable fee.
3	1.6.5	Valid GMP certificate of API manufacturer issued by regulatory body of country shall be submitted.	Valid GMP certificate of API manufacturer is provided. Valid till 25-06-2023.
4	3.2. S.4	• Results of analysis of relevant batch(es) of drug substance performed by drug product manufacturer used during product development and stability studies along with COA of the same batch from drug substance/Active Pharmaceutical ingredient manufacturer. • Detailed analytical procedure for the drug substance by the drug product manufacturer shall be provided. • Analytical method verification studies including specificity, accuracy and repeatability (method precision) for drug substance performed by the drug product manufacturer shall be submitted.	Batch No. A-439 has been manufactured by API lot No. KM-0100918 while COA has only been submitted for API Lot No. KTM-180015 Submitted. Firm has submitted analytical method verification studies but chromatograms for finished product has been submitted.
5	3.2. P.8.3	ADC attested invoices of the drug substance used during product development and stability studies shall be submitted.	ADC attested invoice for API Lot No. KM-0100918 used in Batch No. A-439 has not been provided by the firm.
6	3.2. P.2.3	Justification of not performing terminal sterilization of the drug product.	Firm has submitted that we cannot perform terminal sterilization of ketorolac injection because it is heat sensitive product. **Melting point of the API mentioned in**

			DMF is 165-170 ºC.
7	3.2. P.5.2	Detailed analytical procedure for the drug product by the drug product manufacturer shall be provided.	Submitted.
8	3.2. P.5.3	In process validation protocol 30.45mg of ketorolac tromethamine is used. Justification is required whether overage or potency adjustment.	Firm has submitted that it is potency adjustment. The potency as per COA of drug substance on as is basis is 98.5%. On the basis of as is potency the quantity of powder to be dispenced is calculated as 30.45mg {(100/98.5)×30 = 30.45mg}.
9	3.2. P.8.3	Submit 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.	Submitted.

Decision: Deferred for following;

- **Submission of documents/commercial invoice for the procurement of API Lot No. KM-0100918 with approval from DRAP.**
- **Submission of scientific justification for not performing terminal sterilization of the drug product.**
- **Submission of 7500/- fee for revision of finished product specifications as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**

B; Additional section;

M/s Cure Laboratories (Pvt.) Ltd., Plot # 11-12, Street No. NS-2 RCCI, Industrial Estate, Rawat, Islamabad was granted following additional sections vide letter No. F. 1-13/2017-Lic dated 08-10-2020 in 276th meeting of Central Licensing Board held on 03-09-2020;

i. Tablet section general.
ii. Capsule section general.

266.	Name, address of Applicant / Marketing Authorization Holder	M/s Cure Laboratories (Pvt.) Ltd., Plot # 11-12, Street No. NS-2 RCCI, Industrial Estate, Rawat, Islamabad.
	Name, address of Manufacturing site.	M/s Cure Laboratories (Pvt.) Ltd., Plot # 11-12, Street No. NS-2 RCCI, Industrial Estate, 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 27275 dated 01-10-2021.
	Details of fee submitted	Rs.30,000/- dated 29-09-2021.
	proposed proprietary name / brand name	P-Cip 250mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Ciprofloxacin HCl Eq. to Ciprofloxacin …… 250mg
	Pharmaceutical form of applied drug	Oral tablets.
	Pharmacotherapeutic Group of (API)	Fluoroquinolones Antibiotic.
	Reference to Finished product specification	USP specifications.

	Proposed Pack size	1 x 10's.
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	CIPRO® 250 mg, 500 mg (ciprofloxacin hydrochloride) film coated tablet, for oral use. USFDA Approved, Bayer Healthcare Pharmaceuticals Inc. USA
	For generic drugs (me-too status)	Ciplet 250mg Tablets, Indus Pharma Karachi, R. No. 044461.
	GMP status of the Finished product manufacturer	GMP certificate issued on 18-02-2021 on the basis of inspection conducted on 12-08-2020.
	Evidence of section approval.	Tablet section general vide letter No. F. 1-13/2017-Lic dated 08-10-2020.
	Name and address of API manufacturer.	M/s Citi Pharma (Pvt.) Ltd., 3.5 Km, Head Balloki Road, Phool Nagar, Kasur, 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 Validation/ 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 Ciprofloxacin Hydrochloride 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 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 as per Zone-IV A.
	Stability studies (Drug substance.)	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: (CPH1402007, CPH1402008 & CPH 1403009)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures as per USP Monograph and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product for three trial batches as per Zone-IV A.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against Ciproxin 250mg tablets of Bayer Pakistan (Pvt.) Ltd., by performing quality tests (Description, Identification, Avg. Weight, Dissolution, and Assay, as per USP Monograph). CDP is with the Same Brand Ciproxin 250mg Tablets by Bayer Pakistan (Pvt.) Ltd. at three pH i.e. Acidic (1.2), Acetate Buffer (4.5) & Phosphate Buffer (6.8) and also the similarity factor (f2) is calculated and found satisfactory.
	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., 3.5 Km, Head Balloki Road, Phool Nagar, Kasur, Pakistan.		
API Lot No.	CPH-2011069		
Description of Pack (Container closure system)	10 white colored oblong film coated tablets blistered in an Alu-Alu Blister, then packed in a Unit Carton with leaf 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, 9,12, 18 & 24 (Months)		
Batch No.	T001	T002	T003
Batch Size	1000 Tablets	1000 Tablets	1000 Tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	14-12-2020	14-12-2020	14-12-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Seven Products are approved in 307th Meeting of Registration Board with stability Data. Loxiten 20mg Capsules, Loxiten 30mg Capsules, Loxiten 60mg Capsules, Omexa 20mg Capsules, Omexa 40mg Capsules, Lansasure 15mg Capusles and Lansasure 30mg Capsules.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Citi Pharma (Pvt.) Ltd., Semi Basic (000429) has a GMP Certificate Ref. No. 01/2021-DRAP(FID-2036001-5101) Dated: 6th January 2021. Valid Till: 17th December 2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The Material is locally purchased from Citi Pharma (Pvt.) Ltd. 3.5-km, Head Balloki Road, Phool Nagar, Kasur- Pakistan.
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#	Section	Observation	Submission by the firm.
1.	1.3	Latest GMP certificate/inspection report conducted within last three years could not be confirmed.	Firm has provided GMP certificate issued on 18-02-2021 on the basis of inspection conducted on 12-08-2020.
2.	1.5.3	This section has mentioned 500mg of ciprofloxacin.	Firm has corrected the said section with 250mg of ciprofloxacin.

3.	2.3	Table for literature references for the drug product does not declare the status in pharmacopoeia other than USP.	Corrected table is submitted by the firm with required information.
4.	3.2 S.4.2	Signed copy of analytical method of drug substance shall be submitted.	Submitted
5.	3.2 S.4.3	• Limits provided by the finished product manufacturer in verification of analytical procedure of drug substance is 90-110%. Justification is required. • Performance of repeatability studies has not been done in the verification studies by finished product manufacturer.	• Firm has submitted new limits for drug substance i.e 98% -102%. Submitted
6.	3.2 P.2.1.2	Use of primojel and its compatibility studies shall be submitted as it is not used by the reference product.	Submitted.
7.	3.2 P.2.2.1	Justification of not performing CDP at 15 mint time point.	Firm has referred an article from FDA wherein at page 4, under heading "Approaches for setting Dissolution specifications for new Chemical Entity" for highly soluble and rapidly dissolving drugs products (BCS Classes 1 & 3), generation of an adequate profile sample at 5- or 10-minute intervals may be necessary, and with reference to WHO document, Ciprofloxacin HCl come under BCS class 1&3. *BCS classification of ciprofloxacin HCl is IV. Firm has claimed that it falls in Class I & III.*
8.	3.2 P.4.2	Signed copy of analytical method of drug product shall be submitted.	Submitted.
9.		Justify the dispensing of drug substance for trial batch manufacturing, on the basis of theoretical factor instead of the actual potency determined in Assay analysis of drug substance.	We have dispensed our trial batches on basis of factor calculation for HCL salt because the COA of API Lot # CPH-2011069 of Ciprofloxacin was showing the Assay above 100%. We have checked for assay as well in our own lab and found 100.1%. Due to this reason we have only calculated factor for salt only. *The firm has not adjusted the potency considering the percentage water content.*
10.		As per submitted raw data sheets the dissolution medium is not as per that recommended by the USP monograph of ciprofloxacin tablets.	Firm has submitted that we have performed all the studies with 0.01M HCl as mentioned in USP, However, 0.1M HCl *was erroneously written in some raw data sheets.*
11.		As per submitted analytical record of stability studies the dissolution test at various time points does not qualify S1 stage criteria as recommended by USP general chapter 711.	Firm has submitted that "An amount of Ciprofloxacin Hydrochloride equivalent to NLT 80% (Q) of the labeled amount of ciprofloxacin is dissolved". Statement is clear that drug release should be not less than 80% at the end of test. If we go in General chapter "Dissolution <711>, the first line in "INTERPRETATION" states "Unless otherwise specified in the individual monograph". Accordingly, I have performed the test, and it is qualifying the limits (NLT 80%).

			The interpretation of firm is not in accordance with pharmacopoeial recommendations.

Decision: Deferred for following;

- **Justify the dispensing of drug substance for trial batch manufacturing, on the basis of theoretical factor instead of the actual potency determined in Assay analysis of drug substance.**
- **As per submitted analytical record of stability studies the dissolution test at various time points does not qualify S1 stage criteria as recommended by USP general chapter 711.**
- **Submission of 7500/- fee for revision of finished 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 Cure Laboratories (Pvt.) Ltd., Plot # 11-12, Street No. NS-2 RCCI, Industrial Estate, Rawat, Islamabad.
	Name, address of Manufacturing site.	M/s Cure Laboratories (Pvt.) Ltd., Plot # 11-12, Street No. NS-2 RCCI, Industrial Estate, 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 27276 dated 01-10-2021.
	Details of fee submitted	Rs.30,000/- dated 29-09-2021.
	proposed proprietary name / brand name	P-Cip 500mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Ciprofloxacin HCl Eq. to Ciprofloxacin …… 500mg
	Pharmaceutical form of applied drug	Oral tablets.
	Pharmacotherapeutic Group of (API)	Fluoroquinolones Antibiotic.
	Reference to Finished product specification	USP specifications.
	Proposed Pack size	1 x 10's.
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	CIPRO® 250 mg, 500 mg (ciprofloxacin hydrochloride) film coated tablet, for oral use. USFDA Approved, Bayer Healthcare Pharmaceuticals Inc. USA
	For generic drugs (me-too status)	Ciplet 500mg Tablets, Indus Pharma Karachi, Reg. No. 044462.
	GMP status of the Finished product manufacturer	GMP certificate issued on 18-02-2021 on the basis of inspection conducted on 12-08-2020.
	Evidence of section approval.	Tablet section general vide letter No. F. 1-13/2017-Lic dated 08-10-2020.
	Name and address of API manufacturer.	M/s Citi Pharma (Pvt.) Ltd., 3.5 Km, Head Balloki Road, Phool Nagar, Kasur, 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 Validation/

		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 Ciprofloxacin Hydrochloride 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 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 as per Zone-IV A.
	Stability studies (Drug substance.)	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: (CPH1402007, CPH1402008 & CPH 1403009)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures as per USP Monograph and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product for three trial batches as per Zone-IV A.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against Ciproxin 500mg tablets of Bayer Pakistan (Pvt.) Ltd., by performing quality tests (Description, Identification, Avg. Weight, Dissolution, and Assay, as per USP Monograph). CDP is with the Same Brand Ciproxin 500mg Tablets by Bayer Pakistan (Pvt.) Ltd. at three pH i.e. Acidic (1.2), Acetate Buffer (4.5) & Phosphate Buffer (6.8) and also the similarity factor (f2) is calculated and found satisfactory.
	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., 3.5 Km, Head Balloki Road, Phool Nagar, Kasur, Pakistan.		
API Lot No.	CPH-2011069		
Description of Pack (Container closure system)	10 white colored oblong film coated tablets blistered in an Alu-Alu Blister, then packed in a Unit Carton with leaf 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, 9,12, 18 & 24 (Months)		
Batch No.	T001	T002	T003
Batch Size	20,000 Tablets	20,000 Tablets	20,000 Tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	14-12-2020	14-12-2020	14-12-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.		
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Seven Products are approved in 307th Meeting of Registration Board with stability Data. Loxiten 20mg Capsules, Loxiten 30mg Capsules, Loxiten 60mg Capsules, Omexa 20mg Capsules, Omexa 40mg Capsules, Lansasure 15mg Capusles and Lansasure 30mg Capsules.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Citi Pharma (Pvt.) Ltd., Semi Basic (000429) has a GMP Certificate Ref. No. 01/2021-DRAP(FID-2036001-5101) Dated: 6th January 2021. Valid Till: 17th December 2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The Material is locally purchased from Citi Pharma (Pvt.) Ltd. 3.5-km, Head Balloki Road, Phool Nagar, Kasur- Pakistan.
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.#	Section	Observation	Submission by the firm.
1	1.3	Latest GMP certificate/inspection report conducted within last three years could not be confirmed.	Firm has provided GMP certificate issued on 18-02-2021 on the basis of inspection conducted on 12-08-2020.
2	1.5.12	SOP for batch numbering is for capsule dosage form.	SOP for batch numbering of general tablet is provided by the firm.
3	2.3	Table for literature references for the drug product does not declare the status in pharmacopoeia other than USP.	Corrected table is submitted by the firm with required information.
4	3.2 S.4.2	Signed copy of analytical method of drug substance shall be submitted.	Submitted
5	3.2 S.4.3	• Limits provided by the finished product manufacturer in verification of analytical procedure of drug substance is 90-110%. Justification is required. • Performance of repeatability studies has not been done in the verification studies by the finished product manufacturer.	Firm has submitted new limits for drug substance i.e 98% -102%.
6	3.2 P.2.1.2	Use of primojel and its compatibility studies shall be submitted as it is not used by the reference product.	Submitted.
7	3.2 P.2.2.1	Justification of not performing CDP at 15 mint time point.	Firm has referred an article from FDA wherein at page 4, under heading "Approaches for setting Dissolution specifications for new Chemical

			Entity" for highly soluble and rapidly dissolving drugs products (BCS Classes 1 & 3), generation of an adequate profile sample at 5- or 10-minute intervals may be necessary, and with reference to WHO document, Ciprofloxacin HCl come under BCS class 1&3. *BCS classification of ciprofloxacin HCl is IV. Firm has claimed that it falls in Class I & III.*
8	3.2 P.4.2	Signed copy of analytical method of drug product shall be submitted.	Submitted.
9		Justify the dispensing of drug substance for trial batch manufacturing, on the basis of theoretical factor instead of the actual potency determined in Assay analysis of drug substance.	We have dispensed our trial batches on basis of factor calculation for HCL salt because the COA of API Lot # CPH-2011069 of Ciprofloxacin was showing the Assay above 100%. We have checked for assay as well in our own lab and found 100.1%. Due to this reason we have only calculated factor for salt only. *The firm has not adjusted the potency considering the percentage water content.*
10		As per submitted raw data sheets the dissolution medium is not as per that recommended by the USP monograph of ciprofloxacin tablets.	Firm has submitted that we have performed all the studies with 0.01M HCl as mentioned in USP, However, 0.1M HCl *was erroneously written in some raw data sheets.*
11		As per submitted analytical record of stability studies the dissolution test at various time points does not qualify S1 stage criteria as recommended by USP general chapter 711.	Firm has submitted that; "An amount of Ciprofloxacin Hydrochloride equivalent to NLT 80% (Q) of the labeled amount of ciprofloxacin is dissolved". Statement is clear that drug release should be not less than 80% at the end of test. If we go in General chapter "Dissolution <711>, the first line in "INTERPRETATION" states "Unless otherwise specified in the individual monograph". Accordingly, I have performed the test, and it is qualifying the limits (NLT 80%). *The interpretation of firm is not in accordance with the pharmacopoeial recommendations.*

Decision: Deferred for following;

- **Justify the dispensing of drug substance for trial batch manufacturing, on the basis of theoretical factor instead of the actual potency determined in Assay analysis of drug substance.**
- **As per submitted analytical record of stability studies the dissolution test at various time points does not qualify S1 stage criteria as recommended by USP general chapter 711.**
- **Submission of 7500/- fee for revision of finished product specifications as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**

C; Deferred cases Human (Local manufacturer);

268.	Name and address of manufacturer/ Applicant	M/s Mega Pharmaceuticals (Pvt.) Limited, 27-km, Raiwind Road, Lahore (Tablet General, Antibiotics).
	Brand Name + Dosage Form + Strength	Megalor DS 2.5mg Tablet.
	Composition	Each Film Coated Tablet Contains: Desloratadine ……..…2.5mg
	Diary No. Date of R & I & fee	Dy. No 11357 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Antihistamine.
	Type of Form	Form-5.
	Finished product Specification	Not provided.
	Pack size & Demanded Price	As per SRO.

	Approval status of product in Reference Regulatory Authorities	Could not be confirmed.
	Me-too status	Delort tablet, Medizan Laboratories, Reg. No. 060864.
	GMP status	GMP certificate issued on 30-10-2018on the basis of inspection conducted on 09-07-2018.
	Remarks of the Evaluator [XIII]	• Finished product specification is not provided. • Reference product is Orodispersible tablets and the applied formulation is film coated tablets. Label claim needs revision as per reference product along with applicable fee OR • Provide Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. • Official monograph is available in USP.
	Decision of 308th meeting of Registration Board.	Deferred for following: • Finished product specification. • Reference product is Orodispersible tablets and the applied formulation is film coated tablets. Label claim needs revision as per reference product along with applicable fee OR • Provide 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:	• Firm has revised their formulation from film coated tablets to Orodispersible tablets with submission of 7500/- fee vide slip No. 6767141868 dated 10-09-2021. • Firm has also provided finished product specifications as innovator's specifications. *Revised label claim is as under:* *Each Orodispersible Tablet Contains:* *Desloratadine ……2.5mg*
	Remarks of the Evaluator PEC-[XIII]	• For formulation change from film coated to Orodispersible tablet, full fee is required. • Me too in Orodispersible could not be confirmed. • Orally disintegrating tablets monograph is available in USP.
	Decision: Deferred for the following; • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **For formulation change from film coated to Orodispersible tablet, full fee is required as as per notification No. F. 7-11/2021-B&A/DRAP dated 13-07-2021**	
269.	Name and address of manufacturer/ Applicant	M/s Karsons Pharmaceuticals, Plot No.1, Street No. SS-3, National Industrial Zone, Rawat, Islamabad (Tablet general).
	Brand Name + Dosage Form + Strength	Karzin 10mg Tablets.
	Composition	Each Film Coated Tablet Contains: Cetirizine Dihydrochloride ……. 10mg
	Diary No. Date of R & I & fee	Dy. No 10695 dated 05-03-2019; Rs.20,000/- 04-03-2019.
	Pharmacological Group	Anti-Histamine for systemic use.
	Type of Form.	Form-5.
	Finished product Specification.	Manufacturer Specifications.
	Pack size & Demanded Price	10's, 20's, 30's, 50's, 100's & As per DRAP Policy.
	Approval status of product in Reference Regulatory Authorities.	Zirtek allergy relief 10 mg film-coated tablets, MHRA approved.
	Me-too status.	Serzine 10mg Tablets, Qintar Pharma, Reg. No. 030644.
	GMP status.	Same as above.
	Remarks of the Evaluator PEC [XIII]	• Firm has also provided Cetizex 10mg, Cetikar 10mg & Histozine 10mg Tablet as alternative brand names. • Official monograph of applied formulation is available in

		USP.
	Decision of 307th meeting of Registration Board:	Deferred for updated status of GMP of the firm from QA & LT Division.
	Submission of the firm.	Firm has submitted Inspection report dated 17-02-2019 wherein it is concluded by the FID-III That M/s Karsons Pharmaceuticals, Plot#1, Street#SS-3, National Industrial Zone, Rawat requires to improve the pharmaceutical quality system in general. However, in the opinion of undersigned basic element of GMP compliance reference to schedule B-II are in place and complied with.
	Remarks of the Evaluator PEC XIII	
	Decision of 312th meeting of Registration Board.	Deferred for correction of composition as per reference product.
	Submission by the firm.	Firm has submitted that their formulation is in line with reference product.
	Remarks of the Evaluator PEC-XIII	*Zirtek allergy relief 10 mg film-coated tablets:* Each film-coated tablet contains 10 mg cetirizine dihydrochloride.
	Decision: Approved with USP Specifications. • **Registration Board further decided that registration letter will be issued after submission of applicable fee i.e. 7500/- for revision of finished product specifications as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
270.	Name and address of manufacturer/ Applicant	M/s Reliance Pharma, Plot No. 8, Street No. S-8, Industrial Estate, Rawat, Islamabad.
	Brand Name + Dosage Form + Strength	Reli Sevel tablet 400mg
	Composition	Each film- coated tablet contains: Sevelamer HCl……..…400mg
	Diary No. Date of R & I & fee	Dy. No. 29371; 03-09-2018; Rs.20,000 (03-09-2018)
	Pharmacological Group	Phosphate binder.
	Type of Form.	Form- 5.
	Finished product Specification.	Manufacturers.
	Pack size & Demanded Price	3x 10's & as per SRO
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved.
	Me-too status.	Sevela 400mg tablet of M/s Hilton Pharma (Reg. # 058394)
	GMP status.	Last GMP inspection was conducted on 27-12-2018 and the report concludes the firm to be GMP compliant.
	Remarks of the Evaluator PEC XIII	• General tablet section is available in the firm as mentioned in the submitted GMP inspection report. • 2% overage is applied.
	Decision of 293rd meeting of Registration Board:	Deferred for scientific justification of adding 2% overage in the applied formulation.
	Submission of the firm.	Firm has revised their master formulation wherein they have removed 2% of overage without submission of applicable fee.
	Remarks of the Evaluator PEC XIII	Applicable fee for revision of master formulation shall be submitted.
	Decision: Approved with Innovator's specifications. • **Registration Board further decided that registration letter will be issued after submission of applicable fee i.e. 7500/- for revision of master formulation & finished product specifications as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
271.	Name and address of manufacturer/ Applicant	M/s Scilife Pharma Pvt Ltd., Plot # FD-57/58-A2, Korangi Creek Industrial Park, Karachi. (Contract giver) M/s Opal Laboratories (Pvt.) Ltd., LC-41, L.I.T.E., Landhi, Karachi (contract acceptor)
	Brand Name + Dosage Form + Strength	Duphil 100mg/5ml Syrup.
	Composition	Each 5ml Syrup Contains:

		Doxofylline ……..…100mg
	Diary No. Date of R & I & fee	Dy. No 16166 dated 07-03-2019; Rs.50,000/- dated 07-03-2019.
	Pharmacological Group	Xanthine's/other systemic drugs for obstructive airways disease.
	Type of Form	Form-5.
	Finished product Specification	Manufacturer's specifications.
	Pack size & Demanded Price	60ml, 120ml & As per DPC.
	Approval status of product in Reference Regulatory Authorities	Ansimar, ABC FARMACEUTICI SPA, AIFA approved.
	Me-too status	Agolix Syrup100mg, Opal Laboratories, Reg. No. 067129.
	GMP status	Scilife Pharma: GMP certificate issued on 17-06-2021 on the basis of inspection conducted on 01-03-2021.
	Remarks of the Evaluator	• GMP status of contract acceptor could not be confirmed. • Section approval/manufacturing facility of contract acceptor could not be confirmed. • M/s Scilife Pharma has 06 approved sections vide letter No. F. 2-4/2011-Lic (Vol-I) dated 18-06-2021. • M/s Scilife Pharma has also submitted that they have 09 approved products on contract basis. • Different pack sizes are mentioned. Clarification is required?
	Decision of 312th meeting of Registration Board:	Deferred for following: • GMP status of contract acceptor could not be confirmed. • Section approval/manufacturing facility of contract acceptor could not be confirmed. • Different pack sizes are mentioned. Clarification is required.
	Submission of the firm.	Firm has submitted the following; • GMP certificate of M/s Opal Laboratories issued on 27-05-2021 on the basis of inspection conducted on 24-02-2021. • Section approval letter of M/s Opal Laboratories wherein they have Oral liquid/syrup general section. • 60ml, 120ml pack sizes.
	Remarks of the Evaluator PEC XIII	
	Decision: Approved with Innovator's specifications. • **Registration Board further decided that registration letter will be issued after submission of applicable fee i.e. 7500/- for revision of finished product specifications as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
272.	Name and address of manufacturer/ Applicant	M/s Wnsfeild Pharmaceuticals, Plot # 122, Block- A, Phase- V Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Misodoc tablets 50mg/ 200mcg.
	Composition	Each enteric- coated tablet contains: Diclofenac Sodium…….50mg Misoprostol…….200mcg
	Diary No. Date of R & I & fee	Dy. No. 34356 dated 16-10-2018 Rs.20,000/-Dated 09-10-2018
	Pharmacological Group	NSAIDs
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	2x 10's & As per SRO
	Approval status of product in Reference Regulatory Authorities	MHRA Approved
	Me-too status	Arthopan of M/s Safe Pharma 061790
	GMP status	Last GMP inspection was 16-02-2018 and the report concludes grant renewal of DML 000711 for approved tablet general and Capsule general section, to M/s Siam Pharmaceuticals Islamabad.

	Remarks of the Evaluator PEC-XIII (a)	Clarification regarding Misoprostol ratio in applied formulation.
	Decision of 297th meeting of Registration Board:	Deferred for following: • revision of formulation in accordance with reference product, • confirmation requisite facility of bilayered compression machine • Clarification regarding Misoprostol ratio in the applied formulation.
	Submission of the firm.	• Firm has revised their label claim in line with reference product with submission of 30,000/- fee vide slip No. 18131798976 dated 02-11-2021. • Firm has also provided GMP inspection report dated 10-12-2020 wherein the panel unanimously recommends the grant of cGMP certificate to the firm. Report has also mentioned Bi-layered tablet facility. • Firm has also provided complete step wise manufacturing outline and master formulation in line with reference product wherein it is evident that 1% HPMC dispersion of misoprostol is used in the formulation. Revised label claim is as under; Each Film coated tablet contain; Diclofenac Sodium (In enteric coated core) …… 50mg Misoprostol (In outer layer) ……. 200mcg
	Remarks of the Evaluator PEC XIII	
	Decision: Approved with following label claim; **Each Film coated tablet contain;** **Diclofenac Sodium (In enteric coated core) …… 50mg** **Misoprostol (In outer layer) ……. 200mcg**	

D; Deferred cases veterinary (Local Manufacturer):

273.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin)- Veterinary).
	Brand Name +Dosage Form + Strength	ASL-20 Powder
	Composition	Each kg contains Amoxicillin trihydrate 200gm eq. to amoxicillin base.. 173.92gm Lincomycin HCl ……88mg Spectinomycin sulphate ……..88mg Vitamin-E 50% ……30mg
	Diary No. Date of R& I & fee	Dy. No. 13861 dated 24-05-2021; Rs. 30,000/- vide slip No. 51411031100 dated 20/05/2021
	Pharmacological Group	Antibiotic
	Type of Form	Form-5.
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Tritin-Le powder, Leeds pharma, Reg. No. 082795.
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021
	Remarks of the Evaluator PEC-XIII	• Submitted me too contain 88 grams of each of both Lincomycin HCl & Spectinomycin sulphate while the applied formulation has 88 milligrams of both the actives. • Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm OR revise label claim with applicable fee.
	Decision of 307th meeting of	Deferred for Evidence of approval of applied formulation

	Registration Board.	(generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 88718213437 dated 27-10-2021. *Revised formulation is as under:* *Each kg contains* *Amoxicillin trihydrate 200gm eq. to amoxicillin base.. 173.92gm* *Lincomycin HCl ……88gm* *Spectinomycin sulphate ……..88gm* *Vitamin-E 50% ……..30mg*
	Remarks of the Evaluator PEC-XIII	• Firm has neither submitted revised form-5 nor master formulation for revised formulation. • Full fee is required for change of formulation.
	Decision: Deferred for following; • **Revised form 5, master formulation and manufacturing process.** • **For correction/standardization of composition as per RRA/Innovator's product, full fee is required as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
274.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin)- Veterinary).
	Brand Name +Dosage Form + Strength	Amox-T Powder
	Composition	Each 100gm contains Amoxicillin trihydrate 50gm eq. to amoxicillin base…43.48mg
	Diary No. Date of R& I & fee	Dy. No. 13857 dated 24-05-2021; Rs. 30,000/- vide slip No. 9773518678 dated 20/05/2021
	Pharmacological Group	Penicillin Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	D-Mox Powder, Leads pharma, Reg. No. 082796.
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021
	Remarks of the Evaluator PEC XIII	• Submitted me too product contains Amoxicillin trihydrate 50gm eq. to amoxicillin base 43.48gm while the applied formulation is having 43.48mg. • Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm OR revise label claim with applicable fee.
	Decision of 307th meeting of Registration Board.	Deferred for following: • Submitted me too product contains Amoxicillin trihydrate 50gm eq. to amoxicillin base 43.48gm while the applied formulation is having 43.48mg. • Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm OR revise label claim with applicable fee.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 297459147 dated 27-10-2021. They also revised their specifications from innovator to BP specifications. *Revised formulation is as under:* *Each 100gm contains* *Amoxicillin trihydrate 50gm eq. to amoxicillin base ……43.48gm*
	Remarks of the Evaluator PEC XIII	• Firm has neither submitted revised form-5 nor master formulation for revised formulation. • Full fee is required for change of formulation.

	Decision: Deferred for following; • **Revised form 5, master formulation and manufacturing process.** • **For correction/standardization of composition as per RRA/Innovator's product, full fee is required as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
275.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin) - Veterinary).
	Brand Name +Dosage Form + Strength	Amox-C Powder.
	Composition	Each gm contains Amoxicillin trihydrate ……..20,000 mg Colistin sulphate ……200,000,00 IU
	Diary No. Date of R& I & fee	Dy. No. 13854 dated 24-05-2021; Rs. 30,000/- vide slip No. 45999735407 dated 20/05/2021.
	Pharmacological Group	Antibiotic
	Type of Form	Form-5.
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Anzah-Mox, Bio labs Islamabad, Reg. No. 034568.
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021
	Remarks of the Evaluator PEC XIII	Submitted generic product and applied formulation are not same. Each 1000gm Contains: - Amoxycillin …. 20,000mg. Colistine Sulphate … 2000,0000IU Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm.
	Decision of 307th meeting of Registration Board.	Deferred for Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 46786059278 dated 27-10-2021. *Revised formulation is as under:* *Each 1000gm Contains: -* *Amoxycillin …… 20,000mg.* *Colistine Sulphate …… 2000,0000IU*
	Remarks of the Evaluator PEC XIII	• Firm has neither submitted revised form-5 nor master formulation for revised formulation. • Full fee is required for change of formulation.
	Decision: Deferred for following; • **Revised form 5, master formulation and manufacturing process.** • **For correction/standardization of composition as per RRA/Innovator's product, full fee is required as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
276.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin) - Veterinary).
	Brand Name +Dosage Form + Strength	Amox 10% Powder
	Composition	Each gm contains Amoxicillin trihydrate ……..100mg Colistin sulphate ……500,000 IU
	Diary No. Date of R& I & fee	Dy. No. 13855 dated 24-05-2021; Rs. 30,000/- vide slip No. 81974677578 dated 20/05/2021.
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Innovator's Specification

	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Colimoxin Powder, Selmore Pharmaceutical (034583)
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021
	Remarks of the Evaluator PEC XIII	Submitted me too contain Amoxicillin base 100mg while the applied formulation contains Amoxicillin trihydrate. Label claim needs revision along with applicable fee.
	Decision of 307th meeting of Registration Board.	Deferred for revision of label claim in line with the reference generic product along with applicable fee.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 40702243748 dated 27-10-2021. *Revised formulation is as under:* *Each gm contains* *Amoxicillin base ……..100mg* *Colistin sulphate ……..500,000 IU*
	Remarks of the Evaluator PEC XIII	Firm has neither submitted revised form-5 nor master formulation for revised formulation.
	Decision: Deferred for submission of revised form 5, master formulation and manufacturing process.	
277.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin) - Veterinary).
	Brand Name +Dosage Form + Strength	LSA PLUS Powder.
	Composition	Each gm contains Amoxicillin Trihydrate ……200mg Lincomycin HCl ……88mg Spectinomycin 2HCl …….88mg
	Diary No. Date of R& I & fee	Dy. No. 13851 dated 24-05-2021; Rs. 30,000/- vide slip No. 76700977 dated 20/05/2021.
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Amoxy LS powder, Inshal pharma, Reg. No. 063887.
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021
	Remarks of the Evaluator PEC XIII	Submitted me too contain Amoxicillin Trihydrate 20mg/gm while the applied formulation contains Amoxicillin Trihydrate 200mg/gm.
	Decision of 307th meeting of Registration Board.	Deferred for revision of label claim in line with reference product along with submission of applicable fee.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 0980184451 dated 27-10-2021. *Revised formulation is as under:* *Each 100gm contains* *Amoxicillin Trihydrate ……20gm* *Lincomycin HCl …… 8.8gm* *Spectinomycin 2HCl …… 8.8gm.*
	Remarks of the Evaluator PEC XIII	• Firm has neither submitted revised form-5 nor master formulation for revised formulation. • Full fee is required for change of formulation.
	Decision: Deferred for following; • **Revised form 5, master formulation and manufacturing process.**	

	• **For correction/standardization of composition as per RRA/Innovator's product, full fee is required as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
278.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin) - Veterinary).
	Brand Name +Dosage Form + Strength	COLBAK Powder.
	Composition	Each 100gm contains Amoxicillin Trihydrate …….16gm Clavulanic Acid as potassium clavulanate….4gm
	Diary No. Date of R& I & fee	Dy. No. 13848 dated 24-05-2021; Rs. 30,000/- vide slip No. 7259289940 dated 20/05/2021.
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Clavet Powder, Selmore pharmaceuticals, (034582)
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021
	Remarks of the Evaluator PEC[XIII]	Submitted me too contains Amoxycillin as Trihydrate 160mg/gm and Clavulanic Acid 40mg/gm while the applied formulation has Amoxicillin Trihydrate & Clavulanic Acid as potassium clavulanate respectively. Label claim needs revision as per reference product along with applicable fee.
	Decision of 307th meeting of Registration Board.	Deferred for revision of label claim in line with reference generic product along with applicable fee.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 001875690 dated 27-10-2021. *Revised formulation is as under:* *Each gram contains* *Amoxicillin as Trihydrate ……. 160mg* *Clavulanic Acid ……..4mg*
	Remarks of the Evaluator PEC [XIII]	• Firm has neither submitted revised form-5 nor master formulation for revised formulation.
	Decision: Deferred for submission of revised form 5, master formulation and manufacturing process.	
279.	Name and address of manufacturer / Applicant	M/s Attabak Pharmaceutical, 5-C Industrial Area, I-10/3 Islamabad (Oral powder (Penicillin) - Veterinary).
	Brand Name +Dosage Form + Strength	Amoxi-PB Powder
	Composition	Each 100gm contains Amoxicillin Trihydrate 20gm eq. To Amoxicillin Base ……..17.392gm Clavulanic Acid as potassium clavulanate …..4gm Bromhexine HCl ……..0.5gm
	Diary No. Date of R& I & fee	Dy. No. 13859 dated 24-05-2021; Rs. 30,000/- vide slip No. 0574359455 dated 20/05/2021.
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	100gm, 500gm, 1kg, 2.5kg, 5kg & Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Clavmox-Forte Oral Water-Soluble Powder, Sanna Laboratories, Reg. No. 081697.
	GMP status	New Section granted vide Letter No. F.1-5/96-Lic Dated 12-03-2021 On basis of Inspection conducted on dated 08-2-2021

	Remarks of the Evaluator PEC[XIII]	• Submitted me too contain Amoxicillin as Amoxicillin Trihydrate 16gm/100gm while the applied formulation contains Amoxicillin Trihydrate 20gm eq. To Amoxicillin Base 17.392gm/100gm. Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm OR Revise formulation as per reference product with applicable fee.
	Decision of 307th meeting of Registration Board.	Deferred for Evidence of approval of applied formulation (generic/me too) already approved by DRAP with brand name, Reg. No. and name of the firm OR Revise formulation as per reference product with applicable fee.
	Submission by the firm.	Firm has provided their revised formulation with submission of 7500/- fee vide slip No. 11000860631 dated 27-10-2021. *Revised formulation is as under:* *Each 100gm contains* *Amoxicillin as Trihydrate ……. 16gm* *Clavulanic Acid as potassium clavulanate …..4gm* *Bromhexine HCl ……..0.5gm*
	Remarks of the Evaluator PEC [XIII]	• Firm has neither submitted revised form-5 nor master formulation for revised formulation. • Full fee is required for change of formulation.
	Decision: Deferred for following; • **Revised form 5, master formulation and manufacturing process.** • **For correction/standardization of composition as per RRA/Innovator's product, full fee is required as per notification No. F. 7-11/2012-B&A/DRAP dated 07-05-2021.**	
280.	Name and address of manufacturer / Applicant	M/s Delux Chemical Industries, LT 26 A/1 Landhi Industrial Area, Karachi-22
	Brand Name +Dosage Form + Strength	Reoflor 25% liquid (Oral Solution)
	Composition	Each 100ml contains: Florfenicol …….25% w/v
	Diary No. Date of R& I & fee	Dy. No.512, R&I Dated 20-6-2016, (Rs.20,000/-) (20-6-2016)
	Pharmacological Group	Anti-bacterial in poultry
	Type of Form	Form -5
	Finished product Specifications	Not provided
	Pack size & Demanded Price	100ml, 500 ml, 1000ml, 2.5 litre, 5 litre bottle & Decontrolled
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Nobiflor 25% of M/s Noble Pharma Mirpur AK
	GMP status	Last inspection was conducted on 24-12-2013 and the report concludes renewal of DML by way of formulation.
	Remarks of the Evaluator PEC	• Latest inspection report. • Species: Cattles; Sheep & Goats; Poultry. • Section needs to be verified. • Provide specs. • Firm has not submitted the reply even after being issued letter and reminder dated 13th Nov, 2017 & 4th Jan, 2018 respectively.
	Decision of 278th meeting of Registration Board.	Deferred for submission of latest GMP inspection report conducted within a period of last 1 year by DRAP.
	Submission by the firm.	Firm has submitted GMP inspection report conducted on 22-06-2021 wherein it is concluded that the fir is operating at an acceptable level of GMP compliance at the time of inspection.
	Remarks of the Evaluator PEC [XIII]	Inspection report has also mentioned that firm holds DML No. 000033 (by way of formulation) last renewed w.e.f. 09-01-2011.

		The last inspection was carried out by the panel for renewal of DML on 24-12-13.
	Decision: Deferred for updated GMP and renewal status of the firm.	
281.	Name and address of manufacturer / Applicant	M/s Delux Chemical Industries, LT 26 A/1 Landhi Industrial Area, Karachi-22
	Brand Name +Dosage Form + Strength	Reoflox-C oral solution.
	Composition	Each 100ml solution contains: Enrofloxacin …….25% w/v Colistin Sulphate……50 M.I.U.
	Diary No. Date of R& I & fee	Dy. No. 512, R&I Dated 20-06-2016, (Rs.20,000/-) (20-6-2016)
	Pharmacological Group	Anti-bacterial
	Type of Form	Form -5
	Finished product Specifications	Not provided
	Pack size & Demanded Price	100ml, 500 ml, 1000ml, 2.5-liter, 5-liter bottle & Decontrolled
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Vitaflox-C 25% liquid of M/s Vetz Pharma
	GMP status	Last inspection was conducted on 24-12-2013 and the report concludes renewal of DML by way of formulation.
	Remarks of the Evaluator PEC	• Latest inspection report. • Species: Poultry & Ruminants • Section needs to be verified. • Provide specs. • Firm has not submitted the reply even after being issued letter and reminder dated 13th Nov, 2017 & 4th Jan, 2018 respectively.
	Decision of 278th meeting of Registration Board.	Deferred for submission of latest GMP inspection report conducted within a period of last 1 year by DRAP.
	Submission by the firm.	Firm has submitted GMP inspection report conducted on 22-06-2021 wherein it is concluded that the firm is operating at an acceptable level of GMP compliance at the time of inspection.
	Remarks of the Evaluator PEC XIII	Inspection report has also mentioned that firm holds DML No. 000033 (by way of formulation) last renewed w.e.f. 09-01-2011. The last inspection was carried out by the panel for renewal of DML on 24-12-13.
	Decision: Deferred for updated GMP and renewal status of the firm.	
282.	Name and address of manufacturer/ Applicant	M/s Selmore Pharmaceuticals (Pvt.) Ltd., 36-Km, Multan Road Lahore (Veterinary Penicillin liquid injection).
	Brand Name + Dosage Form + Strength	BPS LA Injection 100ml
	Composition	Each ml Contains: Benzathine Penicillin G ……..…100,000IU Procaine Penicillin G ……..…150,000IU Dihydro Streptomycin Sulphate Eq. To Dihydro Streptomycin ……200mg
	Diary No. Date of R & I & fee	Dy. No 10341 dated 02-07-2019; Rs.20,000/- dated 01-07-2019.
	Pharmacological Group	Natural penicillin/aminoglycosides.
	Type of Form	Form-5.
	Finished product Specification	Manufacturer's specifications.
	Pack size & Demanded Price	Decontrolled.
	Approval status of product in Reference Regulatory Authorities	
	Me-too status	Pencin-La Injection (10ml, 20ml, 50ml, 100ml), Star Laboratories, Reg. No. 063626.
	GMP status	Same as above.

	Remarks of the Evaluator	
	Decision of 312th meeting of Registration Board.	Deferred for confirmation of manufacturing facility (penicillin)
	Submission by the firm.	Firm has submitted section approval letter vide No. F. 1-13/2000-Lic (Vol-II) dated 23-01-2019 wherein they have liquid injection (Penicillin) (veterinary section)
	Remarks of the Evaluator PEC XIII	
	Decision: Approved with Innovator' specifications.	

E; Deferred import veterinary cases:

283	Name and address of Applicant	M/s Meezab Z International, Near Bilal Mosque, Fareed Abad, Jahanian, Punjab Pakistan.
	Detail of Drug Sale License	Name: M/s Meezab Z International Address: Fareed Abad, Jahanian, District Khanewal. Validity: 05th October 2021. Status: License to sell drugs as a distributor (Form No.11).
	Name and address of manufacturer	M/s Al Reef Company for Manufacturing Veterinary Drugs & Agrochemicals, (REEFCO) Alhassan Industrial Estate-Irbid-Jordan.
	Name and address of marketing authorization holder	M/s Al Reef Company for Manufacturing Veterinary Drugs & Agrochemicals, (REEFCO) Alhassan Industrial Estate-Irbid-Jordan.
	Name of exporting country	Jordan.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 9724 dated 04-03-2019
	Fee including differential fee	Rs100,000/- dated 28-02-2019
	Brand Name +Dosage Form + Strength	Amproreef 600 Powder.
	Composition	Each 1gm Contains: Amprolium Hydrochloride…….……..…600mg
	Finished Product Specification	Manufacturer's Specifications.
	Pharmacological Group	Antiprotozoal.
	Shelf life	36 months
	Demanded Price	Decontrolled.
	Pack size	100gm, 250gm, 500gm, 1kg, 5kg, 10kg. Round H.D.P.E. Jar without tamper evident. With H.D.P.E Caps and Aluminum seal stamped with Reefco.
	International availability	N/A
	Me-too status	Cocster-60 Oral water-soluble Powder, M/S. Aamster Laboratories, Reg. No. 101989
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and 65 ± 5%RH of three batches for 36 months and accelerated stability data sheet conducted at 40 ± 2 ºC and 75 ± 5%RH of three batches for six months
	Detail of certificates attached	Original legalized GMP certificate Certificate No: 5/5/10 004744. Certifying Authority: Minister of Agriculture. Date: 08/03/2021. GMP Status: GMP certificate states that firm is subjected to inspection at adequate interval in order to verify GMP. Validity: Valid for five years Original legalized Free sale Certificate Certificate No: 5/5/10 004367. Certifying Authority: Minister of Agriculture. Date: 28/02/2021 Free Sale Certificate Confirms the free sale of the product in exporting country.

		Letter of Authorization Name: M/s Meezab International company. Date of Agreement: 28-02-2021. Validity: Authorization shall remain in force until revoked in writing by M/s Al Reef Company for Manufacturing Veterinary Drugs & Agrochemicals, (REEFCO).
	Remark of the Evaluator [XIII]	
	Decision of 308th meeting of Registration Board.	Deferred for evidence of approval of required manufacturing facility / section by regulatory authority i.e. penicillin and dry powder suspension sections are separate.
	Submission by the firm:	Firm has provided a document issued by the Ministry of Agricultural/Veterinary and Animal Health Department/Pharmacy and Drug Control Division/ in the Hashemite Kingdom of Jordan wherein the manufacturer has the following sections manufacturing facility; i. Oral Liquid (General) ii. Oral Soluble Powder (General) iii. Suspension (General) iv. Penicillin (Powder)
	Remark of the Evaluator [XIII]	
	Decision: Registration Board approved registration of above application with Innovator's specifications, up to 1 Kg pack size and as per Policy for inspection of Manufacturer abroad with verification of filling capacity.	

Agenda Item of Evaluator PEC-II

Case no. 01 Registration applications of newly granted DML or New section (Human)

a. New DML/New Section

- On the recommendations of panel of experts, the **CLB in its 278th** meeting held **on 10th & 11th December, 2020** has considered and approved the following (01) additional section of **M/s Islam Pharmaceuticals, 7-Km, Pasrur Road, Sialkot** Under Drug Manufacturing License Number **000885** (Formulation)

284.	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 26415 Dated: 23/09/2021
	Details of fee submitted	PKR 30,000/- Dated: 04/08/2021
	proposed proprietary name / brand name	Trapam 100mg/2ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml ampoule contains: Tramadol Hydrochloride…….100mg
	Pharmaceutical form of applied drug	Clear and colorless solution filled in USP Type I glass ampoules with green OPC mark and two green color ACF rings
	Pharmacotherapeutic Group of (API)	Analgesics – other opioids
	Reference to Finished product	Innovator

	specifications	
	Proposed Pack size	2ml×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Tramadol Hydrochloride injection 100mg/2ml by M/s Biologici Italia Laboratories S.r.l., Italy, MHRA Approved.
	For generic drugs (me-too status)	Trumed Injection 100mg/2ml by M/s Neutro Pharma (Pvt) Ltd. Reg. No. 065756
	GMP status of the Finished product manufacturer	New Section for liquid ampoule (SVP) General was granted after inspection vide letter No.F. 1-19/2014-Lic (Vol-1) Dated: 18/12/2020
	Name and address of API manufacturer.	M/s Supriya Lifescience Ltd., 07/208, Udyog Bhavan, Sonawala Road, Goregaon (East) MUMBAI - 400 063. 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:(SLL/TDM/0715011,SLL/TDM/0715012, SLL/TDM/0815014)
	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 Tramal 100mg/2ml injection by Searle Company by performing quality tests (Identification, Assay, pH and Volume Variation). All parameters results 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 Supriya Lifescience Ltd., 07/208, Udyog Bhavan, Sonawala Road, Goregaon (East) MUMBAI - 400 063. INDIA
API Lot No.	SLL/TDM/0719021
Description of Pack (Container closure system)	USP Type-I Glass ampoules in PVC Tray, packed in unit carton (2ml×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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21ARn011	21ARn012	21ARn013
Batch Size	2336 ampoules	2336 ampoules	2336 ampoules
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	05-03-2021	05-03-2021	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. (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. 19101668 issued by FDCA valid till 21/10/2022.
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 Tramadol HCl 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.	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:

Section#	Observations	Firm's response
3.2. S.4	• Drug substance specifications submitted by Drug substance manufacturer is of BP standard while Drug product manufacturer has proposed USP standard specifications for drug substance. • Drug substance analytical procedure proposed by Drug substance manufacturer & Drug product manufacturer is different. • Analytical method verification studies have been performed by M/s Islam pharma as per USP method whereas Drug substance manufacturer has claimed BP specifications.	As Tramadol HCl API monograph is available in both USP and BP, most of the tests and limits of API are same in both pharmacopoeia and results of our analysis fall in limits as specified by BP as well (Specification of Drug substance manufacturer). Common tests in BP and USP with their results are presented in tabular form with specification of USP and BP. Furthermore, we undertake that will perform and follow the BP specifications and procedure for analysis of API.
3.2S.4.4	COA of drug substance manufacturer does not declare the Assay test.	By mistake only first page of CoA by drug substance manufacturer was attached in CTD, Assay test result is given on second page.
3.2.S.5	Submitted working standard COA from M/s Islam pharma, declares Sue before date as 24-11-2019, whereas analysis has been submitted	The submitted working standard COA is by drug substance manufacturer, we mistakenly provided Working standard CoA in Drug product section

	after this date.	under section *3.2.P.6 Reference standard or materials*, copy of CoA of reference standard is submitted.
3.2.S.7	• Limits for Assay test mentioned in Drug substance specifications is different from that mentioned in the stability data. • Long term stability studies data has been submitted for 12 months only.	• The data for Real time stability was incomplete in DMF at the time of CTD submission and we requested manufacturer for complete stability data which has been received, complete stability data till 60 months has been submitted.
3.2.P.5.4	COA of only batch has been submitted.	COAs of three batches have been submitted.

Decision: Registration Board deferred the case for following:

- **Adoption of Drug substance specifications as per BP monograph of Tramadol HCl, since the drug substance manufacturer has proposed BP specifications for the drug substance.**
- **Submission of analytical record for the Drug substance analysis as per BP monograph of Tramadol HCl.**
- **Submission of analytical method verification studies for the BP monograph of Tramadol HCl, performed by M/s Islam Pharmaceuticals.**

- **M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat.**

On the recommendations of panel of experts, the CLB in its 278th meeting held on 10th & 11th December, 2020 has considered and approved the grant of Drug Manufacturing License by way of formulation (DML No. 000925) of M/s Carer pharmaceuticals Industries, Plot No. 27, Main Road, Rawat Industrial Estate, Rawat with following four sections:

- Tablet (General) Section
- **Capsule (General) Section**
- Sachet (General) Section
- Ampoule (General) section
- Dry Powder Suspension (General) Section

285.	Name, address of Applicant / Marketing Authorization Holder	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	Name, address of Manufacturing site.	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	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 section approval	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Dy. No. and date of submission	Dy. No 27959 dated 11-10-2021
	Details of fee submitted	Rs.30,000/- dated 28-09-2021
	proposed proprietary name / brand name	ORS Sachet Lemon flavour
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet contains: Sodium Chloride……...2.6g Sodium Citrate Dihydrate…….2.9g Potassium Chloride……...1.5g

		Glucose anhydrous……...13.5g
	Pharmaceutical form of applied drug	Sachet
	Pharmacotherapeutic Group of (API)	Oral Rehydration Salt
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	1 X 20's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	WHO Approved
	For generic drugs (me-too status)	Werisol Sachet of M/s Werrick Pharmaceuticals
	GMP status of the Finished product manufacturer	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General),Capsule (General), section approved.
	Name and address of API manufacturer.	**Sodium Chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India **Sodium Citrate, dihydrate:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India **Potassium Chloride** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India **Glucose,anhydrous** Xiwang Pharmaceutical Co.Ltd.No.237, Tongfu Road, Handian Town, Zouping Country, Binzhou 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, 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, 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	**Sodium chloride:** 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. **Trisodium citrate dihydrate:** 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 chloride:** 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. **Glucose anhydrous:** 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):	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 Werrisol by Werrick Pharma performing quality tests
	Analytical method validation/verification of product	Method verification studies have submitted.

STABILITY STUDY DATA

Manufacturer of API	**Sodium chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Trisodium citrate dihydrate:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Potassium chloride:** Nandu Chemicals (Pvt) Ltd. N-12, Industrial Estate, Hubli India. **Glucose anhydrous:** Xiwang Pharmaceutical Co. Ltd. No. 237, Tongfu Road, Handian Town, Zouping County, Binzhou City, Shandong Province China.		
API Lot No.	**Sodium chloride:** BSCL201112 **Trisodium citrate dihydrate:** 183 **Potassium chloride:** 736 **Glucose anhydrous:** XW20200302		
Description of Pack (Container closure system)	White to off-white crystalline powder filled in laminated sachet.(1 x 20'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.	T001	T002	T003
Batch Size	2500 sachet	2500 sachet	2500 sachet
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	02-2023	02-2023	02-2023
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.	**Sodium chloride:** Firm has submitted copy of GMP certificate (No. 1037/2020-21) of M/s Nandu Chemicals (Pvt) Ltd. India issued by Drugs Control Department Government of Karnataka. The certificate is valid till 17-11-2021. **Trisodium citrate dihydrate:**

		Firm has submitted copy of GMP certificate (No. 1037/2020-21) of M/s Nandu Chemicals (Pvt) Ltd. India issued by Drugs Control Department Government of Karnataka. The certificate is valid till 17-11-2021. **Potassium chloride:** Firm has submitted copy of GMP certificate (No. 1037/2020-21) of M/s Nandu Chemicals (Pvt) Ltd. India issued by Drugs Control Department Government of Karnataka. The certificate is valid till 17-11-2021. **Glucose anhydrous:** Firm has submitted copy of GMP certificate (No. SD20170644) of M/s Xiwang Pharmaceutical Co. Ltd. Xiwang Industry zone Zouping County, Shandong Province China issued by CFDA China. The certificate is valid till 11-01-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoices 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 & accelerated)	The report of Temperature and humidity log is also attached.

Remarks of Evaluator:

Observations	**Firm's response**
Details of the reference product, against which Pharmaceutical equivalence studies have been performed, shall be submitted.	Pharmaceutical studies have been performed against the ORS sachet of M/s Searle.
Submit evidence of availability of "Atomic emission spectrophotometry/ Flame Photometer", required for the analysis of Potassium & sodium in the applied product.	
Complete batch manufacturing records shall be submitted for stability batches.	• Batch manufacturing records of three stability batches have been submitted.
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".	• Analytical method verification studies performed by M/s Carer Pharma submitted
Submit evidence of procurement of each drug substance like ADC attested invoice or DHL slip etc, since only commercial invoice is submitted.	• Firm has submitted commercial invoice and courier slips.

Decision: Deferred for submission of evidence of availability of "Atomic emission spectrophotometry/ Flame Photometer", required for the analysis of Potassium & sodium in the applied product.

286.	Name, address of Applicant / Marketing Authorization Holder	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	Name, address of Manufacturing site.	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat

	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 section approval	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Dy. No. and date of submission	Dy. No 27274 dated 01-10-2021
	Details of fee submitted	Rs.30,000/- dated 21-09-2021
	proposed proprietary name / brand name	Desan Plus Sachet 20mg/1680mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet contains: Omeprazole …….. 20mg Sodium Bicarbonate…….1680mg
	Pharmaceutical form of applied drug	Immediate release powder for oral suspension in sachet
	Pharmacotherapeutic Group of (API)	Proton pump inhibitors
	Reference to Finished product specifications	As Per Innovators Specifications
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Risek Insta Sachet of M.s Getz Pharma
	GMP status of the Finished product manufacturer	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Name and address of API manufacturer.	**Omeprazole:** M/s Everest Organics limited. Regd. Office & factory: Aroor Village, Sadasivpet Mandal, Sangareddy Dist. Telangana **Sodium Bicarbonate:** M/s TATA Chemicals Europe Ltd., Mond House, Winnington Lane, Northwich Cheshire, CW84DT, United Kingdom
	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, 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 monographs of Omeprazole and Sodium Bicarbonate are present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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
	Stability studies	**Sodium bicarbonate:** Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH **Omeprazole:** Real time: 5°C ± 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, 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 Zegerid by Santarus Pharma performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed for omeprazole against the same brand that is Zegerid by Santarus Pharma in Acid media (pH 1.0-1.2), 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 verification studies have submitted.

STABILITY STUDY DATA			
Manufacturer of API	**Omeprazole:** M/s Everest Organics limited. Regd. Office & factory: Aroor Village, Sadasivpet Mandal, Sangareddy Dist. Telangana **Sodium Bicarbonate:** M/s TATA Chemicals Europe Ltd., Mond House, Winnington Lane, Northwich Cheshire, CW84DT, United Kingdom		
API Lot No.	OME/E-347/18 (Omeprazole) & 0000047245 (Sodium Bicarbonate)		
Description of Pack (Container closure system)	White powder filled in Aluminium foil sachet.(1 x 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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T1/21	T2/21	T3/21
Batch Size	1500 Sachets	1500 Sachets	1500 Sachets
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	12-2022	12-2022	12-2022
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.	**Omeprazole:** Copy of GMP certificate (Certificate No.L.Dis. No.1221/E1/2019) for M/s Everest Organics Ltd. Aroor Village, Sadasivpet Mandal, Medak District – 502291 Telangana India issued by Drug Control Adminstration Government of Telgana issued on 10-09-2019 and, valid for three years. **Sodium Bicarbonate:** Copy of Drug manufacturing license (License no. UK API 10762 Insp GMP 10762/1649-0005) for M/s Ata Chemicals Europe Limited Issued by Medicines and Healthcare Products Regulatory Agency United Kingdom is submitted, valid upto 20-09-2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice 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:		
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.**		
287.	Name, address of Applicant / Marketing Authorization Holder	M/s ,Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	Name, address of Manufacturing site.	M/s ,Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	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 section approval	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Dy. No. and date of submission	Dy. No 27273 dated 01-10-2021
	Details of fee submitted	Rs.30,000/- dated 21-09-2021
	proposed proprietary name / brand name	Desan Plus Sachet 40mg/1680mg

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet contains: Omeprazole …….40mg Sodium Bicarbonate…….1680mg
	Pharmaceutical form of applied drug	Immediate release powder for oral suspension in sachet
	Pharmacotherapeutic Group of (API)	Proton pump inhibitors
	Reference to Finished product specifications	As Per Innovators Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Risek Insta Sachet of M.s Getz Pharma
	GMP status of the Finished product manufacturer	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General),Ampoule (General),Capsule (General), section approved.
	Name and address of API manufacturer.	**Omeprazole:** M/s Everest Organics limited. Regd. Office & factory: Aroor Village, Sadasivpet Mandal, Sangareddy Dist. Telangana **Sodium Bicarbonate:** M/s TATA Chemicals Europe Ltd., Mond House, Winnington Lane, Northwich Cheshire, CW84DT, United Kingdom
	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, 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 monographs of Omeprazole and Sodium Bicarbonate are present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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
	Stability studies	**Sodium bicarbonate:** Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH **Omeprazole:** Real time: 5°C ± 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, 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 Zegerid by Santarus Pharma performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).

		CDP has been performed for omeprazole against the same brand that is Zegerid by Santarus Pharma in Acid media (pH 1.0-1.2), 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 verification studies have submitted.		
STABILITY STUDY DATA				
Manufacturer of API		**Omeprazole:** M/s Everest Organics limited. Regd. Office & factory: Aroor Village, Sadasivpet Mandal, Sangareddy Dist. Telangana **Sodium Bicarbonate:** M/s TATA Chemicals Europe Ltd., Mond House, Winnington Lane, Northwich Cheshire, CW84DT, United Kingdom		
API Lot No.		OME/E-347/18 (Omeprazole) & 0000047245 (Sodium Bicarbonate)		
Description of Pack (Container closure system)		White powder filled in Aluminium foil sachet.(1 x 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: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		T1/21	T2/21	T3/21
Batch Size		1500 Sachets	1500 Sachets	1500 Sachets
Manufacturing Date		01-2021	01-2021	01-2021
Date of Initiation		12-2022	12-2022	12-2022
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.	**Omeprazole:** Copy of GMP certificate (Certificate No.L.Dis. No.1221/E1/2019) for M/s Everest Organics Ltd. Aroor Village, Sadasivpet Mandal, Medak District – 502291 Telangana India issued by Drug Control Adminstration Government of Telgana issued on 10-09-2019 and, valid for three years. **Sodium Bicarbonate:** Copy of Drug manufacturing license (License no. UK API 10762 Insp GMP 10762/1649-0005) for M/s Ata Chemicals Europe Limited Issued by Medicines and Healthcare Products Regulatory Agency United Kingdom is submitted, valid upto 20-09-2021		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Omeprazole: Firm has submitted copy of invoice from M/s Everest Organics Limited, 1st Floor, LakeviewPlot No. 127-128, Amar Co-operative Society Madhapur Hydrabad, India. Sodium bicarbonate: Firm has submitted copy of Invoice from Toss enterprises 1st Floor, Sattar Villa A, 32-1-C-1/6, Block 6, P.E.C.H.S., Osman Issabhai Memon Road, (Near Hill Park), Karachi.Firm also submitted GD from TATA chemicals Europe Limited to Toss		

		chemicals.
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:

Section#	Observation	Firm's response
1.5.15 – 1.5.20	Commitments not submitted	Submitted.
3.2.S.5	Relevant information shall be submitted.	COA of working standard of Omeprazole submitted.
3.2.S.7	Justification shall be submitted for stability studies of Omeprazole at refrigerating conditions.	USP monograph of Omeprazole recommends "cold" storage conditions.
3.2.P.5.2	Reference shall be submitted for the selection of dissolution parameters	Dissolution parameters have been adopted from US FDA Dissolution database. https://www.accessdata.fda.gov/scripts/cder/dissolution/dsp_SearchResults.cfm
3.2.P.8	Documents for the procurement of API with approval from DRAP (in case of import) shall be submitted. In-use stability studies shall be submitted for the reconstituted powder. Raw data sheets shall be submitted for stability studies.	Copy of commercial invoice & GD submitted. The applied product is to be used immediately after reconstitution, hence in-use stability study was not performed. Raw data sheets have been submitted.

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.**

288.	Name, address of Applicant / Marketing Authorization Holder	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	Name, address of Manufacturing site.	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	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 section approval	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension

		(General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Dy. No. and date of submission	Dy. No 24057 dated 01-09-2021
	Details of fee submitted	Rs.30,000/- dated 10-08-2021
	proposed proprietary name / brand name	Carawat Inj 10 ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampule contains: Water for Injection……10ml
	Pharmaceutical form of applied drug	Sterile Liquid Injection
	Pharmacotherapeutic Group of (API)	Solvent
	Reference to Finished product specification	BP Pharmacopoeia
	Proposed Pack size	100's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Approved by MHRA and USFDA, also available in BP & USP
	For generic drugs (me-too status)	Surge Laboratories Pvt Ltd Brand Name W.F.I Strength 5ml /ampoule
	GMP status of the Finished product manufacturer	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Name and address of API manufacturer.	N/A
	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, specifications, analytical procedures, 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, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	N/A
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and 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 W.F.I 10ml by Surge Laboratories by performing quality tests (Acidity, Conductivity, pH, Sterility and endotoxin tests).
	Analytical method validation/verification of product	In Analytical procedure of Carawat 10 ml (water for injection) all tests are Qualitative so validation of Analytical Procedure is not applicable in Product.
STABILITY STUDY DATA		
Manufacturer of API	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial	

	Estate, Rawat		
API Lot No.	NA		
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, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T003	T005
Batch Size	1000 ampoules	1000 ampoules	1000 ampoules
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	12-2022	12-2022	12-2022
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.	N/A
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice 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)	

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.**

289.	Name, address of Applicant / Marketing Authorization Holder	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	Name, address of Manufacturing site.	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	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 section approval	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Dy. No. and date of submission	Dy. No 24056 dated 01-09-2021
	Details of fee submitted	Rs.30,000/- dated 10-08-2021
	proposed proprietary name / brand name	Carawat Inj 5 ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampule contains: Water for Injection …… 5ml
	Pharmaceutical form of applied drug	Sterile Liquid Injection
	Pharmacotherapeutic Group of (API)	Solvent
	Reference to Finished product specifications	BP Pharmacopoeia
	Proposed Pack size	100's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Approved by MHRA and USFDA
	For generic drugs (me-too status)	Surge Laboratories Pvt Ltd., Brand Name W.F.I Strength 5ml /ampoule
	GMP status of the Finished product manufacturer	New license granted on 18/03/2021 Tablet (General & General Antibiotic) Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General), section approved.
	Name and address of API manufacturer.	N/A
	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, specifications, analytical procedures, 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, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	N/A
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and 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 W.F.I 5ml by Surge Laboratories by performing quality tests (Acidity, Conductivity, pH, Sterility and endotoxin tests).
	Analytical method validation/verification of product	N/A

STABILITY STUDY DATA

Manufacturer of API	M/s, Carer Pharmaceuticals Industries Plot # 27, Main Road, Rawat Industrial Estate, Rawat		
API Lot No.	NA		
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, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T002	T004	T006
Batch Size	1000 ampoules	1000 ampoules	1000 ampoules
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	12-2022	12-2022	12-2022
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.	N/A
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice 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:

Observation	Firm's response
• Provide validation of analytical procedures in section 3.2.S.4.3 of module 3 or else provide scientific justification if validation of analytical procedure is not required.	• Since this product does not require any analytical testing like assay etc therefore there is no need to perform the validation or verification studies

• 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) in section 3.2.S.4.4 of module 3 as per the decision of 293rd meeting of Registration Board. • Provide details of the container closure system of the drug substance in section 3.2. S.6. • Provide results of stability studies of the drug substance in section 3.2.S.7 or else provide scientific justification if the stability studies are not required to be performed. • Provide validation of analytical procedures of drug product in section 3.2.P.5.3 of module 3 or else provide scientific justification if validation of analytical procedure is not required. • Justify why the tests for nitrates are not performed during the stability studies. • Submit signed copy of batch manufacturing record of all the three stability batches.	• COA of drug substance analysis at bulk stage has been submitted. • Distilled Water for Injection is Contained at about 80oC in SS Container (316L) for less than 24Hours. • In Analytical procedure of Carawat 5 ml (WATER FOR INJECTION) all tests are Qualitative so validation of Analytical procedure is not applicable in product. • 9th month long term stability study data has been submitted along with performance of test of nitrates.

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.**

290.	Name, address of Applicant / Marketing Authorization Holder	M/s Carer Pharmaceuticals Industries, Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	Name, address of Manufacturing site.	M/s Carer Pharmaceuticals Industries, Plot # 27, Main Road, Rawat Industrial Estate, Rawat
	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.28924 dated 22-10-2021
	Details of fee submitted	PKR 30,000/- dated 11-10-2021
	The proposed proprietary name / brand name	Gabril 100mg capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Pregabalin…….100mg
	Pharmaceutical form of applied drug	Hard gelatin capsule
	Pharmacotherapeutic Group of (API)	Anticonvulsants
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	2 × 7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lyrica 100mg capsule of Upjohn UK limited (USFDA Approved)

	For generic drugs (me-too status)	ZEEGAP 100mg Capsule of M/s Hilton pharma
	GMP status of the Finished product manufacturer	New license granted on 18/03/2021 Tablet (General), Dry Powder Suspension (General), Sachet (General), Ampoule (General), Capsule (General) section approved.
	Name and address of API manufacturer.	M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Address: 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, 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 regarding nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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.
	Stability studies of drug substance	The firm has submitted 06 months accelerated and 36 months real time stability study data of drug substance.
	Module-III (Drug Product):	The firm has submitted details of manufactures, 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 submitted pharmaceutical equivalence of developed formulation (Batch # T-001) against the innovator product that is Lyrica 100 mg Capsule by Pfizer Pharma performing quality tests (Identification, Assay, Dissolution). CDP has been performed with the same comparator product that is Lyrica 100 mg Capsule by Pfizer Pharma in acid media (pH 1.2), acetate buffer pH 4.5 & Phosphate Buffer (pH 6.8). The values for f_1 and f_2 are in the acceptable range.
	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 Zhejiang Huahai Pharmaceutical Co., Ltd. Address: Chuannan, Duqiao, Linhai, Zhejiang, 317016, China
API Lot No.	D5248-19-069
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: 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	1500 Capsules	1500 Capsules	1500 Capsules
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	01-2021	01-2021	01-2021
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
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.	The firm has submitted copy of approval of DML for M/s Zhejiang Huahai pharmaceutical co., Ltd, China issued by Zheijiang Drug Administration. It is valid till 12-01-2025.
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 Pregabalin (1.114 Kg, Batch # D5248-19-069) dated 12-12-2020. The invoice is not attested by AD (I & E) of concerned 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 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	The firm has not submitted compliance record of 21 CFR 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)	The firm has submitted record of data logger for temperature and humidity monitoring of stability chambers.
REMARKS OF EVALUATOR		

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.**

M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore.

The Central Licensing Board in its 270th meeting held on 23rd May, 2019 has considered and approved the grant of Drug Manufacturing License to M/s Pacific Pharmaceuticals Ltd. Ravi lane, Plot No., 384, Sundar industrial Estate, Raiwind Road, Lahore by way of Formulation vide approval letter No. F. 1-56/2011 Lic dated 24th June, 2019 with following (03) sections.

S No.	Name of Section
1.	LVP (General) Section
2.	SVP (General) Section
3.	Ophthalmic General) Section

291.	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 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. 8511 dated 25-10-2021
	Details of fee submitted	Rs.30,000/- dated 12-08-2021
	proposed proprietary name / brand name	Easy-Spa Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule contains: Pholoroglucinol dihydrate …….40mg Trimethyl phloroglucinol ……0.04mg
	Pharmaceutical form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	ATC Code: A03AX12 Musculotropic Antispasmodic
	Reference to Finished product specification	IH specification
	Proposed Pack size	1 x 4 ml
	Proposed unit price	--
	status in reference regulatory authorities	Spasfon (ANSM France Approved)
	For generic drugs (me-too status)	Spasfon (ANSM France Approved)
	Name and address of API manufacturer.	Taixing Yinxin Chemical Co., LTD. Address: No. 18 Zhonggang Road, Economic Development Zone, Taixing, Website: www.taixingyinxinchem.com Tel: +86-523-87998158 City: Taixing Province: Jiangsu, 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 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)	**Phloroglucinol** Long-term stability studies were performed at a storage temperature of 30°C±2°C/65%±5% RH for 36 months. Accelerated stability studies were performed at a temperature of 40±2°C/75%±5% RH for 6 months. **Trimethyl Phloroglucinol** Long-term stability studies were performed at a storage temperature of 30°C±2°C/65%±5% RH for 36 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 "Spasfon Injection" by Himont 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	Taixing Yinxin Chemical Co., LTD. Address: No. 18 Zhonggang Road, Economic Development Zone, Taixing, Website: www.taixingyinxinchem.com Tel: +86-523-87998158 City: Taixing Province: Jiangsu, China		
API Lot No.	TX20200408 (Phloroglucinol) TMB20200301 (Trimethyl phloroglucinol)		
Description of Pack (Container closure system)	Glass ampoule type I		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% RH ± 5% RH Accelerated: 40°C ± 2°C / 75% RH ± 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.	GSTT0012021	GSTT0022021	GSTT0032021
Batch Size	10 liter	10 liter	10 liter
Manufacturing Date	05/01/2021	05/01/2021	05/01/2021

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.	Copy of GMP certificate in the name of Taixing Yinxin Chemical Co., LTD. Address: No. 18 Zhonggang Road, Economic Development Zone, Taixing, China valid upto 17-12-2022 issued by Nanjing Pharmaceutical Association.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice not attested by AD I&E DRAP, Lahore, has been submitted.

Batch No.	Quantity Imported	Date of approval by DRAP
TX20200408 (Phloroglucinol)	600 g	
TMB20200301 (Trimethyl phloroglucinol)	700 g	

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:

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 shall submit valid DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin before issuance of registration letter.**

292.	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 LVP 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 23823 dated 31-08-2021
	Details of fee submitted	Rs.30,000/- dated 12-08-2021
	proposed proprietary name / brand name	Pacipar IV Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains 10mg paracetamol. 100ml contain 1000 mg Paracetamol.
	Pharmaceutical form of applied drug	IV Infusion

	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specification	Innoator's specification
	Proposed Pack size	1 x 100 ml
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Provas Infusion of M/s Sami pharma
	Name and address of API manufacturer.	M/s Hebei Jiheng (Group) Pharmaceutical Co., 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. 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)	**Paracetamol** 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 "Paracetamol 10 mg/ml Solution for Infusion" Solution by: 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	
Manufacturer of APIs	Hebei Jiheng (Group) Pharmaceutical Co., No. 1 Weiwu Street Industrial Park Hengshui City, Hebei Province, 053000 China
API Lot No.	011909031
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.	PI0111O	PI0211O	PI0311O
Batch Size	500 liters	500 liters	500 liters
Manufacturing Date	11/2019	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**
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Paracetamol** Copy of GMP certificate (certificate#HE20160062) in the name of Hebei Jiheng (Group) Pharmaceutical Co., No. 1 Weiwu Street Industrial Park Hengshui City, Hebei Province, 053000 China valid upto 02-02-2024 issued by HEBEI Drug Administration.
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** 011909031 | 5875 | 03-10-2019 Firm has submitted that Invoice stated the address Mis Pacific Pharmaceuticals Ltd. 30th Km Multan Road, Lahore because the procurement department at that time of Purchasing was operating from Multan road plant. Now, at current situation all procurement done from Sundar Plant.
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#	Observations	Firm's response
3.2. S.4.4	Date of analysis by M/s Pacific Pharma has been mentioned prior to date of manufacturing of drug substance.	Firm has declared it a typographical error and has submitted corrected COA.
3.2. P.7	Details of the construction of material of the primary packaging container shall be submitted.	Low Density Polyethylene for Pharmaceutical Blow Moulding.
3.2. P.8	Following shall be submitted: • Complete batch manufacturing record of stability trial batches.	Complete batch manufacturing record of stability trial batches has been submitted.
Specify the section in which applied product will be manufactured.		Product will be manufactured in LVP Section.

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.**

293.	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 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. 24882 dated 08-09-2021
	Details of fee submitted	Rs.30,000/- dated 12-08-2021
	proposed proprietary name / brand name	Xiben IV solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100 ml bottle contains 400 mg of Ibuprofen
	Pharmaceutical form of applied drug	IV Infusion
	Pharmacotherapeutic Group of (API)	ATC Code: G02CC01 Nonsteroidal anti-inflammatory drug
	Reference to Finished product specification	Innovator's Specs
	Proposed Pack size	1 x 100 ml
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Caldolor injection approved by TGA of Australia.
	For generic drugs (me-too status)	Flozeline IV Infusion of M/s Mediflow (Reg.# 079600)
	Name and address of API manufacturer.	M/s Shandong Xinhua Pharmaceutical Co. Ltd. Address: East Chemical Zone of Zibo High & New Technology Development Zone, Zibo Shandong, China Tel: 086-533-2196812
	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)	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 "Ibuprofen 400mg/100ml Solution for Infusion" by B. Braun Karachi
	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	Shandong Xinhua Pharmaceutical Co. Ltd. Address: East Chemical Zone of Zibo High & New Technology Development Zone, Zibo Shandong, China. Tel: 086-533-2196812		
API Lot No.	17091940 (Ibuprofen)		
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: 9 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9 (Months)		
Batch No.	IB0111O	IB0211O	IB0311O
Batch Size	2000 liter	2000 liter	2000 liter
Manufacturing Date	11/2019	11/2019	11/2019

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)	**N/A**
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Ibuprofen** Copy of GMP certificate (Certificate# SD20190969) in the name of Shandong Xinhua Pharmaceutical Co. Ltd. Address: East Chemical Zone of Zibo High & New Technology Development Zone, Zibo Shandong, China valid up to 01-08-2024 issued by Shandong Food & Drug Administration China
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 issued in the name of M/s Pacific Pharmaceuticals, 30th Km, Multan Road, Lahore, dated 30-11-2017.
4.	Data of stability batches will be supported by attested respective	Firm has submitted data of stability batches along with batch manufacturing record and analytical record.

	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 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:

Section#	Observations	Firm's response
3.2.S.4	Date of analysis of drug substance has been mentioned before the issuance of DML.	Date of analysis has been corrected in the COA.
3.2.S.7	Long term stability studies data is not as per Zone-Iva.	Long term stability studies data is not as per Zone-Iva conditions has been submitted for 60 months.
3.2.P.1	Justification of using Arginine in the applied formulation, since the innovator product referred by firm contains trometamol.	L-Arginine & trometamol both act as buffering agents to adjust the pH. Due to unavailability of trometamol, L-Arginine was used in applied formulation.
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.	Pharmaceutical equivalence studies have been submitted against the Ibuprofen Infusion of M/s B. Braun.
3.2.P.8	Following shall be submitted: i. Complete BMRs of three stability batches.	Firm has submitted batch manufacturing records of three 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.**

M/s Jasm Pharmaceutical (Pvt) Ltd,
Plot 4-A, Export Processing Street, Risalpur Industrial Estate, **Nowshera.**
The Central Licensing Board in its **276th** meeting held on **03rd September, 2020** has considered and approved the grant of Drug Manufacturing License Number **(000920), M/s Jasm Pharmaceutical (Pvt) Ltd,** Plot 4-A, Export Processing Street, Risalpur Industrial Estate, Nowshera by way of Formulation vide approval letter No. F. 3-5/2017-Lic dated 30th Sep, 2020 with following (05) sections.

S No.	Name of Section
1.	Tablet Section (General)
2.	Capsule (Cephalosporin)
3.	Dry Powder Section (General)
4.	Liquid Syrup Section (General)
5.	Oral Liquid Syrup Section
6.	Cream/Ointment Section (General)

294.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	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	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Dy. No. and date of submission	Dy. No. 27892 dated 08-10-2021
	Details of fee submitted	Rs.30,000/- dated 02-09-2021
	proposed proprietary name / brand name	Pylenol 250mg/5ml Oral Suspension
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml Contains: Paracetamol …….250 mg
	Pharmaceutical form of applied drug	Oral Suspension
	Pharmacotherapeutic Group of (API)	Analgesic and Antipyretic
	Reference to Finished product specification	USP
	Proposed Pack size	90 ml / bottle or as per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Calpol 250mg/5mL Suspension by M/s SmithKline Beecham USFDA Approved.
	For generic drugs (me-too status)	Fevenor Plus suspension of M/s Vision pharmaceuticals (Reg.#056310)
	GMP status of the Finished product manufacturer	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s Zenith Chemical Industries (Pvt) Limite Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind 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)	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 72 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 Calpol Suspension 120 mg/5mL by GSK Pharmaceutical 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 **Zenith Chemical Industries (Pvt) Limited.** Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind Pakistan.		
API Lot No.	ZPAR20-001		
Description of Pack (Container closure system)	90 ml / bottle packed 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.	P05	P19	30
Batch Size	500 Bottles	500 Bottles	500 Bottles
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	16-10-2020	21-10-2020	24-10-2020
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 Ref No. 141/2019-Drap(AD-813875--228) issued by DRAP
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	N/A

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

Remarks of Evaluator:

Section#	Observation	Firm's response
3.2. S.4.3	Analytical method verification studies for Assay method by HPLC shall be submitted, performed by M/s JASM Pharmaceuticals.	Submitted.
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 hand book of pharmaceutical excipients for the quantities of preservative.
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 preservative effectiveness studies at 9th month time point of long term stability studies.
3.2. P.8	• 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.	

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.**

295.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	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	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Dy. No. and date of submission	Dy. No. 27892 dated 08-10-2021
	Details of fee submitted	Rs.30,000/- dated 02-09-2021
	proposed proprietary name / brand name	Pylenol 500mg Tablet
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Tablet Contains: Paracetamol…500mg
	Pharmaceutical form of applied drug	Tablet

	Pharmacotherapeutic Group of (API)	Analgesic and Antipyretic
	Reference to Finished product specifications	USP
	Proposed Pack size	20X10's Tablets or as per SRO
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Panadol original Tablet approved by MHRA of UK
	For generic drugs (me-too status)	Panadol 500mg tablet of M/s GSK (Reg.#000817)
	GMP status of the Finished product manufacturer	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s **Zenith Chemical Industries (Pvt) Limite** Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind 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 Acetaminophen 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 72 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 Calpol Tablet 500mg by GSK Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Calpol Tablet 500mg by GSK Pharmaceutical the values for f2 are in 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 **Zenith Chemical Industries (Pvt) Limited** Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind Pakistan.
API Lot No.	ZPAR20-001
Description of Pack (Container closure system)	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, 3 & 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	P02	P20	P32
Batch Size	500 Packs	500 Packs	500 Packs
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	15-10-2020	21-10-2020	25-10-2020
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 Ref No. 141/2019-Drap (AD-813875--228) issued by DRAP
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	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Manual record submitted

Remarks of Evaluator:

Section#	Observation	Firm's response
3.2. S.4.3	Analytical method verification studies shall be submitted, performed by M/s JASM Pharmaceuticals.	Submitted.
3.2.P.2.1	• Use of primogel in the batch formulation shall be justified since innovator product has not used it. Also submit drug excipient compatibility study for primogel.	Firm has referred to the Hand book of Excipients, for literary reference of compatibility.
3.2.P.2.2.1	• Comparative Dissolution studies have been performed in two mediums only i.e., pH 4.5 & pH 6.8.	CDP study has been submitted for pH 1.2.
3.2.P.3.5	Process validation protocol does not mention the details of critical process parameters, critical quality attributes and sampling plan.	Revised process validation protocol has been submitted.
3.2. P.8	• Submitted accelerated stability data sheet of batch# P32, reflect significant change in the results of Assay test at 6th month time point. • Raw data sheet for the performance of Assay test shall be submitted wherein details of weight of standard, weight of sample and calculation formula applied are mentioned. • Justification shall be submitted for performing Assay analysis with one standard injection only, without establishing system suitability. • Submitted chromatograms reflect that the	• Firm has submitted 9th month real time stability study. • Firm has referred to the AMV study for the performance of system suitability test. • Firm has submitted that test has been performed as per USP specified method. • Firm has submitted that it was a clerical mistake and corrected the stability sheets.

	gradient program of mobile phase as described by USP monograph of "Paracetamol tablets", has not been applied. • Submitted stability 3data sheets mention different batch number of drug substance than that of which COA has been submitted. • Record for temperature and humidity monitoring of stability chambers (real time and accelerated) shall be submitted, with data of at least daily basis.	

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.**
- **Results of 6 months accelerated stability studies of first three commercial batches shall be submitted to PE&R division, establishing the fact that no significant change occurred during these studies.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

296.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	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	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Dy. No. and date of submission	Dy. No 27894 dated 08-10-2021
	Details of fee submitted	Rs.30,000/- dated 02-09-2021
	proposed proprietary name / brand name	Negzum 20mg Capsule
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Esomeprazole as enteric coated pellets……20mg
	Pharmaceutical form of applied drug	Red/Transparent Hard Gelatin Capsules filled with Esomeprazole enteric coated Pellets.
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor (PPI)
	Reference to Finished product specification	USP
	Proposed Pack size	2×7's 14 capsules or as per SRO
	Proposed unit price	As per SRO
	status in reference regulatory authorities	NEXIUM 20 mg CAPSULES

		by M/s AstraZeneca Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Nexum capsule of M/s Getz pharma
	GMP status of the Finished product manufacturer	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt.) Limited, Plot No. 22-23, Industrial Triangle, Kahuta 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)	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 72 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (P18, P28, P38)
	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 Ezium 40 mg by Searle Pharmaceuticals by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Ezium 40 mg by Searle Pharmaceuticals 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	M/s **Vision Pharmaceuticals (Pvt.) Limited** Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan
API Lot No.	EMZ046205
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: 6 months

	Accelerated: 6 months			
Frequency	Accelerated: 0, 3 & 6 (Months) Real Time: 0, 3, 6 (Months)			
Batch No.	P10	P24	P34	
Batch Size	7000 Cap	7000 Cap	7000 Cap	
Manufacturing Date	10-2020	10-2020	10-2020	
Date of Initiation	18-10-2020	22-10-2020	26-10-2020	
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. F.3-26/2019-Addl.Dir. (QA & LT-I) issued by DRAP valid till 10/02/2022.		
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	N/A		
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Manual record submitted		
Remarks of Evaluator:				
297.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.		
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd. Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.		
	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	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved		
	Dy. No. and date of submission	Dy. No. 27961 dated 11-10-2021		
	Details of fee submitted	Rs.30,000/- dated 02-09-2021		
	proposed proprietary name / brand name	Negzum 40mg Capsule		
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Esomeprazole as enteric coated pellets…40mg		
	Pharmaceutical form of applied drug	Red/Transparent Hard Gelatin Capsules filled with		

		Esomeprazole enteric coated Pellets.
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor (PPI)
	Reference to Finished product specifications	USP
	Proposed Pack size	2×7's 14 capsules or as per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	NEXIUM 40 mg CAPSULES by M/s AstraZeneca Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Nexum capsule of M/s Getz pharma
	GMP status of the Finished product manufacturer	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt.) Limited, Plot No. 22-23, Industrial Triangle, Kahuta 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)	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 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (P18, P28, P38)
	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 Ezium 40 mg by Searle Pharmaceuticals by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against same brand that is Ezium 40 mg by Searle Pharmaceuticals 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	M/s Vision Pharmaceuticals (Pvt.) Ltd, Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan	

API Lot No.	EMZ046205		
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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3 & 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	P18	P28	P38
Batch Size	7000 Cap	7000 Cap	7000 Cap
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	20-10-2020	24-10-2020	27-10-2020
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. F.3-26/2019-Addl.Dir. (QA & LT-I) issued by DRAP valid till 10/02/2022.
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	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Manual record submitted

Remarks of Evaluator:

Section#	Observation	Firm's response
3.2. S.4.3	Analytical method verification studies shall be submitted, performed by M/s JASM Pharmaceuticals.	Analytical method verification studies submitted in section 3.2.P.5.3 is also applicable for drug substance.
3.2. S.5	Reference standard of Esomeprazole has been presented, whereas USP monograph of "Esomeprazole delayed release capsules", declares use of "Omeprazole" reference standard.	COA of working standard of Omeprazole has been submitted.
3.2.P.1	Justify the quantity of 197.86mg of Esomeprazole magnesium Pellets 22.5% equivalent to 40mg of Esomeprazole.	Calculation for the equivalency factor has been submitted.
3.2.P.2.2.1	• Details of the reference product, used for the performance of Pharmaceutical equivalence studies, shall be submitted.	Pharmaceutical equivalence & CDP has been performed against the Nexium capsules of M/s Getz Pharma.
3.2. P.8	• Raw data sheet for the performance of Assay & dissolution test shall be submitted wherein details of weight of standard, weight of sample and calculation formula applied are mentioned. • Justification shall be submitted for performing Assay analysis with one standard injection	• Raw data sheets have been submitted. • Firm has submitted to the system suitability performance in the analytical method verification studies.

	only, without establishing system suitability.	
Decision: Registration Board deferred the applications of "Negzum 20mg Capsule" & "Negzum 40mg Capsule" for the submission of details of working standard used for the analysis of stability studies along with relevant analytical record.		
298.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM Pharmaceuticals (Pvt) Ltd. Address: Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd Address: Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	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 section.	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Dy. No. and date of submission	Dy.No 245512 dated 02-09-2021
	Details of fee submitted	Rs.30,000/- dated 02-09-2021
	proposed proprietary name / brand name	Celozin 750mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated Tablet Contains: Ciprofloxacin HCl eq.to Ciprofloxacin ……. 750mg
	Pharmaceutical form of applied drug	Film Coated Tablets
	Pharmacotherapeutic Group of (API)	Quinolone Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1x10's Tablets or as per SRO
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Styx 750mg tablet of M/s Saaf Pharma
	GMP status of the Finished product manufacturer	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s Zenith Chemical Industries (Pvt) Limited. Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind 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)	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 72 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 Xirip 750mg Tablets by M/s Dew Max pharmaceuticals by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Xirip 750mg Tablets by M/s Dew Max pharmaceuticals in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values 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 Zenith Chemical Industries (Pvt) Limited.** Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind Pakistan.		
API Lot No.	ZCFX20-013		
Description of Pack (Container closure system)	1x10's Tablets 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, 3 & 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	P16	P27	P29
Batch Size	500 Packs	500 Packs	500 Packs
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	20-10-2020	23-10-2020	24-10-2020
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 Ref No. 141/2019-Drap (AD-813875--228) issued by DRAP

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	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Manual record has been submitted

Firm's response:

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.**

299.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM Pharmaceuticals (Pvt) Ltd. Address: Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd Address: Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	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 section.	New license granted on 29/09/2020 Tablet, Capsule, Dry Powder, Liquid Syrup, Cream Ointment (General Sections) Approved
	Dy. No. and date of submission	Dy.No 245512 dated 02-09-2021
	Details of fee submitted	Rs.30,000/- dated 02-09-2021
	proposed proprietary name / brand name	Celozin 500mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated Tablet Contains: Ciprofloxacin HCl eq.to Ciprofloxacin ……. 500mg
	Pharmaceutical form of applied drug	Film Coated Tablets
	Pharmacotherapeutic Group of (API)	Quinolone Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1x10's Tablets or as per SRO
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Cinolox 500mg tablet of M/s Axis Pharma
	GMP status of the Finished product	New license granted on 29/09/2020

	manufacturer	Tablet, Capsule, Dry Powder, Liquid Syrup , Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s Zenith Chemical Industries (Pvt) Limited. Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind 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)	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 72 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 Cipesta 250mg Tablets by Getz Pharmaceuticals by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is is Cipesta 250mg Tablets by Getz Pharmaceuticals in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values 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 Zenith Chemical Industries (Pvt) Limited. Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind Pakistan.
API Lot No.	ZCFX20-013
Description of Pack (Container closure system)	1x10's Tablets 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, 3 & 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	P12	P25	P41
Batch Size	500 Packs	500 Packs	500 Packs
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	18-10-2020	23-10-2020	28-10-2020
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 Ref No. 141/2019-Drap (AD-813875--228) issued by DRAP
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	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Manual record has been submitted

Firm's response:

Remarks of Evaluator:

Section#	Observation	Firm's response
3.2.S.4.3	Analytical method verification studies for Assay method by HPLC shall be submitted, performed by M/s JASM Pharmaceuticals.	Firm has submitted analytical method verification studies performed by M/s Jasm Pharma.
3.2.P.2.2.1	• Justification shall be submitted regarding performance of CDP against the product of Getz instead of the innovator product. • Performance of CDP studies in only one medium has been justified.	• According to CTD guidelines we considered Getz products as our reference product for Pharmaceutical equivalence • Firm has submitted CDP study in all three mediums now.
3.2.P.5.5	The said section refers to the BP monograph, whereas Finished product specification have been claimed as of USP.	It was a drafting error, while finished product specifications have been claimed as USP.

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.**
- **The firm shall submit pharmaceutical equivalence and comparative dissolution profile data with innovator product i.e., Ciproxin 500mg tablets before issuance of registration letter.**

- On the recommendations of panel of experts, the **CLB in its 278th** meeting held **on 10th & 11th December, 2020** has considered and approved the following (03) additional section of **M/s City Pharmaceutical Laboratories, Plot No. 12-A, 1-5, Sector 5, NewSurvey No. 276, Korangi Industrial Area, Karachi** Under Drug Manufacturing License Number **000723** (Formulation)

S. No.	Name of Section
1.	Sterile Dry Powder Injection (Penicillin)
2.	Capsule (Penicillin)
3.	Dry Powder for Suspension (Penicillin)

300.	Name, address of Applicant / Marketing Authorization Holder	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, 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 on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval leter dated 22-12-2020, wherein approval for "Sterile dry powder for injection (Penicillin)", Capsule (Penicillin), Dry powder for suspension (Penicillin)."
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 17836 dated 25-06-2021
	Details of fee submitted	Rs.20,000/- dated 16-02-2021
	proposed proprietary name / brand name	Ampicillin 500mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ampicillin Sodium Eq. to Ampicillin…500mg
	Pharmaceutical form of applied drug	Powder for Injection
	Pharmacotherapeutic Group of (API)	Anti-bacterial for systemic use, Penicillin for with extended spectrum (J01CA01)
	Reference to Finished product specification	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	status in reference regulatory authorities	Approved by TGA Australia
	For generic drugs (me-too status)	Ampin injection of M/s Bosch Pharma (Reg.#016930)
	Name and address of API manufacturer.	M/s Sterile India Pvt. Limited., Plot no. -100, Sec.56, Phase IV, HSIIDC, Kundli, Sonipat, Harayana, 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, 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 "Ampin Injection 500mg" of M/s Bosch 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 Sterile India Pvt. Limited., Plot no. -100, Sec.56, Phase IV, HSIIDC, Kundli, Sonipat, Harayana, India.		
API Lot No.	00421/014/2020		
Description of Pack (Container closure system)	Type III 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.	TRI-001	TRI-002	TRI-002
Batch Size	3361 vials	3361 vials	3361 vials
Manufacturing Date	12-2020	12-2020	12-2020

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.	Copy of GMP certificate issued by Food & Drug Administration Haryana, valid upto 14-12-2021.
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
00421-03/014/2020 00421-03/014/2020	2540	10Kg 5.8 Kg	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: 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 25-06-2021.

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.**

301.	Name, address of Applicant / Marketing Authorization Holder	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, 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 on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval leter dated 22-12-2020, wherein approval for "Steril dry powder for injection (Penicillin)", Capsule (Penicillin), Dry powder for suspension (Penicillin)."
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 17837 dated 25-06-2021
	Details of fee submitted	Rs.20,000/- dated 16-02-2021
	proposed proprietary name / brand name	Ampicillin 1000mg Injection

	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial Contains: Ampicillin Sodium Eq. to Ampicillin…….1gm
	Pharmaceutical form of applied drug	Powder for Injection
	Pharmacotherapeutic Group of (API)	Anti-bacterial for systemic use, Penicillin for with extended spectrum (J01CA01)
	Reference to Fin0ished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	status in reference regulatory authorities	Approved by TGA Australia
	For generic drugs (me-too status)	Ampin injection of M/s Bosch Pharma (Reg.#016930)
	Name and address of API manufacturer.	M/s Sterile India Pvt. Limited., Plot no. -100, Sec.56, Phase IV, HSIIDC, Kundli, Sonipat, Harayana, 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	Pharmaceutical Equivalence Studies against the reference product of "Ampin Injection 1gm" of M/s BoschS 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 Sterile India Pvt. Limited., Plot no. -100, Sec.56, Phase IV, HSIIDC, Kundli, Sonipat, Harayana, India.

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.	TRI-001	TRI-002	TRI-002
Batch Size	2518 vials	2518 vials	2518 vials
Manufacturing Date	12-2020	12-2020	12-2020

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.	Copy of GMP certificate issued by Food & Drug Administration Haryana, valid upto 14-12-2021.
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
00421-03/014/2020 00421-03/014/2020	2540	10Kg 5.8 Kg	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.	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
1.6.5	Valid GMP certificate issued by the relevant regulatory authority.	Copy of GMP certificate issued by Food & Drug Administration Haryana, valid upto 14-12-2021.
2.3.S.3.2 (a)(i)	Relevant information has not been submitted	Submitted
2.3.S.4.5	• This section declares that specifications have been adopted as per British pharmacopoeia, whereas Acceptance limits presented in section 2.3.S.4.1 are not as per BP monograph for "Ampicillin sodium". • Relevant information shall be presented as per the format of QOS, instead of reproducing the extracts of Module III.	Specifictaions have been corrected as per BP.
2.3.S.5	• Relevant information shall be presented as per the	Submitted

	format of QOS, instead of reproducing the extracts of Module III.	
2.3.P.1 (d)	• Type of glass vial used as intermediate container shall be described.	Glass vial Type III has been used.
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 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.	Firm has submitted analytical method verification studies performed by M/s City Pharmaceuticals.
3.2.S.4.4	• Provide results of analysis of relevant batch(es) of Drug Substance performed used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacturer. • Submitted record reflects that drug substance analysis has been performed by UV spectrophotometer whereas BP monograph of Ampicillin sodium declares HPLC method.	• Drug substance COA from both drug substance and drug product manufacturer has been submitted. • Firm has submitted HPLC analytical record for the drug substance analysis.
3.2.P.1	• Submitted batch formula describe that "1063mg of Ampicillin sodium equivalent to 1gm of Ampicillin", which is not the correct equivalency factor.	Firm has submitted that equivalency factor was declared based upon the potency of drug substance.
3.2.P.2.2.1	• Submitted record of Pharmaceutical equivalence reflects that drug substance analysis has been performed by UV spectrophotometer whereas USP monograph of Ampicillin for injection declares HPLC method for Assay test.	HPLC analytical record has been submitted for the Pharmaceutical equivalence study.
3.2.P.2.6	• Compatibility studies with the reconstitution diluents shall be performed as per the instructions provided in individual label of the drug product.	Submitted.
3.2.P.5.3	• Analytical method validation studies have been submitted for UV spectrophotometric method, instead of the HPLC method recommended by the USP monograph of "Ampicillin for injection".	Firm has submitted HPLC analytical record for the analytical method verification studies.
3.2.P.5.4	• The copies of complete analysis of relevant batches shall be provided	Firm has submitted COA of the drug product batches.
3.2.P.6	• Justification shall be submitted for using BP grade reference standard for Assay analysis as per USP method.	COA of USP reference standard has been submitted.
3.2.P.7	• Type of glass vial used as intermediate container shall be described.	Glass vial Type III has been used. Product approved by MHRA (PL02000/0001) is in type III glass vial.
3.2.P.8.3	• Stability summary sheets must include the actual values of different tests instead of general term "complies". • Assay test during the stability studies analysis has been performed as per in-house UV method, whereas USP monograph of "Ampicillin for injection", recommends HPLC method for the Assay test. • Complete Batch manufacturing record of all three	• Revised stability sheets have been submitted. • HPLC Analytical record for stability batches has been submitted. • Batch manufacturing record of three stability batches has been submitted.

	stability batches.	

- 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 25-06-2021.

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.**

302.	Name, address of Applicant / Marketing Authorization Holder	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, 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 on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 22-12-2020, wherein approval for "Sterile dry powder for injection (Penicillin)", Capsule (Penicillin), Dry powder for suspension (Penicillin)."
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 18624 dated 02-07-2021dated 02-07-2021
	Details of fee submitted	Rs.20,000/- dated 16-02-2021
	proposed proprietary name / brand name	Amoxiclillin 250mg Capsule
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Amoxicillin Trihydrate Eq. to Amoxicillin…250mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Anti-bacterial for systemic use, Penicillin for with extended spectrum (J01CA01)
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	status in reference regulatory authorities	Approved by TGA Australia
	For generic drugs (me-too status)	Amoxil Capsule 250mg of M/s GSK (Reg.#016930)
	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,

		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)	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 "Amoxil Capsule 250mg of M/s GSK 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	Saakh Pharma (Pvt) Ltd. C-7/1, North Western Industrial Zone Port Qasim Karachi.		
API Lot No.	18PN30362		
Description of Pack (Container closure system)	Alu/PVC 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.	TRC-001	TRC-002	TRC-003
Batch Size	5000 capsules	5000 capsules	5000 capsules
Manufacturing Date	12-2020	12-2020	12-2020

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	GMP certificate issued on basis of inspection conducted on 18-06-2020.

	authority of country of origin.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice 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)	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
1.6.5	Valid GMP certificate issued by the relevant regulatory authority.	GMP certificate issued on basis of inspection conducted on 18-06-2020.
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.	Firm has submitted analytical method verification studies performed by M/s City Pharmaceuticals.
3.2.P.8.3	• Complete Batch manufacturing record of all three stability batches.	• Batch manufacturing record of three stability batches has been submitted.
• 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 02-07-2021.		

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.**

303.	Name, address of Applicant / Marketing Authorization Holder	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s City Pharmaceutical Laboratories. Plot No. 12A, Sector 5, I-5 New Serveyno-276, 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 on basis of inspection conducted on 18-11-2020.
	Evidence of approval of manufacturing facility	Firm has submitted copy of section approval letter dated 22-12-2020, wherein approval for "Sterile dry powder for injection (Penicillin)", Capsule (Penicillin), Dry powder for suspension (Penicillin)."
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No 18623 dated 02-07-2021 dated 02-07-2021
	Details of fee submitted	Rs.20,000/- dated 16-02-2021
	proposed proprietary name / brand name	Amoxicillin 500mg Capsule
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Amoxicillin Trihydrate Eq. to Amoxicillin…500mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Anti-bacterial for systemic use, Penicillin for with extended spectrum (J01CA01)
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	status in reference regulatory authorities	Approved by TGA Australia
	For generic drugs (me-too status)	Amoxil Capsule 250mg of M/s GSK (Reg.#016930)
	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, 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)	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 "Amoxil Capsule 250mg of M/s GSK has been submitted.
	Analytical method validation/verification	Firm has submitted verification studies of the drug substance

	of product	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	Saakh Pharma (Pvt) Ltd. C-7/1, North Western Industrial Zone Port Qasim Karachi.		
API Lot No.	18PN30362		
Description of Pack (Container closure system)	Alu/PVC 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.	Amox-Trial-005	Amox-Trial-006	Amox-Trial-007
Batch Size	5000 capsules	5000 capsules	5000 capsules
Manufacturing Date	12-2020	12-2020	12-2020

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 18-06-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice 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)	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
1.6.5	Valid GMP certificate issued by the relevant regulatory authority.	GMP certificate issued on basis of inspection conducted on 18-06-2020.
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.	Firm has submitted analytical method verification studies performed by M/s City Pharmaceuticals.
3.2.P.8.3	• Complete Batch manufacturing record of all three stability batches.	• Batch manufacturing record of three stability batches has been submitted.
• Firm has submitted differential fee of Rs. 10,000 vide deposit slip# 45064638642 dated 11-11-2021.		

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.**

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.

301.	Name, address of Applicant / Marketing Authorization Holder	M/s 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. 22585 dated 17/08/2021
	Details of fee submitted	PKR 30,000/-: dated 24/05/2021
	proposed proprietary name / brand name	Ensol- RL Infusion (500ml)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100mL contains: Sodium Chloride ……..... 0.6%w/v Potassium Chloride……0.04%w/v Calcium Chloride Dihydrate ..... 0.027%w/v Sodium Lactate ……... 0.32%w/v
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Sodium Chloride: Other mineral supplements ATC CODE: A12CA01 Potassium Chloride: Other mineral supplements ATC CODE: A12BA01 Calcium Chloride Dihydrate: Electrolyte replacement ATC CODE: A12AA07 Sodium Lactate: Alkalinizing Agents ATC CODE: A14AB08
	Reference to Finished product specifications	BP
	Proposed Pack size	500mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Compound Sodium Lactate Solution Intravenous Infusion BP of Baxter Healthcare Ltd. UK
	For generic drugs (me-too status)	Compound Sodium Lactate Infusion (Intravenous Infusion BP) of M/S Frontier Dextrose Ltd. (Reg # 052739)
	GMP status of the Finished product	New License Approved. Last inspection conducted on 15 &

	manufacturer	16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Name and address of API manufacturer.	Sodium Chloride: Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China Potassium Chloride: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Calcium Chloride Dihydrate: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Sodium Lactate: Luoyang Longmen Pharmaceutical Co., Ltd County Industrial Zone, Luoning, Henan, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, 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	Sodium Chloride: 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: (2871, 2872 and 2873) Potassium Chloride: 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: (KCL-054F, KCL-055B and KCL-056D) Calcium Chloride Dihydrate: 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: (CCL-253A, CCL- 253B and CCL-253C) Sodium Lactate: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (151201, 151202 and 151203)
	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	NA
	Analytical method validation/verification of product	Method verification studies has been submitted including linearity, accuracy, precision, specificity and robustness.

STABILITY STUDY DATA			
Manufacturer of API	Sodium Chloride: Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China Potassium Chloride: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Calcium Chloride Dihydrate: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Sodium Lactate: Luoyang Longmen Pharmaceutical Co., Ltd County Industrial Zone, Luoning, Henan, China.		
API Lot No.	Sodium Chloride: 20200204 Potassium Chloride: 20200310 Calcium Chloride Dihydrate: 20200215 Sodium Lactate solution: 20010160		
Description of Pack (Container closure system)	500mL 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	400 L	400 L	400 L
Manufacturing Date	11-07-2020	11-07-2020	11-07-2020
Date of Initiation	12-07-2020	12-07-2020	12-07-2020
No. of Batches	03		
Administrative Portion			
7.	Reference of previous approval of applications with stability study data of the firm (if any)	NA	
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Sodium Chloride: Copy of DML Certificate (Certificate No. # 20160106) for Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China issued by China food & Drug Administration valid up to 03-12-2025 is submitted Potassium Chloride: Copy of DML Certificate (Certificate No. # 20150058) for Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China issued by China food & Drug Administration valid up to 15-12-2025 is submitted Calcium Chloride Dihydrate: Copy of DML Certificate (Certificate No. # 20150058) for Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China issued by China food & Drug Administration valid up to 15-12-2025 is submitted	

		Sodium Lactate: Copy of DML Certificate (Certificate No. # 20190099) for Luoyang Longmen Pharmaceutical Co., Ltd County Industrial Zone, Luoning, Henan, China issued by China food & Drug Administration valid up to 29-11-2024 is submitted
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy invoices (invoice# HZA20CS88024 & invoice# LM2020031201) dated: 17-04-2020 & 07-04-2020 from Hangzhou Zhongbao Imp & Exp. Corp. Ltd, China & Luoyang Longmen Pharmaceutical Co., Ltd, China cleared by DRAP Lahore office dated 08-06-2020 & 18-06-2020
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 of Evaluator: Submitted data is in line with BP monograph.		
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.**		
302.	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. 22583 dated 17/08/2021
	Details of fee submitted	PKR 30,000/-: dated 24/05/2021
	proposed proprietary name / brand name	Ensol- RL Infusion (1000ml)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100mL contains: Sodium Chloride……..... 0.6%w/v Potassium Chloride…….0.04%w/v Calcium Chloride Dihydrate.....0.027%w/v Sodium Lactate……...0.32%w/v
	Pharmaceutical form of applied drug	Intravenous Infusion

	Pharmacotherapeutic Group of (API)	Sodium Chloride: Other mineral supplements ATC CODE: A12CA01 Potassium Chloride: Other mineral supplements ATC CODE: A12BA01 Calcium Chloride Dihydrate: Electrolyte replacement ATC CODE: A12AA07 Sodium Lactate: Alkalinizing Agents ATC CODE: A14AB08
	Reference to Finished product specifications	BP
	Proposed Pack size	1000mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Compound Sodium Lactate Solution Intravenous Infusion BP of Baxter Healthcare Ltd. UK
	For generic drugs (me-too status)	Compound Sodium Lactate Infusion (Intravenous Infusion BP) of M/S Frontier Dextrose Ltd. (Reg # 052739)
	GMP status of the Finished product manufacturer	New License 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.	Sodium Chloride: Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China Potassium Chloride: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Calcium Chloride Dihydrate: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Sodium Lactate: Luoyang Longmen Pharmaceutical Co., Ltd County Industrial Zone, Luoning, Henan, 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	Sodium Chloride: 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: (2871, 2872 and 2873)

		Potassium Chloride: 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: (KCL-054F, KCL-055B and KCL-056D) Calcium Chloride Dihydrate: 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: (CCL-253A, CCL- 253B and CCL-253C) Sodium Lactate: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (151201, 151202 and 151203)
	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	NA
	Analytical method validation/verification of product	Method verification studies has been submitted including linearity, accuracy, precision, specificity and robustness.

STABILITY STUDY DATA

Manufacturer of API	Sodium Chloride: Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China Potassium Chloride: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Calcium Chloride Dihydrate: Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China Sodium Lactate: Luoyang Longmen Pharmaceutical Co., Ltd County Industrial Zone, Luoning, Henan, China.		
API Lot No.	Sodium Chloride: 20200204 Potassium Chloride: 20200310 Calcium Chloride Dihydrate: 20200215 Sodium Lactate solution: 20010160		
Description of Pack (Container closure system)	1000mL 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	400 L	400 L	400 L
Manufacturing Date	11-07-2020	11-07-2020	11-07-2020

Date of Initiation	12-07-2020	12-07-2020	12-07-2020
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.	Sodium Chloride: Copy of DML Certificate (Certificate No. # 20160106) for Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China issued by China food & Drug Administration valid up to 03-12-2025 is submitted Potassium Chloride: Copy of DML Certificate (Certificate No. # 20150058) for Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China issued by China food & Drug Administration valid up to 15-12-2025 is submitted Calcium Chloride Dihydrate: Copy of DML Certificate (Certificate No. # 20150058) for Tianjin Haiguang Pharmaceutical Co., Ltd No.5 The seventh street TEDA, Tianjin, China issued by China food & Drug Administration valid up to 15-12-2025 is submitted Sodium Lactate: Copy of DML Certificate (Certificate No. # 20190099) for Luoyang Longmen Pharmaceutical Co., Ltd County Industrial Zone, Luoning, Henan, 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 invoices (invoice# HZA20CS88024 & invoice# LM2020031201) dated: 17-04-2020 & 07-04-2020 from Hangzhou Zhongbao Imp & Exp. Corp. Ltd, China & Luoyang Longmen Pharmaceutical Co., Ltd, China cleared by DRAP Lahore office dated 08-06-2020 & 18-06-2020	
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: Submitted data is in line with BP monograph.			
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.**			

Case no. 02 Registration applications for local manufacturing of (Human) drugs

a. New cases

303.	Name, address of Applicant / Marketing Authorization Holder	M/s Radiant Pharma Pvt Ltd. 43-E, Sundar Industrial Estate, Lahore
	Name, address of Manufacturing site.	M/s Neutro Pharma (Pvt) Ltd. Sheikhupura Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm (manufacturer)	GMP certificate issued on basis of inspection conducted on 31-12-2018 & 28-02-2019.
	Evidence of approval of manufacturing facility	Firm has submitted copy of GMP certificate of M/s Neutro Pharma, declaring the availability of Cephalosporin injectable 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. 13396 dated 18-05-2021
	Details of fee submitted	Rs.50,000/- dated 10-02-2021
	The proposed proprietary name / brand name	Ceftra 1gm IM 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 DRAP policy.
	The status in reference regulatory authorities	Approved by MHRA of UK
	For generic drugs (me-too status)	Oxidil 1gm of M/s Sami
	Name and address of API manufacturer.	M/s Zhuhai United Laboratories Co., Ltd., No. 2428, Anji road, Sanzao town, Jinwan District Zhuhai City, Guangdong 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 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 1gm injection" of M/s Sami 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 Zhuhai United Laboratories Co., Ltd., No. 2428, Anji road, Sanzao town, Jinwan District Zhuhai City, Guangdong province, China.		
API Lot No.	3052004004		
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.	001	002	003
Batch Size	16,600 vials	2.533 packs	2.924 packs
Manufacturing Date	04-19	08-18	01-19

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.	Copy of GMP certificate (certificate# GD20180909) valid upto 05-12-2023 issued by CFDA.
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 & humidity monitoring of stability chambers (real time and accelerated)	Submitted.

Remarks of Evaluator:

Section	**Observation**	**Firm's response**
2.3.S.2.1	Name of drug substance manufacturer is different from that mentioned in section#	It has been corrected as M/s Zhuhai United Laboratories Co., Ltd., No. 2428, Anji

	1.6.5	road, Sanzao town, Jinwan District Zhuhai City, Guangdong province, China.
3.2.S.2	Name of drug substance manufacturer is different from that mentioned in Module II.	It has been corrected as M/s Zhuhai United Laboratories Co., Ltd., No. 2428, Anji road, Sanzao town, Jinwan District Zhuhai City, Guangdong province, China.
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 M/s Neutro Pharma shall be submitted. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	Firm has submitted drug substance specifications, analytical method & method verification studies from M/s Neutro Pharma.
3.2.S.4.4	Provide Certificate of Analysis (CoA) of the Drug Substance, used during product development and stability studies, from Drug Substance manufacturer.	
3.2.S.7	Long term stability studies data of drug substance is not as per Zone-Iva.	Long term stability data as per Zone-IV a condition has been submitted for 36 months.
3.2.P.1	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.	3.5 ml 1% Lidocaine HCl 1% solution has been declared as diluent.
3.2.P.2.2.1	Justification shall be submitted for performance of Pharmaceutical equivalence studies against the Oxidil injection instead of the innovator product i.e., Rocephin.	Pharmaceutical equivalence studies against the Rocephin Injection have been submitted now.
3.2.P.2.6	Compatibility studies shall be performed as per the instructions provided in label of the drug product.	Compatibility study report has been submitted.
3.2.P.5.1	• Description test of submitted specifications mention use for WFI as diluent, whereas Lignocaie injection is recommended for the reconstitution of Ceftriaxone IM injection. Justification shall be submitted in this regard. • Submitted drug product specifications does not include tests of water determination, constituted solution.	• Test of description has been revised for details of diluent. • Test of Loss on drying has been added in the testing method.
3.2.P.5.2	Sample & Standard preparation method described in the Assay test is not as per the USP monograph of "Ceftriaxone for injection".	Testing method has been revised as per USP monograph for the preparation of sample and standard solution (2).
3.2.P.6	COA of primary / secondary reference standard including source and lot number shall be provided.	COA of working standard has been submitted from M/s Neutro pharma.
3.2.P.8	Following shall be submitted: • Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of commercial invoice (Invoice# CEF200220YF) attested by AD I&E DRAP, Lahore dated 28-05-2020 has been submitted for 300 Kg of Ceftriaxone.

	• Record of Digital data logger for temperature & humidity monitoring of stability chamber (real time and accelerated). • 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. • Complete Batch manufacturing records for the stability batches. • Microbiological Reports for sterility testing & Bacterial Endotoxin testing	

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.**

304.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Ltd. Plot No. 29-30, Sector 27, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Ltd. Plot No. 29-30, Sector 27, 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 on 24-01-2019
	Evidence of approval of manufacturing facility	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. 14558 dated 28-05-2021
	Details of fee submitted	Rs.20,000/- dated 29-03-2021 & Rs.10,000/- dated 28-05-2021
	proposed proprietary name / brand name	Ketoride 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	Liquid injectable
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1ml x 5 amber colored ampoules
	Proposed unit price	--
	status in reference regulatory authorities	Approved by US FDA
	For generic drugs (me-too status)	Toradol Injection 30mg/ml of m/s martin Dow ltd., (Reg.#015000)

	Name and address of API manufacturer.	M/s Saurav Chemicals Ltd., Derabassi- Barwala Road, Village Bhagwanpura, tehsil Derabassi, District Sahibzada Ajit Singh Nagar, Punjab, 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	Pharmaceutical Equivalence Studies against the reference product of "Toradol Injection 30mg/ml", 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 Saurav Chemicals Ltd., Derabassi- Barwala Road, Village Bhagwanpura, tehsil Derabassi, District Sahibzada Ajit Singh Nagar, Punjab, India		
API Lot No.	KTM200004		
Description of Pack (Container closure system)	30mg/ml, Clear to slightly pale-yellow color solution, packed in amber glass ampoules, further packed in secondary 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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	542DS01	542DS02	542DS03
Batch Size	4000 Ampoules	4000 Ampoules	4000 Ampoules

Manufacturing Date	03.08.2020	03.08.2020	03.08.2020

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)	Firm has referred to their last inspection report for Estine Tablets 10mg & 20mg conducted on 06-05-2019, approved in 289th 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# Drugs (10) Pb.2019/3217) issued by Food & Drug Administration Punjab valid upto 24-06-2023.
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, 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 pf 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)

Batch No.	Quantity Imported	Date of approval by DRAP
KTM200004	1Kg	17-0-6-2020

Remarks of Evaluator:

Section	Observation	Firm's response
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	Submitted
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
3.2.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 for both compendial as well as non-compendial drug	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

	substance(s) shall be submitted.	have used 100% API without any placebo in Analytical Method Verification Studies of Ketorolac Tromethamine, 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.P.2.2.1	• Justify the quantity of Drug substance declared for each batch, considering the applied label claim of "Ketorolac tromethamine 30mg/ml." • Name of the manufacturer of reference product, used for Pharmaceutical equivalence studies, shall be submitted.	This is to inform you that the theoretical fill volume per ampoule is 1.10ml as mentioned in executed Batch Manufacturing Record. Therefore, for filling of 1.0ml in 4000 ampoules 120gm of API is required while for 1.10ml 132gm of API will be required.
• Submitted BMR recommends speed of stirrer as 250 - 300 rpm, whereas actual speed of stirrer has been recorded as 400rpm. Justification shall be submitted for this variation.		This is to inform you that for manufacturing of trial batch RPM was set as 250-300 RPM, Since Ethanol is used in formulation, therefore, in order to achieve desired uniformity and homogenization RPM was changed during manufacturing to 400RPM. Speed of stirrer will be monitored during process validation on 03 batches and as per observations speed of stirrer will be optimized if required.
• Details of the minimum handling capacity of the compounding Jug/Jar, holding tank, applied for manufacturing of trial batches shall be submitted shall be submitted.		This is to inform you that 2.0 Liters is the minimum capacity of vessel, used for manufacturing of trial batches.
• Submitted batch record reflect that terminal sterilization has not been performed. justification for the selection of aseptic processing over terminal sterilization shall be provided		This is to inform you that we have used Ethanol absolute in formulation of Ketorid (Ketorolac Tromethamine) 30mg/ml Injection. Terminal sterilization can affect Ethanol absolute content in formulation therefore, we have used Aseptic manufacturing process to maintain integrity of Ethanol during manufacturing process.

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.**

305.	Name, address of Applicant / Marketing Authorization Holder	M/s Surge Laboratories (Pvt) Ltd., 10th Km, Faisalabad Road Bikhi, District Sheikhupura
	Name, address of Manufacturing site.	M/s Surge Laboratories (Pvt) Ltd., 10th Km, Faisalabad Road Bikhi, District 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. 2829: 25-01-2021
	Details of fee submitted	PKR 20,000/-: 08-04-2020
	proposed proprietary name / brand name	Nervlok-Heavy Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Bupivacaine Hydrochloride ……. 5mg Dextrose Anhydrous ……. 80mg
	Pharmaceutical form of applied drug	Liquid Injection
	Pharmacotherapeutic Group of (API)	Anesthetic
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	4ml x 5's
	Proposed unit price	MRP as per PRC
	The status in reference regulatory authorities	Marcain Heavy, 0.5% solution for injection. 0.5% w/v Solution for Injection is Aspen Pharma MHRA Approved
	For generic drugs (me-too status)	Sensocaine Spinal 0.5% Injection of M/s Brookes Pharma (Reg. No.: 057745)
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 04-07-2019.
	Name and address of API manufacturer.	M/s Dishman Carbogen Amics Ltd., Survey No. 47 & 48, Paiki Sub Plotno. 1, Village Lodariyal, Taluka, Sanand Dist. Ahmedabad-382 220 , Gujarat 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, 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 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	Pharmaceutical Equivalence study has been submitted against the Marcain spinal injection of M/s Astrazeneca.

	Analytical method validation/verification of product	Firm has submitted analytical method verification data.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions.
	Remarks:	

STABILITY STUDY DATA

Manufacturer of API	M/s Dishman Carbogen Amics Ltd., Survey No. 47 & 48, Paiki Sub Plotno. 1, Village Lodariyal, Taluka, Sanand Dist. Ahmedabad-382 220 , Gujarat estate, India		
API Lot No.	117BAF0005, 119BAF0006		
Description of Pack (Container closure system)	Amber color glass ampoule USP Type-I		
Stability Storage Condition	Real time : 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 60 months Accelerated: 6 months		
Frequency	Accelerated: 0,3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	BPI-DEX-4-001	BPI-DEX-4-002	BPI-DEX-4-003
Batch Size	250 Ampoules	250 Ampoules	250 Ampoules
Manufacturing Date	06-2019	06-2019	06-2019
Date of Initiation	06-2019	06-2019	06-2019
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

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# 21012392) issued by Food & Drug Control Administration Gujarat, has been submitted valid upto 07-01-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice attested by AD DRAP I&E Lahore, dated 08-12-2017 for import of 10Kg of Bupivacaine 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 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	The firm has submitted audit trail reports of products testing.
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:

- In reference glucose monohydrate is mentioned as excipient while frim had initially mentioned it as active. Upon communication of observation the firm has revised the label claim as follows and submitted revised from 5F accordingly:

"Each ml contains:
Bupivacaine Hydrochloride ……. 5mg"

- Moreover, Glucose monohydrate has been added in the list of excipients.

Decision: Approved with Innovator's specifications with following label claim:

"Each ml contains:
Bupivacaine hydrochloride 5mg in Dextrose Injection"

- **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.**
- **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.**

306.	Name, address of Applicant / Marketing Authorization Holder	M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road Lahore
	Name, address of Manufacturing site.	M/s Dyson Research Laboratories 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 27389 dated 17-12-2019
	Details of fee submitted	Rs.20,000/- dated 16-12-2019
	proposed proprietary name / brand name	Oriptin 12.5mg Tablet
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Omarigliptin…….12.5mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Long-acting oral antidiabetic drug of the DPP-4 inhibitor
	Reference to Finished product specifications	As per Innovator's product
	Proposed Pack size	4's 10's and 20's
	Proposed unit price	As per S.R.O
	status in reference regulatory authorities	Approved by PMDA of Japan
	For generic drugs (me-too status)	Omaril Tablets 12.5 mg of M/s Genix Pharma Pvt. Ltd.
	GMP status of the manufacturer	GMP inspection dated 11-01-2019, concluded satisfactory level of GMP compliance.
	Name and address of API manufacturer.	Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd., Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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:	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 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 (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	-----
	Analytical method validation/verification of product	Firm has submitted analytical method verification data.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions.

STABILITY STUDY DATA

Manufacturer of API	M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd., Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, China		
API Lot No.	OMG20190101S		
Description of Pack (Container closure system)	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: 0,1,2,3,4 & 6 (Months) Real Time: 0,1,2,3,4 & 6 (Months)		
Batch No	T-01	T-02	T-03
Batch Size	1000 tablets	1000 tablets	1000 tablets
Manufacturing Date	03-2019	03-2019	03-2019

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)	Firm has referred to onsite inspection report of their product "Sovir 400mg tablets", which was conducted on 06th February, 2018 and was presented in 279th meeting of Registration Board. Registration Board decided to approve registration of "Sovir tablet**"** by M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road 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. Firm has demonstrated audit trail reports (assay analysis on HPLC) for the submitted stability batches.
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. JS20170734) issued by CFDA China. The certificate is valid till 25-12-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Commercial invoice (Invoice#PSPW-190121-1) attested by AD DRAP i&E Lahore dated 06-02-2019 for Import of Omarigliptin.
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 hav been submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
307.	Name, address of Applicant / Marketing Authorization Holder	M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road Lahore
	Name, address of Manufacturing site.	M/s Dyson Research Laboratories 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 27390 dated 17-12-2019
	Details of fee submitted	Rs.20,000/- dated 16-12-2019
	proposed proprietary name / brand name	Oriptin 25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Omarigliptin…….25mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Long-acting oral antidiabetic drug of the DPP-4 inhibitor
	Reference to Finished product specification	As per Innovator's product
	Proposed Pack size	4's 10's and 20's
	Proposed unit price	As per S.R.O
	status in reference regulatory authorities	Approved by PMDA of Japan
	For generic drugs (me-too status)	Omaril Tablets 25 mg of M/s Genix Pharma Pvt. Ltd.

	GMP status of the manufacturer	GMP inspection dated 11-01-2019, concluded satisfactory level of GMP compliance.
	Name and address of API manufacturer.	Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd., Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, 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:	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 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	-------
	Analytical method validation/verification of product	Firm has submitted analytical method verification data.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions.

STABILITY STUDY DATA

Manufacturer of API	M/s Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd., Daixi Street, Luoyang Town, Wujin District, Changzhou, Jiangsu, 213105, China		
API Lot No.	OMG20190101S		
Description of Pack (Container closure system)	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: 0,1,2,3,4 & 6 (Months) Real Time: 0,1,2,3,4 & 6 (Months)		
Batch No	T-01	T-02	T-03
Batch Size	1000 tablets	1000 tablets	1000 tablets
Manufacturing Date	03-2019	03-2019	03-2019

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)	Firm has referred to onsite inspection report of their product "Sovir 400mg tablets", which was conducted on 06th February, 2018 and was presented in 279th meeting of Registration Board. Registration Board decided to approve registration of "Sovir tablet**"** by M/s Dyson Research Laboratories Pvt Ltd. 28 km Ferozepur Road 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. Firm has demonstrated audit trail reports (assay analysis on HPLC) for the submitted stability batches.
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. JS20170734) issued by CFDA China. The certificate is valid till 25-12-2022.
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	Audit trail reports hav been submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

REMARKS OF EVALUATOR

Section #.	Deficiencies	Firm's response
2.3	• Quality Overall Summary (QOS) shall be provided in WHO QOS-PD Template or template approved by Registration Board in its 296th meeting.	• Submitted
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 shall be submitted. • 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 manufacturer.	• Submitted
3.2. S.5	• COA of primary / secondary reference standard including source and lot number shall be provided.	• COA of working standard submitted from drug substance

		manufacturer
3.2. P.2	• Results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 shall be submitted and discussed.	• CDP studies have been submitted against the innovator product of Marizev tablet (12.5mg and 25mg) of Merck with acceptable values of f2 factor.
3.2. P.4.5	• A certificate shall be provided, confirming that the excipient(s) are free from BSE and TSE FOR "Magnesium stearate" used in the formulation.	• TSE/BSE certofocate submitted from the supplier.
3.2. P.5.1	• A copy of the drug product specification(s) including tests, acceptance criteria and reference to analytical procedure shall be provided. • Test for "content uniformity" has not been included in the drug product specifications.	• Test of content uniformity ha sbeen added in the revised testing method.
3.2. P.5.3	• Specificity parameter has been performed by injecting the, placebo+sample, placebo, blank & 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., light, humidity, acid or base hydrolysis, oxidation). Justification shall be submitted for this variation in method. Clarification shall be submitted for this variation.	• Firm has submitted data for forced degradation studies for the parameter of specificity.
3.2. P.5.4	• The copies of complete analysis of at least two batches finished drug product shall be provided.	• Submitted
3.2. P.5.6	• Justify the selection of dissolution parameters i.e., apparatus, dissolution medium, time, speed of apparatus & acceptance criteria.	• Firm has referred to the US FDA guidelines & resulst of Comaprative dissolution profile for selection of acceptance criteria for dissolution.
3.2.P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	• COA of working standard submitted from drug substance manufacturer
3.2.P.8	• Following shall be submitted: i. Documents for the procurement of API with approval from DRAP (in case of import).	•

Decision: Registration Board approved Oriptin 12.5mg Tablet & Oriptin 25mg 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.**

308.	Name and address of manufacturer / Applicant	M/s Pharmasol (Pvt) Ltd. Plot No. 549, Sundar Industrial Estate, Raiwind Road, Lahore.
	Brand Name +Dosage Form + Strength	BENZORIM-A Gel 0.1% / 2.5%
	Diary No. Date of R& I & fee	Dy. No 23982 dated 11-07-2018
	Composition	Each gram contains: Adapalene ……0.1 % w/w (1mg) Benzoyl Peroxide … 2.5 % w/w (25mg)
	Pharmacological Group	Anti- acne preparation
	Type of Form	Form-5
	Finished Product Specification	Manufacturer's Specifications
	Pack size & Demanded Price	15gm, 30 gm, 45gm, 60gm, 90gm / As per SRO

	Approval status of product in Reference Regulatory Authorities.	(USFDA approved), ANSM; France Approved Epiduo Gel by Galderma Australia Pty Ltd , TGA
	Me-too status	Adalene-B Gel by Pharmatec (Reg. No. 076683)
	GMP status	Last inspection dated 08-07-2019 & 25-07-2019 concluded that M/s Pharmasol, Lahore was operating at satisfactory level of GMP compliance.
	Remarks of the Evaluator.	
	Decision: The Board deferred the case for consideration with the other cases submitted on Form 5 for human drug products.	

a. Deferred cases

309.	Name, address of Applicant / Marketing Authorization Holder	"M/s Kaizen Pharmaceuticals Pvt Ltd. E-127-129, North Western Industrial Zone, Bin Qasim, Karachi"
	Name, address of Manufacturing site.	"M/s Kaizen Pharmaceuticals Pvt Ltd. E-127-129, North Western Industrial Zone, Bin 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 21539 dated 22-10-2019
	Details of fee submitted	Rs.50,000 dated 21-10-2019
	The proposed proprietary name / brand name	Azilsart 40mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Tablet Contains: Azilsartan …….. 40mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor blocker.
	Reference to Finished product specifications	Manufacturer specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Azilva Tablet approved by PMDA of Japan.
	For generic drugs (me-too status)	N/A
	GMP status	GMP certificate issued on basis of inspection conducted on 28-08-2019.
	Name and address of API manufacturer.	M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., Chem & API's Industrial Zone, Linhai, Zheijiang , China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS –PD template
	Module-III Drug Substance:	Relevant information has been submitted including Analytical method verification studies & batch analysis.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability studies data has been submitted as per Zone IV a condition.
	Module-III Drug Product:	

	Pharmaceutical Equivalence and Comparative Dissolution Profile	CDP studies against the reference product of "Azilva Tablets" in three dissolution mediums has been submitted with acceptable level of f2 results
	Analytical method validation/verification of product	Firm has submitted analytical method validation data.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions

STABILITY STUDY DATA

Manufacturer of API	M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., Chem & API's Industrial Zone, Linhai, Zheijiang , China.		
API Lot No.	C1011-0148104		
Description of Pack (Container closure system)	Alu-PVC blister 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: 0,1,2,3,4,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No	TF-01	TF-02	TF-03
Batch Size	1200 tablets	1200 tablets	1200 tablets
Manufacturing Date	09-2018	09-2018	09-2018

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).	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 by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	Copy of GMP certificate (ZJ20180032) issued by China Food & Drug Administration, valid upto 14-03-2023 for M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., China
3.	Documents confirming import of API etc.	Not submitted. Firm has submitted copy of Fed Ex courier slip, from which details of shipment could not be verified.
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Yes

	Raw data sheets, COA, summary data sheets etc.	
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

310.	Name, address of Applicant / Marketing Authorization Holder	"M/s Kaizen Pharmaceuticals Pvt Ltd. E-127-129, North Western Industrial Zone, Bin Qasim, Karachi"
	Name, address of Manufacturing site.	"M/s Kaizen Pharmaceuticals Pvt Ltd. E-127-129, North Western Industrial Zone, Bin 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 21538 dated 22-10-2019
	Details of fee submitted	Rs.50,000 dated 21-10-2019
	The proposed proprietary name / brand name	Azilsart 20mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Tablet Contains: Azilsartan …….. 20mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor blocker.
	Reference to Finished product specifications	Manufacturer specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Azilva Tablet approved by PMDA of Japan.
	For generic drugs (me-too status)	N/A
	GMP status	GMP certificate issued on basis of inspection conducted on 28-08-2019.
	Name and address of API manufacturer.	M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., Chem & API's Industrial Zone, Linhai, Zheijiang , China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS –PD template
	Module-III Drug Substance:	Relevant information has been submitted including Analytical method verification studies & batch analysis.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability studies data has been submitted as per Zone IV a condition.
	Module-III Drug Product:	
	Pharmaceutical Equivalence and Comparative Dissolution Profile	CDP studies against the reference product of "Azilva Tablets" in three dissolution mediums has been submitted with acceptable level of f2 results

	Analytical method validation/verification of product	Firm has submitted analytical method validation data.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions

STABILITY STUDY DATA

Manufacturer of API	M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., Chem & API's Industrial Zone, Linhai, Zheijiang , China.		
API Lot No.	C1011-0148104		
Description of Pack (Container closure system)	Alu-PVC blister 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: 0,1,2,3,4,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No	TF-01	TF-02	TF-03
Batch Size	1200 tablets	1200 tablets	1200 tablets
Manufacturing Date	07-2018	07-2018	07-2018

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).	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 by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	Copy of GMP certificate (ZJ20180032) issued by China Food & Drug Administration, valid upto 14-03-2023 for M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., China
3.	Documents confirming import of API etc.	Not submitted. Firm has submitted copy of Fed Ex courier slip, from which details of shipment could not be verified.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
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
311.	Name, address of Applicant / Marketing Authorization Holder	"M/s Kaizen Pharmaceuticals Pvt Ltd. E-127-129, North Western Industrial Zone, Bin Qasim, Karachi"
	Name, address of Manufacturing site.	"M/s Kaizen Pharmaceuticals Pvt Ltd. E-127-129, North Western Industrial Zone, Bin 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 21537 dated 22-10-2019
	Details of fee submitted	Rs.50,000 dated 21-10-2019
	The proposed proprietary name / brand name	Azilsart 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Tablet Contains: Azilsartan …….. 10mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Angiotensin II receptor blocker.
	Reference to Finished product specifications	Manufacturer specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Azilva Tablet approved by PMDA of Japan.
	For generic drugs (me-too status)	N/A
	GMP status	GMP certificate issued on basis of inspection conducted on 28-08-2019.
	Name and address of API manufacturer.	M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., Chem & API's Industrial Zone, Linhai, Zheijiang , China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS –PD template
	Module-III Drug Substance:	Relevant information has been submitted including Analytical method verification studies & batch analysis.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability studies data has been submitted as per Zone IV a conditions.
	Module-III Drug Product:	
	Pharmaceutical Equivalence and Comparative Dissolution Profile	CDP studies against the reference product of "Azilva Tablets" in three dissolution mediums has been submitted with acceptable level of f2 results
	Analytical method validation/verification of product	Firm has submitted analytical method validation data.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long-term conditions
STABILITY STUDY DATA		

Manufacturer of API	M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., Chem & API's Industrial Zone, Linhai, Zheijiang , China.		
API Lot No.	C1011-0148104		
Description of Pack (Container closure system)	Alu-PVC blister 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: 0,1,2,3,4,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No	TF-01	TF-02	TF-03
Batch Size	1200 tablets	1200 tablets	1200 tablets
Manufacturing Date	07-2018	07-2018	07-2018

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).	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 by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	Copy of GMP certificate (ZJ20180032) issued by China Food & Drug Administration, valid upto 14-03-2023 for M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., China
3.	Documents confirming import of API etc.	Not submitted. Firm has submitted copy of Fed Ex courier slip, from which details of shipment could not be verified.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
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

Sr. No.	Section #.	Deficiencies	Response
Module II			
1.	**2.3. S.7**	Long term stability studies shall be submitted as per Zone IVa conditions.	• Submitted
2.	**2.3.P.3.2**	Relevant information shall be submitted as per template of QOS.	• Submitted
3.	**2.3.P.3.3**	A flow diagram shall be presented giving the steps of the process and showing where materials enter the process. The critical steps and points at which process controls, intermediate tests or final product controls are conducted shall be identified.	• Submitted
Module III			
4.	**3.2.S.4**	Analytical record for the analysis of drug substance performed by the drug product manufacturer shall be submitted.	• Analytical record including HPLC chromatograms & raw data sheets have been submitted.
5.	**3.2.S.5**	COA of primary / secondary reference standard including source and lot number shall be provided.	• COA of working standard from M/s Zheijiang Hongyuan Pharmaceutical Co., Ltd., China has been submitted.
6.	**3.2.S.7**	Long term stability studies shall be submitted as per Zone IVa conditions.	• Long term stability studies have been submitted as per Zone IVa conditions.
7.	**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. • Submitted finished product analytical method describes HPLC method for the dissolution analysis, whereas CDP study has been performed by applying UV spectrophotometric method.	• Pharmaceutical equivalence studies have been submitted against the innovator product of "Azilva" tablets. • HPLC record for the performance of CDP studies has been submitted.
8.	**3.2. P.3.5**	A brief description of process validation including the proposed protocol shall be described	Process validation protocol has been submitted.
9.	**3.2. P.5**	Submitted finished product specifications does not include test of content uniformity for Azilsartan.	Firm has submitted analytical record for the performance of Content Uniformity test.
10.	**3.2. P.8**	Documents confirming import of API, approved by DRAP I&E office shall be submitted. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	• Firm has submitted that they have procured the sample of API through courier. Firm has submitted FedEx courier slip in this regard. Copy of commercial invoice no. HY181115-1 (not attested by DRAP), has been submitted for 0.5 Kg of Azilsart. • Submitted.

Decision of 307th meeting: Registration Board deferred all three applied strengths of Azilsart 40mg tablet

(Azilsartan), Azilsart 20mg tablet (Azilsartan) & Azilsart 10mg tablet (Azilsartan) for following reasons:

- Status of the applied formulation in reference regulatory authorities other than PMDA of Japan.
- Comparative evaluation of the indications, dosage other clinical particulars between "Azilsartan Kamedoxomil tablet" & "Azilsartan tablet".

Firm's response:

- The applied molecule is available only in PMDA of Japan as azilva tablet.
- Moreover, firm has submitted following comparison:

S. No.	COMPARATIVE EVALUATION OF STUDY OF CLINICAL DATA		
	Clinical DATA	**Azilsartan**	**Azilsartan Medoxomil**
1	**Metabolism**	Directly enter as an active. No need of conversion from inactive to active form. Does not require hepatic metabolism by CYP2C9. Thus more effective in patients with hepatic compromise.	Azilsartan medoxomil is a pro-drug. It absorbs in gut and biotransforms in liver converting it into its active metabolite azilsartan by enzyme CYP2C9.
2	**Indication**	For the treatment of hypertension	For thr treatment of Hypertension
3	**Dosage**	20 mg - 80 mg	40 mg - 80 mg
4	**Pharmacokinetics:**		
	Bioavailability	60% approximately	60%
	Elimination half-life	11 hours	11 hours
	Peak plasma concentration	1.5 to 3 hours	2 to 3 hours
5	**Adverse effects**	orthostatic hypotension, nausea, muscle spasm, dizziness, asthenis, fatigue, cough, diarrhea	ypotension/orthostatic hypotension, ausea, diarrhea, fatigue, muscle pasm, postural dizziness,

Decision of 312th meeting: Registration Board deferred for further deliberations upon strength of applied formulations wrt USFDA approved formulation.

Firm's response:

- In Pakistan 40 and 80 mg is registered as AzilsartanMedoxomil while USFDA also launched 20 mg strength as Edarbi.
- 10 mg Azilsartan tablet is for children while 20mg is starting dose for Adults.
- AzilvaTablet is available in 3 strength 10, 20 and 40 as Azilsartan.

Sr.#	PARAMETERS	AZILSARTAN	AZILSARTAN MEDOXOMIL
1	**Metabolism**	Directly enter as an active. No need of conversion from inactive to active form. Does not require hepatic metabolism by CYP2C9. Thus, more effective in patients with hepatic compromise.	Azilsartanmedoxomil is a pro-drug. It absorbs in gut and bio transforms in liver converting it into its active metabolite azilsartan by enzyme CYP2C9.
2	**Indication**	For the treatment of hypertension	For the treatment of Hypertension
3	**Tablet Strength**	10,20 and 40 (Azilva Japan) Applied strength (10.20 and 40)	20,40 and 80 (Edarbi USA) Registered strength (40 and 80)
4	**Dosage**	20 mg - 80 mg (Adult) 10mg(children)	40 mg - 80 mg
5	**Drug Interaction**	Azilsartan base has no such type of Hyperkalemia No dosage adjustments required in hepatic and renal compromised patients	1. Since the use of potassium supplements and potassium-containing salt substitutes with an angiotensin II receptor antagonist (e.g., azilsartanmedoxomil) can increase the potential for hyperkalemia, some clinicians have suggested that

			concomitant administration of these agents with azilsartan medoxomil should be avoided. 2.AzilsartanKmedoxomil is converted into active Azilsartan by Liver Enzyme (Cytochrome P450 (CYP) 2C9 3. Should be used with caution with NSAID and other Potassium Drugs
6	**Residual Solvents in Raw Material**	Class 1 Solvents: Dichloromethane Class 3: Ethanol, Isopropanol	Class 1 solvents: Dichloromethane Class 2 Tetrahydrofuran Class 3 Solvents: Methanol, Acetone, Ethyl Acetate

- Azilsartan innovator is AZILVA available in 10mg, 20mg and 40mg.
- Azilsartan medoxomil innovator is available as EDARBI 20mg, 40mg and 80mg.

Decision: Registration Board approved Azilsart 40mg Tablet & Azilsart 20mg Tablet as per 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.**

Moreover, Registration Board deferred the application of Azilsart 10 mg tablets for further deliberation upon the indication & dosage of 10mg strength in paediatric population.

312.	Name, address of Applicant / Marketing Authorization Holder	M/s JASM PHARMACEUTICALS (PVT) LTD
	Name, address of Manufacturing site.	M/s JASM Pharmaceuticals (Pvt) Ltd. Address: Plot # 4A, Export Processing street, Risalpur Industrial Estate, Nowshera. Khyber Pukhtunkhwa.
	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
	Details of fee submitted	PKR 30,000/-: dated
	The proposed proprietary name/brand name	Pylenol Suspension 120 mg/5ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml Contains: Paracetamol ……. 120 mg
	Pharmaceutical form of applied drug	Oral Suspension
	Pharmacotherapeutic Group of (API)	Analgesic and Antipyretic
	Reference to Finished product specifications	USP
	Proposed Pack size	90 ml / bottle or as per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Calpol 120mg/5mL Suspension by M/s SmithKline Beecham USFDA Approved.
	For generic drugs (me-too status)	

	GMP status of the Finished product manufacturer	New license granted on 29/09/2020 Tablet, Capsule , Dry Powder, Liquid Syrup , Cream Ointment (General Sections) Approved
	Name and address of API manufacturer.	M/s Zenith Chemical Industries (Pvt) Limited. Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind 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 Acetaminophen 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 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: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (P01 , P13 , P26)
	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 Calpol Suspension 120 mg/5mL by GSK Pharmaceutical by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP NA
	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 Zenith Chemical Industries (Pvt) Limited. Moza Dhonday, Jia Baga Raiwind Kahna Road Raiwind Pakistan.
API Lot No.	ZPAR20-001
Description of Pack (Container closure system)	90 ml / bottle packed 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.	P01	P13	P26
Batch Size	500 Bottles	500 Bottles	500 Bottles
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	15-10-2020	19-10-2020	23-10-2020
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 Ref No. 141/2019-Drap(AD-813875--228) issued by DRAP
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	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Manual record submitted

Remarks of Evaluator:

Section#	Observation	Firm's response
3.2. S.4.3	Analytical method verification studies for Assay method by HPLC shall be submitted, performed by M/s JASM Pharmaceuticals.	Submitted
3.2.P.2.1.1	Submit compatibility studies of the Drug Substance(s) with excipients or provided evidence that the qualitative composition of the formulation is similar to innovator / reference product.	Composition of the formulation is similar to that of the reference product.
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 monographs of the preservative excipients from the "Hand book of Pharmaceutical excipients".
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. • You are advised to submit scientific rationale for claiming USP specifications for finished drug product while the Drug substance used is of BP specifications.	We have submitted a dossier of Pylenol suspension 120mg/5ml along with stability study. All results are coming within the range and going forward in the reliable way. The real time stability will be completed after 2 year from manufacturing date. However, JASM Pharmaceutical is a new License holder we couldn't perform microbiological study but now we have fully functional microbiological lab and will start respective testing within the stability. After completion of the real time stability study we will submit all stability data along with the

		test of anti-microbial preservative and efficacy of preservative as recommended by ICH Q1 (R2) guideline and USP chapter <51> will be included in finish product specification.
3.2. P.8	• Significant change has been reported in the Assay result during accelerated stability studies of Batch# P01 & P13. • 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.	It was a clerical mistake, actual results were 99.40%v instead of 94.4.0%.

Decision of 312th meeting: Deferred for submission of results of content of antimicrobial preservative & efficacy o preservative at the next time point of real time stability studies.

Remarks of Evaluator: Firm has submitted preservative effectiveness study at 9th moth time point of long-ter stability studies.

Decision of 313rd meeting: Approved.

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

313.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. **Contract manufacturing by** M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Keuz injection 20mg
	Composition	Each vial contains: Esomeprazole as sodium (lyophilized powder).....20mg
	Diary No. Date of R& I & fee	Dy. No.7062; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Proton pump inhibitor
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	1's vial; As per PRC's price
	Approval status of product in Reference Regulatory Authorities.	Nexium IV(USFDA approved)
	Me-too status	Contour 20mg Injection of M/s S.J.&G. Fazul Ellahie
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.
	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.

	Evaluation by PEC:	• Firm has submitted that bulk lyophilization will be done in our lyophilization facility and our product filling will be done at sterile powder filling injectable area. • Moreover firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision of 295th meeting: Deferred for following clarifications: a. Confirmation for permission to M/s SJG&Fazul Ellahi for bulk lyophilization of Esomeprazole from Licensing Division. b. Whether M/s SJG&Fazul Ellahi has manufacturing facility for dry powder injection. **c.** Confirmation whether Contour 40mg injection (Esomeprazole) is by powder filling or lyophilization.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Approved with Innovator's specifications. Registration letter will be issued after submission of applicable fee for revision of manufacturing outline as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
314.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. Contract manufacturing by M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Keuz injection 40mg
	Composition	Each vial contains: Esomeprazole as sodium (lyophilized powder) ….....40mg
	Diary No. Date of R& I & fee	Dy. No.7065; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Proton pump inhibitor
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	1's vial; As per PRC's price
	Approval status of product in Reference Regulatory Authorities.	Nexium IV(USFDA approved)
	Me-too status	Nexum 40mg Injection of M/s Getz
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.

	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.
	Evaluation by PEC:	• Firm has submitted that bulk lyophilization will be done in our lyophilization facility and our product filling will be done at sterile powder filling injectable area. • Moreover firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision: Deferred for following clarifications: a. Confirmation for permission to M/s SJG&Fazul Ellahi for bulk lyophilization of Esomeprazole from Licensing Division. b. Whether M/s SJG&Fazul Ellahi has manufacturing facility for dry powder injection. **c.** Confirmation whether Contour 40mg injection (Esomeprazole) is by powder filling or lyophilization.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Approved with Innovator's specifications. Registration letter will be issued after submission of applicable fee for revision of manufacturing outline as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
315.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. Contract manufacturing by M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Tikonin injection 200mg
	Composition	Each vial contains: Tiecoplanin (lyophilized powder)…….....200mg
	Diary No. Date of R& I & fee	Dy. No.7055; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	1's vial; As per PRC price
	Approval status of product in Reference Regulatory Authorities.	Targocid 200mg powder for solution for injection/infusion (MHRA approved)
	Me-too status	Targocid injection 200mg of M/s Hoechst Pakistan Ltd
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration

		section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.
	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.
	Evaluation by PEC:	• Firm has submitted that ready to fill powder will be procured and powder filling will be done at sterile powder injectable area. • Moreover, firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/ product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision of 295th meeting: Deferred for clarification from Licensing Division whether firm either has lyophilization or dry powder injection or both facilities.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Deferred for clarification whether innovator/reference product is manufactured by way of lyophilization or otherwise.	
316.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. Contract manufacturing by M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Tikonin injection 400mg
	Composition	Each vial contains: Tiecoplanin (lyophilized powder)…….....400mg
	Diary No. Date of R& I & fee	Dy. No.7054; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	1's vial; As per PRC price
	Approval status of product in Reference Regulatory Authorities.	Targocid 400mg powder for solution for injection/infusion (MHRA approved)
	Me-too status	Targocid injection 400mg of M/s Hoechst Pakistan Ltd
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.

	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.
	Evaluation by PEC:	• Firm has submitted that ready to fill powder will be procured and powder filling will be done at sterile powder injectable area. • Moreover firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision of 295th meeting: Deferred for clarification from Licensing Division whether firm either has lyophilization or dry powder injection or both facilities.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Deferred for clarification whether innovator/reference product is manufactured by way of lyophilization or otherwise.	
317.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. Contract manufacturing by M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Venko injection 500mg
	Composition	Each vial contains: Vancomycin as hydrochloride…….500mg
	Diary No. Date of R& I & fee	Dy. No.7059; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	1's vial; As per PRC's price
	Approval status of product in Reference Regulatory Authorities.	(USFDA approved**)**
	Me-too status	Maparix 500mg Injection of M/s S.J.&G. Fazul Ellahie
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.
	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.

	Evaluation by PEC:	• Firm has submitted that ready to fill powder will be procured and powder filling will be done at sterile powder injectable area. • Moreover firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/ product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision of 295th meeting: Deferred for clarification from Licensing Division whether firm either has lyophilization or dry powder injection or both facilities.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Deferred for clarification whether innovator/reference product is manufactured by way of lyophilization or otherwise.	
318.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. Contract manufacturing by M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Venko injection 1Gm
	Composition	Each vial contains: Vancomycin as hydrochloride…….1gm
	Diary No. Date of R& I & fee	Dy. No.7064; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	1's vial; As per PRC's price
	Approval status of product in Reference Regulatory Authorities.	(USFDA approved**)**
	Me-too status	Maparix 1gm Injection of M/s S.J.&G. Fazul Ellahie
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.
	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.
	Evaluation by PEC:	• Firm has submitted that ready to fill powder will be procured and powder filling will be done at sterile powder injectable area.

		• Moreover firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision of 295th meeting: Deferred for clarification from Licensing Division whether firm either has lyophilization or dry powder injection or both facilities.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Deferred for clarification whether innovator/reference product is manufactured by way of lyophilization or otherwise.	
319.	Name and address of manufacturer / Applicant	M/s Zephyr Pharmatec Pvt. Ltd., A-39, S.I.T.E. II, Super Highway, Karachi. Contract manufacturing by M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi.
	Brand Name +Dosage Form + Strength	Ozop injection 40mg
	Composition	Each vial contains: Omeprazole as sodium (lyophilized powder)…….40mg
	Diary No. Date of R& I & fee	Dy. No.7057; 22-06-2017; Rs.50,000/- (22-06-2017)
	Pharmacological Group	Proton pump inhibitor
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications
	Pack size & Demanded Price	1's vial; As per PRC's price
	Approval status of product in Reference Regulatory Authorities.	Omeprazole 40mg powder for solution for infusion (UK-MHRA approved**)**
	Me-too status	Fymezole dry powder injection IV 40mg of M/s Fynk Pharmaceuticals
	GMP status	Last inspection report of M/s Zephyr Pharmatech conducted on 30-01-2018 concluding good level of GMP compliance. Last GMP Inspection of M/s S.J. & G. Fazul Ellahie conducted on 02-05-2018 with conclusive remarks as under: "The firm has complied/improved according to the directions of the FID. Panel was satisfied for the improvements under taken by the firm to comply with the observations dated 12th July 2017. Further the panel advised the firm to continue the improvements process"
	Remarks of the Evaluator.	M/s Zephyr Pharmatec has 9 approved sections, and the firm has no product already registered under the contract manufacturing as confirmed by relevant registration section. M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. has approved Lyophilization (sterile area) powder injection general section.
	Previous Decision:	Registration Board in its 283rd meeting deferred for deferred for clarification of applied dosage form whether lyophilized powder or lyophilized cake.
	Evaluation by PEC:	• Firm has submitted that bulk lyophilization will be done in our lyophilization facility and our product filling will be done at sterile powder filling injectable area. • Moreover firm has submitted GMP inspection report dated 29-08-2019, wherein following observation has been

		recorded under the section title of "Lyophilization (sterile area) powder injectable (general)": "Well equipped separate proper lyophilized powder/product filling. Packing activity is also carried out under the supervision of qualified person. Contour 40mg injection (Esomeprazole) was under production process with requisite documentation system in place."
	Decision of 295th meeting: Deferred for following clarifications: a. Confirmation for permission to M/s SJG&Fazul Ellahi for bulk lyophilization of Esomeprazole from Licensing Division. b. Whether M/s SJG&Fazul Ellahi has manufacturing facility for dry powder injection. **c.** Confirmation whether Contour 40mg injection (Esomeprazole) is by powder filling or lyophilization.	
	Evaluation by PEC: In response to the Incharge PEC letter (No. F.13-11/2017-PEC) dated 08-10-2020, Assitant Director (Lic) has replied vide their letter No.F.2-44/84-Lic(Vol-IV) dated 10-11-2021 has replied as under: "As per record pf Licensing Dicvision, DRAP, Islamabad M/s M/s S.J.&G. Fazul Ellahie (Pvt.) Ltd. E/46, S.I.T.E. Karachi under DML No. 000083 (Formulation) possess both licensed sections with the title of 'Dry Powder injection (General) Lyophilized & Dry Powder Injection (General)"	
	Decision: Approved with Innovator's specifications. Registration letter will be issued after submission of applicable fee for revision of manufacturing outline as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

Case no. 03 Registration applications of import cases

a. New Cases (Human)

320.	Name, address of Applicant / Importer	M/s Biocare Pharmaceutica. 807 Shadman-1, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0063-032069D Address: 807 Shadman-1, District Lahore. Address of Godown: First floor B-C, Street No. 3, Near LGS School, Shah Jamal District Lahore. Validity: 17-04-2022. Status: License to sell drugs as distributor Renewal: N/A. Valid Drug sales License is attached with CTD dossier Module 1.
	Name and address of marketing authorization holder (abroad)	License Holder/Supplier: World Medicine İlaç San. Ve Tic. A.S. Address:- Temmuz Mahallesi, Camiyolu Cad. No:50 Güneşli / İstanbul, Turkey Tel:- +90 212 474 70 50
	Name, address of manufacturer(s)	Manufactured By:- Mefar İlaç Sanayii A.Ş. (World Medicine Contract manufacturer) Address Manufacturing site: Ramazanoglu Mah. Ensar Cad. No : 20 Kurtkoy / Pendik, TR 34906 Istanbul, Turkey, Post Code: 34906 TEL: (+90) 216 378 44 00
	Name of exporting country	Turkey

	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted legalized CoPP certificate (No.2020/2332) dated 12-08-2020 issued by Republic of Turkey Ministry of health Turkish Medicines and Medical Device Agency. 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 12-8-2022. **GMP Certificate:** Legalized copy of GMP certificate# (TR/GMP/2018/333) issued by Turkish Medicines & Medical Devices Agency valid upto 01-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of legalized distribution agreement signed by both parties Biocare Pharmaceutica & World Medicine İlaç San. Ve Tic. A.S. Agreement cleanly mention manufacturer World Medicine İlaç San. Ve Tic. A.S appoints M/s Biocare Pharmaceutica to register/market/sell/Distribute their product Fluzamed (Fluconazole) 200 mg/100 ml in Pakistan. Agreement validity is 5 years with automatically 1 year renewal clause.
	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. 1925417: 30-12-2020
	Details of fee submitted	PKR 50000 /-: 30-12-2020
	proposed proprietary name / brand name	FLUZAMED
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	200 mg/100 ml (2 mg/ml) Fluconazole per vial
	Pharmaceutical form of applied drug	Solution for IV Infusion
	Pharmacotherapeutic Group of (API)	Antimycotics for Systemic Use, Triazole derivatives, Antifungal
	Reference to Finished product specifications	In-House / Innovator Specification
	Proposed Pack size	1's
	Proposed unit price	Rs 1008/- single dose vial
	The status in reference regulatory authorities	Fluconazole 200 mg/100 ml (2mg/ml) Fresenius Kabi USA (USFDA Approved-076145) & Diflucan (Fluconazole) 200 mg/100 ml injection vial by Pfizer Australia Pty Ltd (TGA Approved). It is also approved by EMA (European Medicine Agency), UK MHRA & PMDA (Japan).

	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	M/s Synergene Active Ingredients Pvt. Ltd. Address: Flat No.402, Bhanu Enclave, Sunder Nagar, Erragadda, Hyderabad-500038, Telangana, 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 accelerated study is complete for 3 batches at 40±2 °C/75±5%RH. The real time Zone IVA stability data is conducted at 30±2°C/65±5%RH. The stability study data is till 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 has been established by conducting all the quality tests against the Pfizer reference product Triflucan (Fluconazole) Solution for IV Infusion 200 mg- 100 ml (2 mg/ml).
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	100 ml marked type I transparent glass vial closed with grey bromo-butyl rubber stopper and transparent Aluminum/plastic flip off cap.
	Stability study data of drug product, shelf life and storage conditions	• 24 months real time stability data at 30°C ± 2°C / 65% ± 5%RH of 03 batches (Zone IVA) • 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches

Evaluation by PEC:

Section#	Observations	Firm's response
1.5.6	Pharmacopoeial reference of the finished product has been declared as European Pharmacopoeia, whereas no EP monograph is available for the applied product.	Firm has declared it an error and has submitted revised Form 5F, wherein product specifications have been referred as "In-House". Moroever firm has submitted following commitment from the manufacturing authorization holder: "We, World Medicine İlaç San. Ve Tic. A.S. Temmuz Mahallesi, Camiyolu Cad. No:50 Güneşli / İstanbul, Turkey, as marketing authorization holder hereby declare that for Fluzamed (Fluconazole) 200 mg/100 ml Solution for IV Infusion product; BP pharmacopoeia only has monograph for IV Infusion product as same with our product. Our specifications meet requirements for BP. We can revise it to BP specifications after registration. Monograph for USP Fluconazole Injection removed current pharmacopoeia. It is Official 1-May-2018 to 7-Nov-2018. Our specifications were determined according to ICH and international requirements. Therefore, we confirm after registration we will provide our product Fluzamed (Fluconazole) 200 mg/100 ml solution for IV infusion under BP Specification/reference standard and write BP in Pack accordingly."
1.3.5	Original legalized COPP/Free sale certificate, translated in English, shall be submitted.	Submitted
2.3	Table for literature references for the Drug Substance and Drug Product, declare that EP monograph exists for the applied drug product. Evidence of above cited monograph shall be submitted.	Relevant information has been submitted as per the WHO QOS PD template.
2.3.S.3	Relevant information against this section shall be submitted in Module II, instead of referring to other modules.	
2.3.S.4.2	• Analytical method has been submitted for Fluconazole solution for injection instead of drug substance "Fluconazole".	
2.3.S.4.3	• Information has been submitted for Fluconazole solution for injection instead of the drug substance "Fluconazole"	
All the tables in the WHO QOS PD template shall be filled as such instead of replacing them with any other format. Also, the information in the module II shall be submitted under relevant sections, instead of referring it to other modules.		
3.2. P.2.2.1	The US FDA approved label of Fluconazole injection in 0.9% Sodium chloride, recommends pH range of 4.0-8.0, whereas Comparative Results of analysis of Test and Reference Products, specifies the pH range of 3.0 – 7.5. Justification shall be submitted in this regard.	Firm has submitted revised pH limits of 4.0-8.0 as per innovator. The results of pH test in submitted batch analysis, falls in the same range as of innovator.
3.2. P.5.1	• Test for content of sodium, chloride, as recommended by USP monograph for	Considered the purpose of being in the product, it is seen that there is no need for relevant control.

	applied product, has not been included in the specifications.	
3.2. P.5.2	• Submitted procedure for Assay test is not per any of the USP, IP or JP monograph for "Fluconazole Injection." Justification shall be submitted in this regard.	Firm has claimed in-house specifications and has also submitted undertaking as mentioned against section 1.5.6
3.2. P.5.6	The section mentions that "Analytical test methods are validated in-house methods". Justification shall be submitted for applying in-house methods, whereas pharmacopoeial monographs are available for the applied product.	
3.2.P.8	Significant changes have been observed in the accelerated stability studies of following batch: • 1514001	MA holder has submitted that there is no out of limit situation/changes in the accelerated stability data of the 1514001 numbered batch. There was typo/error in previous file, it has been corrected.

Decision: Deferred for following:

- **Justification of applying in-house specifications for the drug product analysis, whereas USP & BP monograph is available for the applied product.**
- **Justification of significant change in the accelerated stability studies data of batch# 1514001.**
- **Registration Board further directed the firm to submit comparison between in-house, USP & BP specifications.**

321.	Name, address of Applicant / Importer	M/s Biocare Pharmaceutica. Address:- 807 Shadman-1, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0063-032069D Address: 807 Shadman-1, District Lahore. Address of Godown: First floor B-C, Street No. 3, Near LGS School, Shah Jamal District Lahore. Validity: 17-04-2022. Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	License Holder/Supplier: World Medicine İlaç San. Ve Tic. A.S. Address:- Temmuz Mahallesi, Camiyolu Cad. No:50 Güneşli / İstanbul, Turkey Tel:- +90 212 474 70 50
	Name, address of manufacturer(s)	Manufactured By:- Mefar İlaç Sanayii A.Ş. Address Manufacturing site : Ramazanoglu Mah. Ensar Cad. No: 20 Kurtkoy / Pendik, TR 34906 Istanbul, Turkey, Post Code: 34906 TEL: (+90) 216 378 44 00
	Name of exporting country	Turkey
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted legalized CoPP certificate (No.2020/2331) dated 12-08-2020 issued by Republic of Turkey Ministry of health Turkish Medicines and Medical Device Agency. 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 12-8-2022.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of legalized distribution agreement signed by both parties Biocare Pharmaceutica & World Medicine İlaç San. Ve Tic. A.S. Agreement cleanly mention manufacturer World Medicine İlaç San. Ve Tic. A.S appoints M/s Biocare Pharmaceutica to

		register/market/sell/Distribute their product Sertofen (Dexketoprofen Trometamol) 50 mg/2ml in Pakistan. Agreement validity is 5 years with automatically 1-year renewal clause.
	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 3325 dated 28-01-2021
	Details of fee submitted	PKR 50000 /-: 30-12-2020
	proposed proprietary name / brand name	SERTOFEN, DEXTANOL, DEXKETO
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2 ml of ampoule contains 73.8 mg Dexketoprofen Trometamol equivalent to 50 mg Dexketoprofen.
	Pharmaceutical form of applied drug	Solution for Intramuscular (IM) or Intravenous (IV) Injection.
	Pharmacotherapeutic Group of (API)	Propionic acid derivatives. Analgesics, antipyretics, Non-steroidal anti-inflammatory drugs (NSAIDs)
	Reference to Finished product specifications	In-House / Innovator specification
	Proposed Pack size	5 ampoules Pack (5 Amp)
	Proposed unit price	Rs 600/Pack of 5 ampoules. Rs. 120 per ampoule
	The status in reference regulatory authorities	Dexketoprofen Trometamol 50mg/2ml (IM/IV) solution for injection is an EMA (European Medicine Agency) approved
	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	ZHEJIANG RAYBOW PHARMACEUTICAL CO., LTD. Address: No. 18, Nanyangsan Road, Linhai, Taizhou City, Zhejiang Province, China 317036

	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 accelerated study is complete for 3 batches at 40±2 °C/75±5%RH. The real time Zone IVA stability data is conducted at 30±2°C/65±5%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 has been established by conducting all the quality tests against the reference original product Arveles® (Dexketoprofen Trometamol) 50 mg/2ml Solution for Injection of Menarini International Ltd.
	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 primary packaging for product Sertofen (Dexketoprofen Trometamol) 50 mg/2 ml Solution for Injection is a type amber colored glass ampoule which has 2 ml nominal capacity.
	Stability study data of drug product, shelf life and storage conditions	• 24 months real time stability data at 30°C ± 2°C / 65% ± 5%RH of 03 batches (Zone IVA) 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches

Evaluation by PEC:

Observations	**Firm's response**
• **1.5.6.** Pharmacopoeial reference of the finished product has been declared as European Pharmacopoeia, whereas no EP monograph is available for applied product.	Firm has declared it an error and has submitted revised Form 5F, wherein product specifications have been referred as "In-House".
• **2.3.** Table for literature reference for the drug substance & product, declare that USP & EP monograph exists for the drug substance, while EP monograph also exist for applied drug product. Explanation/Evidence of above cited monograph shall be submitted.	Relevant information has been submitted as per the WHO QOS PD template.
• **2.3.S.3.** Relevant information against this section shall be submitted in Module II, instead of referring to other Modules.	
• Analytical method has been submitted for Fluconazole solution for injection instead of the drug	

substance "Fluconazole". • Information has been submitted for Fluconazole solution for injection instead of the drug substance "Fluconazole"	
• [Module 2 (QOS)]. All the table in the WHO QOS PD template shall be filled as such instead of replacing them with any other format. Also, information in the module II shall be submitted under relevant sections, instead of referring it to other Modules.	
• **3.2.S.4.2.** Justification shall be submitted for applying titration method for the Assay test.	Titration is used to determine Assay in routine test, although it is not a specific method but we use a HPLC method to determine organic impurities which can achieve overall specificity according to ICH Q6A.
• **3.2.S.4.3.** Analytical method verification studies for drug substance, including specificity, accuracy and repeatability (method precision) performed by the manufacturer shall be submitted.	API supplier performs the analytical method validations of the drug substance. Our company take the analysis results of API supplier as reference. Our company does not repeat these tests.
• **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 of the same batch from drug substance / Active pharmaceutical ingredients manufacturer.	Submitted.
• **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 test (mention 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.	Pharmaceutical equivalence studies against the reference product of Arveles Soultion for infusion has been submitted.
• **3.2.P.3.1.** The manufacturing site address mention under this section is different from that declared in CoPP.	Manufacturing address revised as per the details of COPP
• **3.2.P.3.3.** Submitted manufacturing process does not include step of terminal sterilization. Justification shall be submitted for not performing terminal sterilization.	The API Dexketoprofen trometamol cannot tolerate high temperature and ester bond can be broken with high temperature.
• **3.2.P.5.1.** Submitted drug product specifications declare the pH range as 6.5-8.5, whereas the reference product has declared pH range of 7.0-8.0. Justification shall be submitted in this regard.	Firm has revised the pH range to 7.0 – 8.0. The complete analyses of our product are examined , the pH limit is within the range of 7.0 -8.0.

Decision: Deferred for submission of analytical method verification studies of drug substance performed by the drug product manufacturer.

322.	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: by way of 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/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) **CoPP:** Firm has submitted original legalized COPP (DA/6-110/2016/3287) issued on 1-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.	
	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 2037744 Dated 03-03-2020
	Details of fee submitted	Rs.100,000/- Dated 03-03-2020
	The proposed proprietary name / brand name	Briganix 180 Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet Contains: Brigatinib…...……180mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	In house
	Proposed Pack size	30's in HDPE bottle
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Alunbrig 90mg tablet (Takeda uk ltd.)
	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	M/s AnHui youcare kaiyue pharmaceutical co. ltd. gongye dadao, taihe bengbu city, anhui 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 Alunbrig tablet of M/s Takeda Pharma 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
323.	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: by way of 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/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) **CoPP:** Firm has submitted original legalized COPP (DA/6-110/2016/3286) 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.	
	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 2037744 Dated 03-03-2020
	Details of fee submitted	Rs.100,000/- Dated 03-03-2020
	The proposed proprietary name / brand name	Briganix 90 Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet Contains: Brigatinib…...……90mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anticancer
	Reference to Finished product specifications	In house
	Proposed Pack size	30's in HDPE bottle
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Alunbrig 90mg tablet (Takeda uk ltd.)
	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	M/s AnHui youcare kaiyue pharmaceutical co. ltd. gongye dadao, taihe bengbu city, anhui 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 Alunbrig tablet of M/s Takeda Pharma 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 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.1.3.3	• The section declares that "Brigatinib does not exhibit Polymorphism", whereas EMA assessment report of the innovator product declare that "Polymorphism has been observed for Brigatinib." Clarification shall be submitted for this variation.	• Firm has submitted revised COA from both Drug substance & Drug product manufacturer wherein Polymorphic From has been declared as "A" & test of XPRD has been included.
3.2.S.4	• EMA assessment report of the innovator product recommend test of "Solid form confirmation (XRPD)", whereas drug substance specifications & COA submitted form drug substance manufacturer does not include any such test for Solid form confirmation. • 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	• Firm has submitted revised COA from both Drug substance & Drug product manufacturer wherein Polymorphic From has been declared as "A" & test of XPRD has been included. • Tabulated results of Analytical method validation studies have been submitted from M/s Beacon Pharma.

	Analysis (CoA) of the same batch from Drug Substance/Active Pharmaceutical Ingredient manufacture.	
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.	• We have used Pregelatinized Starch (Starch 1500) BP, sodium Starch Glycolate (Primojel) • BP, Ludipress, Magnessium Stearate BP, Colloidal Anhydrous Silica (Aerosil 200) BP & Microcrystalline Cellulose (Avecil PH I 02) in the formulation of Briganix 90mg Tablet as excipients. • These excipients are complies with Current Pharmacopoeia Monograph (British Pharmacopoeia & United States Pharmacopoeia). These excipients are pharmaceutically inert substance and we have used these excipients below IIG limit of FDA Orange Book as well as we have done extensive analysis of the product after formulation and found satisfactory result of Assay , dissolution results & impurity profile. • Also we have done stability study during development 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, specifies the dissolution limit as "NLT Q in 20 minutes", whereas submitted specifications declare the dissolution limits as "NLT 70 (Q)% in 45 minutes". Also, the speed of paddle apparatus recommended by US FDA is 70rpm, whereas submitted drug product testing method declares speed of paddle apparatus as 75rpm. • Justify the variation in time point of dissolution & rpm of paddle apparatus.	• For dissolution method, we have used US FDA data base for medium, apparatus, volume and time point. • However, please note that, for comparative dissolution time points were selected as 5, 10, 15, 20, 30 & 45 minutes. Based on the US FDA data base, dissolution time point covered 45 minutes in method of analysis.

Decision: Registration Board deferred the applications of Briganix 90 Tablet & Briganix 180 Tablet for submission of COAs of last three commercial batches of drug substance from Drug substance manufcaturer.

324.	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): **CoPP:** Firm has submitted original legalized COPP (DA/6-110/2016/3306) 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/6-110/06/4950) issued by M/s Beacon Pharmaceuticals limited valid upto 16-07-2021.	
	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 8004 dated 11-03-2021
	Details of fee submitted	Rs.50,000/- dated 01-02-2021
	The proposed proprietary name / brand name	Tofacinix 5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains Tofacitinib citrate INN equivalent to Tofacitinib 5mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-rheumatic, immunosuppressant
	Reference to Finished product specifications	In house
	Proposed Pack size	30's in Alu-Alu Blister
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Xeljanz XR Tablet 5 mg (Pfizer labs)
	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 Xeljanz XR Tablet 5 mg (Pfizer labs) 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	Alu-Alu Blister
	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.

Evaluation by PEC:

Section #.	Deficiencies	Firm's response
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of Drug substance/Active Pharmaceutical Ingredient by both Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method	• COA s form both drug substance and drug product manufacturer submitted. • Analytical method verification report submitted from M/s Beacon Pharma. • Submitted COA declares the polymorphic form as A.

	precision) performed by 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. • Submitted COA does not reflect the polymorphic form of the drug substance.	
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.	• We have used Pregelatinized Starch (Starch 1500) BP, Croscarmellose Sodium BP, Magnesium Stearate BP, Colloidal Anhydrous Silica (Aernsil 200) BP, Microcrystalline Cellulose (Avecil PH I 02) BP, Opadry II Blue (85G506--t2) in the formulation in Tofacinix 5mg Tablet • These excipients are complying with Current Pharmacopoeial Monograph (British Pharmacopoea & United States Pharmacopoea). These excipients are pharmaceutically inert substance and we have used these excipients bellow the IIG limit of FDA Orange Book as well as we have done extensive a1dysis of the product after formulation and found satisfactory result of assay, dissolution results & impurity profile. • Also we have done stability study during development stage and found satisfactory result of the product. • So we can conclude that these excipicnts are not incompatible with API.
3.2.P.2.2.1	• Comparative dissolution studies have been performed against Xeljanz XR tablet, whereas applied product is immediate release tablet. • Submitted CDP data declare the extended release profile of the applied drug, whereas the label claim is of immediate release tablet.	• Firm has submitted new CDP study data in three dissolution mediums (i.e., pH 1.2, pH 4.5 & pH 6.8), wherein results of f2 factor are in acceptable range.
3.2.P.5.2	• US FDA review document of the Innovator product, specifies the dissolution limit as "NLT Q in 15 minutes" in 0.1N HCl, whereas submitted specifications declare the dissolution limits as "NLT 75% in 30 minutes" using water as dissolution medium. • Justify the variation in time point of dissolution & rpm of paddle apparatus.	• For dissolution method we have used US FDA data base for medium, apparatus, volume and time point. • However, please note that, for comparative dissolution time points were selected as 5, I 0, 15, 20 & 30 minutes. Based on the US FDA Dissolution guidelines, dissolution time point covered 30 minutes in method of analysis.

Decision: Registration Board deferred the application for justification for adopting dissolution parameters & specifications for batch release, in variation from that recommended by the US FDA for innovator's product,

Case no. 04 Registration applications of drugs for which stability study data is submitted

a. **Exemption from onsite verification of stability data**

325.	Name and address of manufacturer / Applicant	M/s Getz Pharma (Private) Limited 29-30, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Emclide Tablets 25mg+5mg
	Diary No. Date of R& I & fee	Dy No. 2176, Rs: 50,000/- 19-11-2015
	Composition	Each film coated tablet contains: Empagliflozin…….25mg Linagliptin….5mg
	Pharmacological Group	Sodium glucose cotransporter 2 inhibitor, Dipeptidyl peptidase 4 inhibitor
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	14 Tablets, Rs. 12,500— Rs. 892.85/ tablet
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved Glyxambi
	Me-too status	N/A
	GMP status	Date of inspection: 26th June 2018 Acceptable level of compliance.
	Remarks of the Evaluator.	

STABILITY STUDY DATA			
Drug	Emclide Tablets 25mg+5mg		
Name of Manufacturer	M/s Getz Pharma (Private) Limited 29-30, Korangi Industrial Area, Karachi		
Manufacturer of API	Empagliflozin Jiangsu Yongan Pharmaceutical Co. LTD Add. No. 18, 237 Provincial Highway, Jiangsu Huaian Economic Development Zone	Linagliptin M/s Fuxin Long Rui Pharmaceutical Co. LTD Fluoride Industrial Park Fuxin City Liaoning Province	
API Lot No.	Empagliflozin 20161218	Linagliptin 160530	
Description of Pack (Container closure system)	Alu-Alu blister packed 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: 6 months Accelerated: 6 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6 (months)		
Batch No.	397DS03	397DS04	397DS05
Batch Size	2500 Tablets	2500 Tablets	2500 Tablet
Manufacturing Date	05-2017	05-2017	05-2017
Date of Initiation	05-2019	05-2019	06-2019
No. of Batches	03		
Date of Submission	28-06-2018 (Dy No. 22511)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
S. No.	**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 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.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Empagliflozin: Firm has submitted COA of Empagliflozin (Batch # 20161218) from M/s Jiangsu Yongan Pharmaceutical Co. Ltd., China. COA (Batch # 20161218) from M/s Getz Pharma (Pvt.) Ltd is also submitted. Linagliptin: Firm has submitted COA of Linagliptin (Batch # 160530) from M/s Fuxin Long Rui Pharmaceutical Co. Ltd., China. Copy of COA (Batch # 160530) from M/s Getz Pharma (Pvt.) Ltd is also submitted.
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	Empagliflozin: 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 Linagliptin: 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.	Empagliflozin: Firm has submitted copy of Drug Manufacturing License (DML # Su20160324) of M/s Jiangsu Yongan Pharmaceutical Co. Ltd., China issued by Jiangsu Drugs Administration, China. The certificate is valid till 06-12-2025. Linagliptin: Firm has submitted copy of Drug Manufacturing License (DML # LIAO20150233) of Fuxin Long Rui Pharmaceutical Co. Ltd., China issued by Liaoning Medical Products Administration, China. The certificate is valid till 20-12-2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted import License No. 0570/17-DRAP (K) dated 28-02-2017 confirming import of 500g Empagliflozin from M/s Jiangsu Yongan Pharmaceutical Co. Ltd., China for Batch No. 20161218. Firm has submitted import License No. 1632/16-DRAP (K) dated 14-06-2016 confirming import of 300g Linagliptin from M/s Fuxin Long Rui Pharmaceutical Co. Ltd., China for Batch No. 160530.

<table>
<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>Firm has submitted that same excipients has been used as used by innovator ‘GLYXAMBI Tablets 25mg + 5mg’. However, there is only difference in film coating materials Therefore, Drug-excipients compatibility studies were not performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Empagliflozin + Linagliptin Tablets 25mg + 5mg and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><th colspan="3">Emclide Tablet 25mg + 5mg</th></tr>
<tr><th>Batch No.</th><th>Bach size</th><th>Mfg. Date</th></tr>
<tr><td>397DS03</td><td>2500 Tablets</td><td>12.05.2017</td></tr>
<tr><td>397DS04</td><td>2500 Tablets</td><td>17.05.2017</td></tr>
<tr><td>397DS05</td><td>2500 Tablets</td><td>18.05.2017</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “GLYXAMBI”. The details are as follows:
<table>
<tr><th>Feature</th><th>Reference product</th><th>Product of Getz Pharma</th></tr>
<tr><td>Brand name</td><td>GLYXAMBI Tablets 25mg + 5mg</td><td>Emclide Tablet 25mg + 5mg</td></tr>
<tr><td>Batch No.</td><td>002263</td><td>397DS06</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer</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>Submitted</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>Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.</td></tr>
<tr><td colspan="3">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.
• 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 05-07-2021.</td></tr>
<tr><td>326.</td><td>Name and address of manufacturer / Applicant</td><td>M/s Helix A/56, SITE, mangopir, Karachi</td></tr>
<tr><td></td><td>Brand Name +Dosage Form + Strength</td><td>Brevi Oral solution</td></tr>
<tr><td></td><td>Composition</td><td>Each ml contains:-
Brivaracetam ……. 10mg</td></tr>
<tr><td></td><td>Diary No. Date of R& I & fee</td><td>Dy. No 6709 dated 20-06-2017, Rs.50,000/-</td></tr>
<tr><td></td><td>Pharmacological Group</td><td>Antiepileptics</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>As per PRC, 60ml & 120ml</td></tr>
<tr><td></td><td>Approval status of product in</td><td>Approved by USFDA</td></tr>
</table>

	Reference Regulatory Authorities	
	Me-too status (with strength and dosage form)	--
	GMP status	GMP certificate was issued based on inspection conducted on 29 october 2020.
	Remarks of the Evaluator[II]	

Now the firm has submitted stability data detailed as under:

STABILITY STUDY DATA

Drug	Brevi/Vetam oral solution 10mg/ml
Name of Manufacturer	M/s Helix A/56, SITE, mangopir, Karachi
Manufacturer of API	Brivaracetam: M/s Chengda Pharmaceuticals Co., Ltd, Zhejiang.
API Lot No.	NP1713-1806001
Description of Pack (Container closure system)	120ml amber glass bottle packed in unit carton with product 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: 0,1,2,3 & 6 months Real Time: 0,3,6 months

Product name	Batch Nos.	Batch size	Date of manufacturing	Date of initiation
Brevi/Vetam oral solution 10mg/ ml	TF001,TF002,TF003	2000ml each	08-2018	09-08-2018
Date of submission	20-08-2019 (Dy.no 15009)			

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Documents To Be Provided	**Status**
COA of API	Yes
Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.	Copy of DML (DML # 20100526) issued by CFDA for the M/s Chengda Pharmaceuticals Co., Ltd, Zhejiang.
Protocols followed for conduction of stability study and details of tests.	Yes
Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc.	Yes
Documents confirming import of API etc.	License to import Brivaracetam from M/s Changda Pharmaceutical Co., Ltd. Jiashan, Zheijiang, China, issued by ADC, DRAP, Karachi has been submitted. Detailed as under:
All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Yes

Batch No.	**Invoice No.**	**Quantity Imported**	**Date of approval by DRAP**
NP1713-1806001	C02S05ZEP180357	800gm	18-07-2018

<table>
<tr><td colspan="2">Commitment to continue real time stability study till assigned shelf life of the product.</td><td>Yes</td></tr>
<tr><td colspan="2">Commitment to follow Drug Specification Rules, 1978.</td><td>Yes</td></tr>
<tr><td colspan="3">REQUEST OF EXEMPTION ROM ON SITE INSPECTION</td></tr>
<tr><td colspan="3">Now the firm has requested for Exemption from On-site Investigation of their submitted stability data provided the following documents in conjunction with the checklist approved by the Registration Board.</td></tr>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm.</td><td>Following has been reported regarding HPLC software & stability chambers:
The HPLC software is 21CFR Compliant as per record available with the firm.
Audit trail on the testing reports of “Brevi solution for infusion” has been available on upgraded HPLC 21CFR.
Audit trail on the testing reports of “c-zyn ophthalmic solution 0.24%” has available on upgraded HPLC 21CFR.
Firm has adequate monitoring & control for stability chambers. Firm has installed software for recording the temperature/ Humidity of the chamber.</td></tr>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Submitted for batch# NP1713-1806001</td></tr>
<tr><td>3.</td><td>Method used for analysis of API along with COA.</td><td>Firm has submitted COA and method of analysis of API.</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>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.</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>Copy of DML (DML # 20100526) issued by CFDA for the M/s Chengda Pharmaceuticals Co., Ltd, Zhejiang.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>License to import Brivaracetam from M/s Changda Pharmaceutical Co., Ltd. Jiashan, Zheijiang, China, issued by ADC, DRAP, Karachi has been submitted.
Detailed as under:
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>NP1713-1806001</td><td>C02S05ZEP180357</td><td>800gm</td><td>18-07-2018</td></tr>
</table></td></tr>
<tr><td>7.</td><td>Authorized Protocols/SOP for the development & stability testing of trial batches.</td><td>Firm has submitted authorized stability protocols for the development of applied product</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>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.
<table>
<tr><th colspan="3">Tri-Plat 60mg tablet</th></tr>
<tr><th>Batch No.</th><th>Date of Mfg.</th><th>Batch Size</th></tr>
<tr><td>TF001</td><td>08-2018</td><td>2000 ml</td></tr>
<tr><td>TF002</td><td>08-2018</td><td>2000 ml</td></tr>
<tr><td>TF003</td><td>08-2018</td><td>2000 ml</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data</td><td>N/A</td></tr>
</table>

	(where applicable)	
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submnitted 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.	Firm has submitted audit trail reports for HPLC analysis for all the three batches of Brevi/vetam oral solution.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of Evaluator[II]:		
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.** • **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 05-07-2021.**		

b. Verification of stability study data

327.	Name and address of manufacturer / Applicant	M/s High Q Pharmaceuticals B-64, Karsaz Road, KDA-1, Karachi
	Brand Name +Dosage Form + Strength	Lasodex 60 mg Capsules
	Diary No. Date of R& I & fee	Dy No. 1368, Rs: 50,000/- 24-11-2016
	Composition	Each capsule contains: Dexlansoprazole (dual delayed release pellets)….60mg
	Pharmacological Group	Drugs For Peptic Ulcer And Gastro-Oesophageal Reflux Disease (Gord) Proton Pump Inhibitors ATC Code: A02BC06
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	14's, 30's Alu alu blister, AS per brand leader
	Approval status of product in Reference Regulatory Authorities.	Dexilant-USFDA approved
	Me-too status	Not applicable
	GMP status	GMP certificate issued to M/s High-Q Pharmaceuticals based on inspection conducted on 15.02.2019
	Remarks of the Evaluator.	• Dissolution parameters stated in finished product testing method are not as recommended by USFDA.

STABILITY STUDY DATA	
Drug	Lasodex 60 mg Capsules
Name of Manufacturer	M/s High Q Pharmaceuticals B-64, Karsaz Road, KDA-1, Karachi
Manufacturer of API	M/s Alphamed Formulations Pvt. Ltd Survey No. 225, Sampanbole Village , Shamirpet Mandal, India
API Lot No.	BVA16002 (Not mentioned on Commercial invoice)
Description of Pack (Container closure system)	Alu-Alu blister packed 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: 6 months Accelerated: 6 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6 (months)		
Batch No.	T001	T002	T003
Batch Size	700 Caps	**700** Caps	700 Caps
Manufacturing Date	08-2017	08-2017	08-2017
Date of Initiation	08-2019	08-2019	08-2019
No. of Batches	03		
Date of Submission	06-04-2018 (Dy No. 12988)		

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.	yes
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.	Yes (date 31-01-2017) 0.9kg
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

REMARKS OF EVALUATOR[2]

Brand name resemblance with Lansodex of Getz.

Report on Investigation of Authenticity / Genuineness of data submitted for registration of Lasodex (Dexlansoprazole) 30mg and Lasodex (Dexlansoprazole) 60mg Capsules by M/s High-Q Pharmaceuticals, Plot # 224 & 225/1, Korangi Industrial Area, Karachi.

Reference No: F.13-11/2017-PEC (Pt) dated 25th September, 2019

Investigation Date and Time: 23rd September, 2021.

Investigation Site: Factory premises of M/S. High-Q Pharmaceuticals, Korangi Industrial Area, Karachi.

Background:

Chairman Registration Board considered the applications of M/S. High-Q Pharmaceuticals, Korangi Industrial Area, Karachi for registration of Lasodex (Dexlansoprazole) 30mg & Lasodex (Dexlansoprazole) 60mg Capsules and constituted a three member panel to investigate the authenticity / genuineness of data (import of raw material and stability data). Panel was advised to conduct inspection of the firm and to submit report for further consideration.

Composition of Panel:

1. Prof. Dr. Rafeeq Alam Khan, Dean. Faculty of Pharmacy, Ziauddin University, Karachi (Member Registration Board).

2. Dr. Saif-ur-Rehman Khattak, Director/ FGA, CDL, Karachi.
3. Ms. Sanam Kauser, Assistant Director, CDL, DRAP, Karachi.

Scope of investigation:

Investigation of the authenticity / genuineness of data (import of raw material and stability data), manufacturing of stability batches and stability studies on these batches.

Tools for Investigation:

The investigation was conducted by using a structured questionnaire of DRAP. For objective evidence physical inspection of the facilities for manufacturing and quality control, material used and retained, personnel involved, ongoing studies, printed data and integrity and security of data in respective databases were also audited. The details of investigation may be summarized as under:

Sr. No.	Question	Observation by panel
1.	Do you have documents confirming the import of API?	The firm has purchased 3kg Dexlansoprazole dual delayed release pellets 22.5%w/w from M/s.VISION PHARMACEUTICALS and used in stability batches of 30 mg and 60mg Lasodex Capsules.
2.	What was the rationale behind selecting the particular manufacturer of API?	A SOP for induction and approval of new vendors is in place and implemented. M/s. Vision Pharma was inducted following the SOP. In addition, this vendor has GMP certificate issued by DRAP which is valid uptil 10th Feb 2022.
3.	Do you have documents confirming the import of API reference standard and impurity standards?	Invoice of API , working standard of API & Impurity standard is available.
4.	Do you have certificate of Analysis of the API, reference standards and impurity standards?	CoA of the API, working standard and impurity standard available.
5.	Do you have any approval of API or GMP certificate of API manufacturer issued by regulatory authority of country of origin?	The firm has GMP certificate of ~~(~~M/s Vision Pharmaceuticals, Islamabad-Pakistan~~)~~ issued by DRAP which is valid till 10th February, 2022.
6.	Do you use API manufacturer method of testing?	Testing method of API manufacturer is used for the testing of Dexlansoprazole pellets.
7.	Do you have stability studies reports on API?	Reports are available.
8.	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	The stability testing has been performed as per SIM method by API manufacturer The test for degradation products is not included in the stability reportshared by the manufacturer of API, however, the firm has performed this test during stability studies; the results are found compliant to specification.
9.	Do you have method for quantifying the impurities in the API?	Method for quantifying the impurities is available
10.	Do you have some remaining quantities of the API, its reference standard and impurities standards?	The firm has some remaining quantity of the API and its reference standard.
11.	Have you used pharmaceutical grade excipients?	Not applicable, as no excipient is added before encapsulation i.e., the API is received as dual delayed release pellets and are filled in capsule shells as such. However the capsules shells used were of pharmaceutical grade
12.	Do you have documents confirming the import of the used excipients?	Not Applicable
13.	Do you have test reports and other records on the excipients used?	Test reports and other documents are available for empty gelatine capsules.
14.	Do you have written and authorized protocols for the development of API tablets	The firm has written and authorized protocol for development of Lasodex 30mg / 60mg capsules.

	/ capsules?	
15.	Have you performed Drug-excipient compatibility studies?	Not applicable, as no excipients are added before encapsulation.
16.	Have you performed comparative dissolution studies?	The firm has performed comparative dissolution studies on their capsules with dexilant capsules (Takeda Japan). The profiles for both strengths are comparable to dexilant capsules.
17.	Do you have product development (R&D) section	The firm has product development (R&D) section with requisite manufacturing facilities while testing is done in fully equipped central lab
18.	Do you have necessary equipment available in product development section for development of Dexlansoprazole Capsules?	All the necessary equipment are available in product development section however, the encapsulation is done in production area using qualified encapsulation machine.
19.	Are the equipment in product development section qualified?	The equipment in product development section (R&D) are qualified.
20.	Do you have proper maintenance / calibration / re-qualification program for the equipment used in PD section?	PD equipment are included in site equipment maintenance, calibration and qualification program.
21.	Do you have qualified staff in product development section with proper knowledge and training in product development?	The firm has adequately qualified and trained staff in product development section.
22.	Have you manufactured three stability batches for the stability studies of capsules as required?	The firm has manufactured three stability batches each for 30mg and 60mg capsules.
23.	What was the criteria for fixing the batch size of stability batches?	The batch size was fixed considering the factors like (i) Complexity of process; in this case it is simple i.e., just filling of pellets in capsules and controlling the fill weight, (ii) start-up waste, (iii) Number of capsules required for one full specification testing, (iv)Number of complete testing to be performed as per approved test frequency for accelerated and real time samples and (v) suitable quantity for reference.
24.	Do you have complete record of production of stability batches?	The firm has complete record of production of stability batches.
25.	Do you have protocols for stability testing of stability batches?	The firm has detailed protocols for stability testing of stability batches.
26.	Do you have developed and validated the method for testing of stability batches?	The firm has validated HPLC methods provided by Manufacturer of the API with the necessary force depredation studies.
27.	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Full validation studies are performed.
28.	Do you have documents confirming the qualification of equipment / instruments being used in the test and analysis of product's API and the finished drug?	The firm has documents confirming the qualification of equipment / instruments being used in the test and analysis of Dexlansoprazole API and the finished product.
29.	Do your method of analysis stability indicating?	Analytical method used in stability studies is stability indicating as evidenced by force degradation studies.
30.	Do your HPLC software is 21CFR compliant?	HPLC software is 21CFR compliant.
31.	Can you show Audit Trail reports on API testing?	Audit Trail reports of API (Dexlansoprazole pellets) and Laxodex Capsules are available.
32.	Do you have some remaining quantities of degradation products and stability batches?	The firm has remaining quantity of stability batches only.
33.	Do you have commitment batches kept on	Three batches each of 30mg and 60mg capsules are

	stability testing?	kept on real time & accelerated stability testing.
34.	Do you have valid calibration status for the equipment used in API tablets production in analysis?	The firm has valid calibration status for the equipment used in production and analysis of Dexlansoprazole Capsules**.**
35.	Do proper and continuous monitoring and control are available for stability chamber?	The firm has adequate monitoring and control available for stability chambers.
36.	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Related manufacturing area, equipment, personnel and utilities are GMP compliant
37.	**Specific Queries by PEC/Board** To verify the dissolution testing of pellets at pH 5.5 for confirmation of dual delayed release action.	As per direction of the PEC results of dissolution testing of the pellets at pH 5.5 were reviewed. It was concluded that the results lie within the limits (less than 35% in three hours).

Conclusions:

1. On the basis of risk-based approach the genuineness / authenticity of stability data submitted by the firm for registration of Lasodex 30mg and Lasodex 60mg (Dexlansoprazole) Capsules are verifiable to satisfactory level.
2. The related manufacturing area, equipment, personnel and utilities are GMP compliant and suited for the manufacturing of Lesodex 30mg and Lasodex 60mg (Dexlansoprazole) Capsules.

Recommendations:

1. Since Lasodex 30mg and Lasodex 60mg (Dexlansoprazole) Capsules are modified release (delayed release) capsules therefore, post registration bioequivalence studies should be conducted on the product before marketing.
2. Firm must develop specific identification test for dexlansoprazole in the pellets and the finished product.
3. The firm may kindly be granted necessary registration of Lasodex 30mg and Lasodex 60mg (Dexlansoprazole) Capsules.

Note: The firm has submitted written undertaking for post registration bioequivalence studies on the capsules (copy enclosed).

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.**
- **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.**

Case no. 05 Priority Registration of Remdesivir Containing Drug Products:

328.	Name and address of Manufacturer Applicant	M/s AJM Pharma. Plot No. 44, Sector No. 27, Korangi Industrial Area, Karachi, Pakistan
	Drug Sale license details	DSL No.: 064 Address: AJM Pharma (Pvt) Ltd 1st Floor, Shafi Court, Merewether Road, Civil Lines, Karachi Validity: 23-02-2023 Status: By way of Wholesale
	Manufacturer	M/s Eva Pharma for Pharmaceuticals and Medical Appliances, 176, El Sadate St., Kafr El Gabal -Pyramids, Giza, Egypt
	Market Authorization Holder	M/s Eva Pharma for Pharmaceuticals and Medical Appliances, 176, El Sadate St., Kafr El Gabal -Pyramids, Giza, Egypt
	Country of Origin	Egypt
	Brand Name+DosageForm+Strength	Ajvir 100mg/20ml Concentrate for solution for IV Infusion
	Composition	Each 20ml contains: Remdesivir ……100mg
	Diary No. Date of R&I & fee	Dy. No.18690; 29-07-2020; Rs.100,000
	Pharmacological Group	Anti-Viral

	Type of Form	Form 5A
	Finished Product Specification	Innovator's specifications
	Pack Size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities.	Approved by US FDA
	Me-too status	Redzi Injection
	Details of certification	• Copy of GMP certificate issued by Drugs Control Department, Government of Karnataka, valid upto 17-03-2022. • Original Letter of Authorisation from M/s Eva Pharma for Pharmaceuticals and Medical Appliances in the name of M/s AJM Pharma (Pvt.) Ltd. • Original legalized COPP (certificate# 01046/2020/H) issued by Egyptian Drug Authority, dated 01-07-2020, wherein status of product has been declared as under: ➢ Product License in exporting country: As an Emergency Use Authorization License ➢ Product actually ion the market in exporting country: Hospital Use only. • Copy of GMP certificate (Certificate# 650/2020) issued by Egyptian Drug Authority valid upto 14/07/2021.
	Remarks of Evaluator: • Firm has submitted fee of Rs. 7500 vide deposit slip# 1395795694 for revision of From 5F for brand name as per the COPP as under: **"Remdesivir-Eva Pharma Concentrate for solution for IV infusion"** • Firm has submitted stability studies data sheets of three batches for both accelerated and long-term stability studies data as per refrigerating conditions from M/s Eva Pharma for Pharmaceuticals and Medical Appliances. • Firm has also submitted "SOP for Data collection of ADR and Reporting to Authorities".	
	Decision: The Board deferred the case for deliberation regarding the grant of Emergency Use Authorization of Remedesvir for import cases.	

Agenda of AD PE&R

Case NO. I: Registration applications submitted on form 5F

329.	Name, address of Applicant / Marketing Authorization Holder	M/s Islam Pharmaceuticals (DML # 000885) 7-KM Pasrur Road Sialkot
	Name, address of Manufacturing site.	M/s Bio-Mark Pharmaceuticals (DML # 000863) Plot No 527, 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.10998 dated 09/04/2021
	Details of fee submitted	PKR 50,000/-: dated 24/03/2021
	proposed proprietary name / brand name	DESICA 0.5mg/5ml Syrup
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Desloratadine…….0.5mg (As per Innovator's specifications)

	Pharmaceutical form of applied drug	Oral Liquid
	Pharmacotherapeutic Group of (API)	Antihistamines- H1 antagonist
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	30ml, 60ml, 90ml & 120ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	NEO-CLARITYN M/S Merck Sharp & Dohme Ltd Spanish Agency for Medicines and Health Products (AEMPS)
	For generic drugs (me-too status)	Desora 0.5mg/ml syrup by M/s Continental Pharma Reg. # 055192
	GMP status of the Finished product manufacturer	New license granted on 12/06/2017 Oral Liquid (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Morepen Laboratories Ltd. Village-Masulkhana, Parwanoo, Distt. 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 6 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (19J225, 19K228 & 19K229)
	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 Eslor 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.	DCH 8070		
Description of Pack (Container closure system)	PET Bottle Amber Color, 120ml		
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, 3, 6 (Months)		
Batch No.	19J225	19K228	19K229
Batch Size	5000 Bottles	5000 Bottles	5000 Bottles
Manufacturing Date	09/2019	10/2019	10/2019
Date of Initiation	15-10-19	15-10-19	15-10-19
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.	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, Distt, Solan. It is valid till 30-04-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying import of 5.0Kg of Desloratadine INH attested by Assistant Director (I&E) dated 28-11-2018.
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 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 & accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks OF Evaluator:

Desloratadine Syrup has already been approved with the name of Varidene Syrup by Registration Board in Minut meeting 297th held on 12-15th January, 2021 was applied on Form-5F (CTD) by Variant Pharmaceuticals for cont manufacturing by M/s Bio-Mark Pharmaceuticals.

Decision: Approved.

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

330.	Name, address of Applicant / Marketing Authorization Holder	M/s Herbion Pakistan (Pvt.) Ltd. Industrial Triangle, Kahuta road, Humak, Islamabad (DML No. 000795)
	Name, address of Manufacturing site.	M/s Herbion Pakistan (Pvt.) Ltd. Industrial Triangle, Kahuta road, Humak, Islamabad (DML No. 000795)

	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.7884 dated 10/03/2021
	Details of fee submitted	PKR 20,000/- dated 05/03/2021
	proposed proprietary name / brand name	Ista tablets 25 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin Phosphate monohydrate eq. to Sitagliptin..25mg
	Pharmaceutical form of applied drug	Oblong shaped, bi-planer, Pink colored film coated tablets, bisect line on both sides
	Pharmacotherapeutic Group of (API)	DPP-4 inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	14's and 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Januvia 25 mg tablet by M/s Merck, USFDA Approved.
	For generic drugs (me-too status)	Sitaglu Tablets 25 mg by M/s Hilton Pharma, R.No. 055158
	GMP status of the Finished product manufacturer	Firm has been granted GMP certificate (F.3-9/2018-Addl.Dir. (QA & Lt-I)-49 dated 17-07-2019.
	Name and address of API manufacturer.	Anhui Haikang Pharmaceutical Co.,Ltd. No. 21, Huancheng West Road, Daguan District, Anqing, Anhui 24600, China. 246000
	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 Sitagliptin Phosphate 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 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20130421, 20130420, 20130419)

	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 Sitaglu 25 mg tablet by M/S Hilton Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Sitaglu 25 mg tablet by M/S Hilton Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The results 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	Anhui Haikang Pharmaceutical Co.,Ltd. No. 21, Huancheng West Road, Daguan District, Anqing, Anhui 24600, China. 246000		
API Lot No.	20010401		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's and 28'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.	170010820	170021020	170031020
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	09-11-2020	09-11-2020	09-11-2020
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. 20190399 issued by FDA Anuhai Province valid till 31/12/2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Form-06 and attested Invoice from DRAP I&E dated 03-07-2020 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 & accelerated)	Submitted

Remarks OF Evaluator:

S.No.	Observations	Firm's Response
i.	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.'	• Drug Substance specifications and analytical procedures used by the **API manufacturer** for routine testing of sitagliptin is submitted. • Drug Substance specifications and analytical procedures used by the **Drug product manufacturer** for routine testing of sitagliptin is submitted**.**
ii.	Submit data in section 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."	
iii.	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 analytical method of drug substance.	• Verification studies of drug substance is submitted. • The opted analytical method of drug product is pharmacopeial and firm has performed all the testing parameters in compliance with the pharmacopeia.
iv.	Submit COA of reference standard / working standard in section 3.2.S.5 which is actually used in the analysis of drug substance and product, since the submitted COA of working standard was expired in 2019 while the drug substance and drug product testing was carried out in 2020.	• COA of reference standard/ working used in analysis of drug substance is submitted.
v.	Justify the adaptation of dissolution specifications as well as its analytical method.	• Firm has stated that: 'The dissolution studies of Sitagliptin phosphate monohydrate tabltes were conducted as per FDA guidelines 2018. The analytical method of dissolution was not present in any monograph so anlytical method validation was performed for dissolution.

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.**

331.	Name, address of Applicant / Marketing Authorization Holder	M/s Herbion Pakistan (Pvt.) Ltd. Industrial Triangle, Kahuta road, Humak, Islamabad
	Name, address of Manufacturing site.	M/s Herbion Pakistan (Pvt.) Ltd. Industrial Triangle, Kahuta road, Humak, 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.7885 dated 10/03/2021
	Details of fee submitted	PKR 20,000/-: dated 05/03/2021
	proposed proprietary name / brand name	Ista tablets 50 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin Phosphate monohydrate eq. to Sitagliptin…50mg
	Pharmaceutical form of applied drug	Oblong shaped bi-planar yellow colored tablets bisect line on both sides.
	Pharmacotherapeutic Group of (API)	DPP-4 inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	14's and 28's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Januvia 50 mg tablet by M/s Merck, USFDA Approved.
	For generic drugs (me-too status)	Sitaglu Tablets 50 mg by M/s Hilton Pharma, R.No. 055159
	GMP status of the Finished product manufacturer	Firm has been granted GMP certificate (F.3-9/2018-Addl.Dir. (QA & Lt-I)-49 dated 17-07-2019.
	Name and address of API manufacturer.	Anhui Haikang Pharmaceutical Co.,Ltd. No. 21, Huancheng West Road, Daguan District, Anqing, Anhui 24600, China. 246000
	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 Sitagliptin Phosphate 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 organic 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 Batches: (20130421, 20130420, 20130419)
	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 Sitaglu 50 mg tablet by M/S Hilton Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Sitaglu 25 mg tablet by M/S Hilton Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The results 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	Anhui Haikang Pharmaceutical Co.,Ltd. No. 21, Huancheng West Road, Daguan District, Anqing, Anhui 24600, China. 246000		
API Lot No.	20010401		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's and 28'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, 9, 12, 18 and 24 (Months)		
Batch No.	171010820	171021020	171031020
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	09-11-2020	09-11-2020	09-11-2020
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. 20190399 issued by FDA Anuhai Province valid till 31/12/2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Form-06 and attested Invoice from DRAP I&E dt: 03-7-2020 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:

S.No	Observations	Firm's Response
i.	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	• Drug Substance specifications and analytical procedures used by the **API**

	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.'	**manufacturer** for routine testing of sitagliptin is submitted. • Drug Substance specifications and analytical procedures used by the **Drug product manufacturer** for routine testing of sitagliptin is submitted**.**
ii.	Submit data in section 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."	
iii.	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.	• Verification studies of drug substance is submitted. • The opted analytical method of drug product is pharmacopeial and firm has performed all the testing parameters in compliance with the pharmacopeia.
iv.	Submit COA of reference standard / working standard in section 3.2.S.5 which is actually used in the analysis of drug substance and product, since the submitted COA of working standard was expired in 2019 while the drug substance and drug product testing was carried out in 2020.	• COA of reference standard/ working used in analysis of drug substance is submitted.
v.	Justify the adaptation of dissolution specifications as well as its analytical method.	• Firm has stated that: 'The dissolution studies of Sitagliptin phosphate monohydrate tabltes were conducted as per FDA guidelines 2018. The analytical method of dissolution was not present in any monograph so anlytical method validation was performed for dissolution.

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.**

332.	Name, address of Applicant / Marketing Authorization Holder	M/s Herbion Pakistan (Pvt.) Ltd. Industrial Triangle, Kahuta road, Humak, Islamabad
	Name, address of Manufacturing site.	M/s Herbion Pakistan (Pvt.) Ltd. Industrial Triangle, Kahuta road, Humak, 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.7886 dated 10/03/2021
	Details of fee submitted	PKR 20,000/-: dated 05/03/2021
	proposed proprietary name / brand name	Ista tablets 100 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin Phosphate monohydrate eq. to Sitagliptin…….100 mg
	Pharmaceutical form of applied drug	Round shaped green color tablets plain on both sides
	Pharmacotherapeutic Group of (API)	DPP-4 inhibitor
	Reference to Finished product specifications	USP
	Proposed Pack size	14's and 28's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Januvia 100 mg tablet by M/s Merck, USFDA Approved.
	For generic drugs (me-too status)	Sitaglu Tablet 100mg by M/s Hilton Pharma, R.No.055160
	GMP status of the Finished product manufacturer	Firm has been granted GMP certificate (F.3-9/2018-Addl.Dir. (QA & Lt-I)-49 dated 17-07-2019.
	Name and address of API manufacturer.	Anhui Haikang Pharmaceutical Co.,Ltd. No. 21, Huancheng West Road, Daguan District, Anqing, Anhui 24600, China. 246000
	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 Sitagliptin Phosphate 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 organic 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 Batches: (20130421, 20130420, 20130419)
	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 brand that is Januvia 100 mg tablet by M/S Merck by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Januvia 100 mg tablet by M/S Merck in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The results 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	Anhui Haikang Pharmaceutical Co.,Ltd. No. 21, Huancheng West Road, Daguan District, Anqing, Anhui 24600, China. 246000		
API Lot No.	20010401		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's and 28'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, 9, 12, 18 and 24 (Months)		
Batch No.	172010820	172021020	171031020
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	09-11-2020	09-11-2020	09-11-2020
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. 20190399 issued by FDA Anuhai Province valid till 31/12/2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Form-06 and attested Invoice from DRAP I&E dated 03-07-2020 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:

S.No.	Observations	Firm's Response
i.	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	• Drug Substance specifications and analytical procedures used by the API manufacturer for routine testing of sitagliptin

	routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required.'	is submitted. • Drug Substance specifications and analytical procedures used by the Drug product manufacturer for routine testing of sitagliptin is submitted**.**
ii.	Submit data in section 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."	
iii.	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.	• Verification studies of drug substance is submitted. • The opted analytical method of drug product is pharmacopeial and firm has performed all the testing parameters in compliance with the pharmacopeia.
iv.	Submit COA of reference standard / working standard in section 3.2.S.5 which is actually used in the analysis of drug substance and product, since the submitted COA of working standard was expired in 2019 while the drug substance and drug product testing was carried out in 2020.	• COA of reference standard/ working used in analysis of drug substance is submitted.
v.	Justify the adaptation of dissolution specifications as well as its analytical method.	• Firm has stated that: 'The dissolution studies of Sitagliptin phosphate monohydrate tabltes were conducted as per FDA guidelines 2018. The analytical method of dissolution was not present in any monograph so anlytical method validation was performed for dissolution.

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.**

333.	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt) Ltd Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad
	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.13083 dated: 055/05/2021

	Details of fee submitted	PKR 50,000/- dated 13/04/2021
	proposed proprietary name / brand name	ORNID 500mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Ornidazole …500mg
	Pharmaceutical form of applied drug	Light orange color, Oblong shaped Film coated tablets.
	Pharmacotherapeutic Group of (API)	AGENTS AGAINST AMOEBIASIS AND OTHER PROTOZOAL DISEASES
	Reference to Finished product specification	Innovator's Specifications
	Proposed Pack size	10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ARROW 500mg Tablets by M/s Teva Pharma (New Zealand) Limited, MEDSAFE Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	New license granted on 11/02/2019. Tablet section approved.
	Name and address of API manufacturer.	M/s Hunan Jiudian Hongyang Pharmaceuticals Co., Ltd. Tongguan Circular Economy Industrial Base, Wang Cheng Economic and Technological Development Zone, Hunan, 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 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: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (201803A01, 201803A02 & 201803A03)
	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 Biteral 500mg Tablet by DEVA Pharmaceuticals (Pvt) Ltd, Turkey by performing quality tests (Identification, Assay, Dissolution, Uniformity of

		dosage form). CDP has been performed against the same brand that is Biteral 500mg Tablet by DEVA Pharmaceuticals (Pvt) Ltd, Turkey 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, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Hunan Jiudian Hongyang Pharmaceuticals Co., Ltd. Tongguan Circular Economy Industrial Base, Wang Cheng Economic and Technological Development Zone, Hunan, China.		
API Lot No.		WT201808A03		
Description of Pack (Container closure system)		Alu-PVC blister packed in unit carton (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: 12 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 2, 3, 4, 5, 6 (Months) Real Time: 0, 3, 6, 9, 12, (Months)		
Batch No.		NDP-902 (T-01)	NDP-902 (T-02)	NDP-902 (T-03)
Batch Size		1000tab	1000tab	1000 tab
Manufacturing Date		07-2019	07-2019	07-2019
Date of Initiation		02-09-2019	02-09-2019	02-09-2019
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				
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 Sofovir-V 400mg/100mg Tablets which was conducted on 5th & 15th October, 2018 and was presented in 286th meeting of Registration Board held on 14-16th November, 2018. 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 GMP certificate No. HN20180310 issued by CFDA valid till 22/05/2023.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.178/2019-ADC (I&E) dated 13/01/2020 is submitted wherein the permission to import Ornidazole 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.	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 & accelerated)	Submitted

Remarks OF Evaluator:

S.No.	Observations	Documents submitted/ Firm's reply
i.	ADC attested invoice dated 10-01-2020, whereas, batches were developed in July 2019. Justification is required.	Firm has submitted ADC attested invoice dated 08-02-2019 and the trial batch was manufactured in 07-2019
ii.	Dissolution test limit in NLT 80% in 60 minutes in 3.2.P.5.1 NLT 80% in 30 min is in 3.2.P.5.2. Clarification is required.	Firm has stated that it was typographical mistake in 3.2.P.5.1 The correct limit is NLT 80% in 30 minutes.
iii.	CDP is not performed with innovator brand approved in reference regulatory authority. Justification is required.	Firm has stated: 'As its mentioned in 293rd Meeeting of Registration Board and also WHO guidelines CDP will be done against Innovator/ Reference comparator product. We select Biteral 500mg Tablet (Manufactured by DEVA Holding Istanbul (PIC/S member country i.e. Turkey)). And according to 275th Registration Board Meeting we can use product of any country which is Pharmaceutical Inspection Convention member and Pharmaceutical Inspection Co-operation scheme (PIC/S) should also be made the part of reference country.'
iv.	Specify API lot number used in manufacturing of batches along with complete batch manufacturing record of test batches.	Firm has stated: 'We use Ornidazole Batch no. WT201808A03, which is also mentioned in analytical method validation protocol.' ADC clearance is also attached. Trial manufacturing record of test batches is also submitted.
v.	In 3.2.P.5.4, Tablet upper weight limit is 879mg for coated tablets while average weight of tablets in batches is more than 880mg per tablet. Scientific justification is required.	Firm has stated: 'The targeted weight of the tablet was 850mg and according to USP & BP limit of wight variation 850±5% (807.5-892.5) and all the readings are within range.'
vi.	Weight variation test is not mentioned in specifications of finished product (3.2.P.5). Justification is required.	Firm has stated: 'Weight variation is our in-process test for finished product which is performed during compression of the tablet, so not mention in specifications of finished product. The weight variation of coated tablet is also performed and already provided.'
vii.	As per CDP results drug show more than 80% release in 0.1N HCl pH 1.2 in 10 minutes, while, in batch analysis and stability studies the drug release in more than 80% in 60 minutes. Clarification is required.	Firm has stated: 'First of all, in stability studies the specifications for dissolution in NLT 80% in 30 minutes. Yes, our finished product shows more than 80% release in 0.1N HCl pH 1.2 in 10 minutes, and our results of dissolution are almost 100% on completion of time.'
viii.	Justify the adaptation of dissolution parameters and specs in the light if WHO/ ICH guidelines.	Firm has stated: 'As this is non compendial API and also have no data on any stringent site, so we develop or dissolution procedure according to Chapter 1092 of USP i.e. The Dissolution

		Procedure: Development and Validation. And ornidazole tablet is immediate release dosage form. So, we follow 6.5.1 and 2.4.1 point of USP. And ornidazole drug has PKa value 2.4 shows its solubility in acidic media so we selct 0.1N HCl (pH 1.2) as mentioned in USP.

Decision: Deferred for following submissions:

- **Evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.**
- **Justification for not performing pharmaceutical equivalence and CDP studies against the innovator product.**
- **Scientific justification for adaptation of acceptance criteria for dissolution test i.e. NLT 80% in 30 minutes since the product show more than 80% drug release within 10 minutes in the same dissolution medium when tested during CDP studies.**

New Licence (Veterinary) M/s Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore (DML#000935)		
Oral Liquid Section (Veterinary) **10 Products/ 10 molecules**		
334.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili EnroCol 20% Oral Liquid
	Composition	Each 100ml contains Enrofloxacin …… 20gm Colistin Sulphate … 50 MIU
	Diary No. Date of R& I & fee	PKR 30,000, R &I:28446, date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml, 100ml ,250ml, 500ml, 1 L, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Sunro E20 Oral Liquid (D-Haans Pharma Azad Kashmir) Reg No.102238
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
335.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili CRD Oral Liquid
	Composition	Each 1000ml contains: Tylosin Tartrate ….. 100gm Colistin sulfate…… 500MIU Doxycyline (as Hyclate) ….. 200gm Bromhexine……. 5gm
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28441, date: 15th October 2021
	Pharmacological Group	Antibiotic + mucolytic agent
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml,100ml, 250ml, 500ml, 1L ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Ztylo plus oral liquid (Zoic International Pharma Lahore) Reg No: 080932
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	• Me-too status not confirm.
	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.	
336.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Coli 20 Oral Liquid
	Composition	Each 1000ml contains: Colistin sulphate ……. 2,000,000,000 IU
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28437, date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5

	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100ml , 250ml , 500ml and 1 Litre , Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Colibar Oral Solution(Baariq pharmaceuticals Lahore **)** Reg No: **075784**
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
337.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Flor C Oral Liquid
	Composition	Each 100ml contains: Florfenicol…… 10gm Colistin sulphate…….. 2.5gm
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28442, date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml, 100ml,250ml, 500ml, 1 L
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Co-Flor Liquid (Wimits Pharmaceuticals pvt Ltd Lahore) Reg No: 078326
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
338.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	MiliBrom 50 Oral Liquid
	Composition	Each 1000ml contains: Bromhexine hydrochloride……. 50gm
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28448: date: 15th October 2021
	Pharmacological Group	Mucolytic agent
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml,100ml , 250ml , 500ml and 1L, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Brom- Z Oral Liquid (Zoic International Lahore) Reg No: 090662
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
339.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Tilmico 25 Oral Liquid
	Composition	Each 1000ml contains: Tilmicosin (base)…. 250gm
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28445, date: 15th October 2021
	Pharmacological Group	Macrolide Antibiotic

	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml,100ml , 250ml , 500ml and 1 Litre, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Zotil-250 Oral liquid (Zoic International pharma Lahore **)** Reg No: 080936
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
340.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Toltrazuril Oral Liquid
	Composition	Each ml contains: Toltrazuril …… 25mg
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28451, date: 15th October 2021
	Pharmacological Group	Anticoccidial agent
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml, 100ml ,250ml, 500ml, 1 L, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Ultrazuriq Oral Solution, (Baariq Pharmaceuticals Lahore) Reg No: 071093
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
341.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Hepa Plus Oral Liquid
	Composition	Each 100ml contains: DL-Methionine…… 5g L-Lysine Monochloride…… 10g Choline chloride……. 19g Cyanocobalamin ….. 1mg Sorbitol……10g
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28450, date: 15th October 2021
	Pharmacological Group	Nutritional supplements
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml, 100ml ,250ml, 500ml, 1 L, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Zoic Hepa Oral Solution (Zoic International Pharma Lahore) Reg No: 094463
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
342.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Adek Oral Liquid
	Composition	Each 1000ml Contains.

		Vitamin A ….30,000,000I.U Vitamin D3 ….1,000,000I.U Vitamin E …5000mg Vitamin K3 ….6000mg
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28431, date: 15th October 2021
	Pharmacological Group	Multivitamins
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml,100ml, 250ml, 500ml, 1L ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Adekbar Oral liquid (Baariq Pharmaceuticals Lahore) Reg No: 073950
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
343.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Ez Sel Oral Liquid
	Composition	Each 1000ml solution contains: Vitamin E ……150,000gm Selenium as Sodium Selenite …… 2300 mg Zinc as Zinc sulphate …… 8000mg
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28443, date: 15th October 2021
	Pharmacological Group	Multivitamin and minerals
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	50ml, 100ml ,250ml, 500ml, 1 L, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Sel-Ez- Oral liquid(Selmore pharmaceuticals) ,R.No: 073949
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	• Me-too status not confirm.
	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.	
Oral Powder Section (Veterinary) 10 Products/ 10 molecules		
344.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	MiliFosfocin Oral Powder
	Composition	Each Kg contains: Fosfomycin calcium …. .200g Tylosin tartrate ….. …….100g Fructose…… ……..180g Sodium Phosphate….. …150g Magnesium sulphate…. .100g
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28430, date: 15th October 2021
	Pharmacological Group	Antibacterial , Electrolytes
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm, 50gm , 100gm , 250gm , 500gm ,1kg and 5kg, Decontrolled
	Approval status of product in	N/A

	Reference Regulatory Authorities	
	Me-too status (with strength and dosage form)	Fosfo 20 Oral Powder (Evergreen Pharmaceuticals (Pvt) Ltd Lahore Reg No: 088861
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
345.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Linco 4.4% Powder
	Composition	Each 100g contains: Lincomycin HCl Monohydrate….. 4.4gm
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28433, date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100gm , 250gm , 500gm , 1kg , 5kg , 10kg and 15kg, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Linc Hans 4.4% Powder(D-Haans Pharma Pvt Ltd Azad Kashmir) Reg No: 102213
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
346.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili Linco C Oral Powder
	Composition	Each gm contains Lincomycin Hydrochloride ……. 100mg Colistin sulphate……... 800,000 IU
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28438, date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm, 50gm , 100gm , 250gm , 500gm and 1kg, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Z-lincolis water soluble powder (Zoic International Pharma Lahore) , Reg No: 080941)
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
347.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	MiliNeo 72% Oral Powder
	Composition	Each 1000gm contains: Neomycin Sulphate…… 720g
	Diary No. Date of R& I & fee	PKR 30,000 , R &I: 28442, date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100gm , 250gm , 500gm and 1kg, Decontrolled

	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Neozoc 720 Water Soluble Powder Zoic International Pharma Lahore Reg No: 090682
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
348.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Mili NOC 400 Oral Powder
	Composition	Each 100gm contains Neomycin sulphate …20gm Colistin sulphate …24MIU Oxytetracycline ….20gm
	Diary No. Date of R& I & fee	PKR 30,000, R &I date: 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm, 50gm , 100gm , 250gm , 500gm and 1kg, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Sulphamed-50 water soluble powder(D-Haans Pharma Pvt Ltd Azad Kashmir) Reg No: 102229
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	• Me-too status not confirm.
	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.	
349.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	MiliTyldox C Oral Powder
	Composition	Each 1000gm contains: Tylosin tartrate ……. 100gm Doxycycline HCl ….. 200gm Colistin sulphate …… 500MIU
	Diary No. Date of R& I & fee	PKR 30,000, R &I date:28440, 15th October 2021
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm , 50 gm , 100gm ,500gm and 1kg, Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Doxi -Tylo C Water Soluble Powder(Baariq Pharmaceuticals Lahore) Reg No: 079815
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
350.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	MiliColi 50 (ORAL POWDER)
	Composition	Each 1000gm contains Colistin sulphate ……. 500,000,000IU
	Diary No. Date of R& I & fee	PKR 30,000, R&I: 28444 date: 15th October 2021

	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100gm , 250gm , 500gm and 1 kg ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Colibect water soluble powder (Bariq Pharma Lahore Reg No**:** 075791)
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	• Me-too status not confirm from available database.
	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.	
351.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Amanta Mil -10% Oral Powder
	Composition	Each 100gm contains: Amantadine HCl….. 10g
	Diary No. Date of R& I & fee	PKR 30,000, R &I:28435, date: 15th October 2021
	Pharmacological Group	Antiviral
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm, 50gm , 100gm , 250gm , 500gm and 1kg ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Hansredin 10% water soluble Powder (D-Haans Pharma Pvt Ltd Azad Kashmir) Reg No: 102206
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
352.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	Levamil 50 Oral Powder
	Composition	Each gm contains: Levamisole HCL… 500mg
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28432, date: 15th October 2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm, 50gm , 100gm , 250gm , 500gm and 1kg , Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status (with strength and dosage form)	Levazoc -50 Water Soluble Powder (Zoic International Pharma) Reg No: 090661
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	
353.	Name and address of manufacturer / Applicant	Mili Vet pharmaceuticals (Pvt) Ltd Had Bast, Mouza Kamas, Tehsil Raiwind, District Lahore
	Brand Name +Dosage Form + Strength	MilizymE Oral Powder

	Composition	Each gram contains: Lysozyme …22.0% Vitamin E 50 SD …0.5%
	Diary No. Date of R& I & fee	PKR 30,000 , R &I:28449 date: 15th October 2021
	Pharmacological Group	Enzyme & Vitamin
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	20gm ,50gm , 100gm , 250gm , 500gm and 1kg ,Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Vitozyme Oral Powder (Selmore pharma) Reg.No: 049622
	GMP status	09-10-2020 & 23-04-2021 Grant of DML, Panel recommended grant of DML.
	Remarks of the Evaluator	
	Decision: Approved with innovator's specification.	

Deferred Cases

354.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Vectin 3.15% Injection (10ml)
	Composition	Each ml contains:- Ivermectin …… 31.5mg
	Diary No. Date of R& I & fee	Dy No.12008 : 21.04.2021 PKR. 20,000/-; 20.04.2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	10ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Elvomec Star Injection 3.15% (Selmore Pharma) R # 063728
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
355.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Vectin 3.15% Injection (50ml)
	Composition	Each ml contains:- Ivermectin …… 31.5mg
	Diary No. Date of R& I & fee	Dy No. 12009 : 21.04.2021 PKR. 20,000/-; 20.04.2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	50ml vial /Decontrolled

	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Elvomec Star Injection 3.15% (Selmore Pharma) R # 063728
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
356.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Vectin 3.15% Injection (100ml)
	Composition	Each ml contains:- Ivermectin …… 31.5mg
	Diary No. Date of R& I & fee	Dy No. 12010 : 21.04.2021 PKR. 20,000/-; 20.04.2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	100ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Elvomec Star Injection 3.15% (Selmore Pharma) R # 063728
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
357.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Vectin 1.05% Injection (10ml)
	Composition	Each ml contains:- Ivermectin …… 10.5mg
	Diary No. Date of R& I & fee	Dy No.12011 : 21.04.2021 PKR. 20,000/-; 20.04.2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	10ml vial /Decontrolled
	Approval status of product in Reference	N/A

	Regulatory Authorities	
	Me-too status	I-Mectin Injection (International Pharma) Reg # 063618
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
358.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Vectin 1.05% Injection (50ml)
	Composition	Each ml contains:- Ivermectin …… 10.5mg
	Diary No. Date of R& I & fee	Dy No.12012 : 21.04.2021 PKR. 20,000/-; 20.04.2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	50ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	I-Mectin Injection (International Pharma) Reg # 063618
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
359.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Vectin 1.05% Injection (100ml)
	Composition	Each ml contains:- Ivermectin …… 10.5mg
	Diary No. Date of R& I & fee	Dy No.12013 : 21.04.2021 PKR. 20,000/-; 20.04.2021
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	100ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A

	Me-too status	I-Mectin Injection (International Pharma) Reg # 063618
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
360.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Meloxter-8 Injection (50ml)
	Composition	Each ml contains:- Meloxicam ……..... 8mg
	Diary No. Date of R& I & fee	Dy No.12148 : 22.04.2021 PKR. 20,000/-; 22.04.2021
	Pharmacological Group	NSAID
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	50ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Mexibak 8% Injection (Attabak Pharma) Reg # 049779
	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	
	Prevoius decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
361.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	Meloxter-8 Injection (100ml)
	Composition	Each ml contains:- Meloxicam ……..... 8mg
	Diary No. Date of R& I & fee	Dy No.12149 : 22.04.2021 PKR. 20,000/-; 22.04.2021
	Pharmacological Group	NSAID
	Type of Form	Form 5
	Finished product Specifications	BP (Vet) Specifications
	Pack size & Demanded Price	100ml vial /Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Mexibak 8% Injection (Attabak Pharma) Reg # 049779

	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	
	Previous decision	The Board in its 308th meeting deferred the case for scientific rationale of related strength of the same formulation.
	Evaluation by PEC	Firm has submitted: • Registration Board parameters for registration is Me-too availability. • Me-too is available for the applied strengths approved by DRAP.
	Decision: Approved with BP (Vet) Specifications specification.	
362.	Name and address of manufacturer / Applicant	Aamster Laboratories Plot No. 18 St#SS-2, National Industrial Zone Rawat, Islamabad.
	Brand Name +Dosage Form + Strength	TRIMED-300 Oral Water Soluble Powder
	Composition	Each 100g contains:- Oxytetracycline HCl ……25g Neomycin sulphate ……. .25g Colistin sulphate ……..30MIU
	Diary No. Date of R& I & fee	Dy. 19073, 30-09-2019, Rs.20,000
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	100gm,250gm,500gm,1Kg,5Kg,10Kg, / Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Oxycol Forte Powder (Attabak Pharma) Reg No. 071068
	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	• The firm has applied for In-House specifications and the product is not present in available pharmacopoeia (USP, BP, IP, JP). • The firm has changed the quantity of Colistin sulphate from 300MIU to 30MIU without submission of fee.
	Previous decision	The Board in its 293rd meeting deferred the case for submission of fee Rs. 20,000/- for change of strength of Colistin sulphate from 300MIU to 30MIU.
	Evaluation by PEC	Firm has submitted Rs. 20,000/- vide challan number: 2006930 dated 02-012020.
	Decision: Approved with innovator's specification.	

Case No.01. Request for Change in Registration Status of Products from M/s Getz Pharma (Pvt) Ltd, 29-30, Sector 27, Korangi Industrial Area, Karachi to M/s Getz Pharma (Pvt) Ltd, Plot No.01, Sector 25, Korangi Industrial Area, Karachi

Registration Board in its 312th meeting held on 14th – 16th September, 2021 considered the request of M/s Getz Pharma (Pvt) Ltd, Plot No.01, Sector 25, Korangi Industrial Area, Karachi (DML No. 000933) for change in registration status of following products from M/s Getz Pharma (Pvt) Ltd, 29-30, Sector 27, Korangi Industrial Area, Karachi (DML No. 000284) to their name. Detail is given as under:

I	II	III	IV	V
S.No.	**Reg. No.**	**Product Name & Composition**	**Initial date of registration/ Remarks of RRR Section regarding Renewal Status**	**Diary No/Date/Fees.**
1.	026164	Leflox Tablets Each tablet contains:- Levofloxacin…..250mg	29/09/2000 Renewal application for year 2015 was submitted 02.08.2015 i.e. **late but within sixty days.**	Dy.No.19839 Date 15-07-2021 Rs.30,000 Invoice # 01976202 Date:15-06-2021 Dy. No. 21990 Date 11-08-2021
2.	026163	Leflox 500mg Tablets Each tablet contains:- Levofloxacin 500mg	29/09/2000 Renewal application for year 2015 was submitted 02.08.2015 i.e. **late but within sixty days.**	Dy.No.19840 Date 15-07-2021 Rs.30,000 Invoice # 34226044542 Date:15-06-2021 Dy. No. 21991 Date 11-08-2021

Administrative Documents in the light of SOP approved by the Registration Board in its 283rd meeting

i. Copy of DML No. 000933 issued w.e.f. 25-05-2021

ii. Panel Inspection report for grant of DML dated 09-03-2021.

iii. Approved sections verified from Licensing Division's letter for issuance of DML (dated 07th June, 2021):
- Tablet (General)
- Capsule (General)
- Dry Powder Suspension (General)

iv. NOC from M/s Getz Pharma (Pvt) Ltd, 29-30, Sector 27, Korangi Industrial Area, Karachi dated 14-06-2021.

v. Relevant undertakings & commitments.

The firm has further submitted that in accordance with WHO Variations Guidelines, they have submitted following documents of pilot scale batch manufactured at new manufacturing facility.

- ✓ Copy of Drug Manufacturing License.
- ✓ Copy of Inspection Report.
- ✓ Comparative dissolution tests in the routine release medium from current and new manufacturing sites.
- ✓ Commitment to perform Process Validation on three batches which includes comparative dissolution with f_2 calculation as necessary.
- ✓ Copy of release and shelf-life specifications.
- ✓ Batch analysis data on one batch from the new site and comparative data on the last three batches from the previous site.
- ✓ Stability Protocol and stability study report (initial time point) of pilot scale batch.
- ✓ Stability commitment to place the first 03 production-scale batch of the FPP produced at the new site into the long-term stability programme.

In the light of SOP approved by the Board in it 283rd meeting, after screening for administrative documents, the applications were forwarded to Pharmaceutical Evaluation Cell for scrutinization/ evaluation. Detail of submitted documents & remarks of evaluator have been mentioned as under:

POST REGISTRATION VARIATION (CHANGE OF MANUFACTURING SITE)

Following is a tabulated comparison of the variation guidelines of three different Regulatory agencies:

FDA SUPAC IR (OSD) GUIDELINES	European Commission Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorizations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures	WHO guidelines on variations to a prequalified product (TRS No. 981, 2013, Annex 3)
Level 2 Changes **1.** Definition of Level changes consist of site changes within a contiguous campus, or between facilities in adjacent city blocks, where the same equipment, SOP's, environmental conditions (e.g., temperature and humidity) and controls, and personnel common to both manufacturing sites are used, and where no changes are made to the manufacturing batch records, except for administrative information and the location of the facility. **2. Test Documentation** **a. Chemistry Documentation** Location of new site and updated batch records. None beyond application/compendial release requirements. One batch on long-term stability data reported in annual report. **b. Dissolution Documentation** None beyond application/compendial release requirements. **c.** In Vivo Bioequivalence Documentation	B.II.b.1 Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product. (IB) e) Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products Documentation: **1.** Proof that the proposed site is appropriately authorised for the pharmaceutical form or product concerned. **2.** Where relevant, the batch numbers, corresponding batch size and the manufacturing date of batches (≥ 3) used in the validation study should be indicated and the validation data presented, or validation protocol (scheme) to be submitted. **3.** The variation application form should clearly outline the 'present' and 'proposed' finished product manufacturers as listed in section 2.5 of the application form. **4.** Copy of approved release and end-of-shelf life specifications if relevant. **5.** Batch analysis data on one production batch and two pilot-scale batches simulating the production process (or two production batches) and comparative data on the last three batches from the previous site; batch data on the next two production batches should be available on request or reported if outside specifications (with proposed action). **6.** For semisolid and liquid formulations in which the active substance is present in non-dissolved form, appropriate	28 Addition or replacement of a manufacturing site for part or all of the manufacturing process for an FPP involving: 28c all other manufacturing operations except batch control and/or release testing Conditions to be fulfilled 1. No change in the batch formula, description of manufacturing process and process controls, equipment class & process controls of critical steps and intermediates or FPP specifications. 2. Satisfactory inspection in the last three years either by WHO or an SRA. 3. Site appropriately authorized by an NMRA (to manufacture the pharmaceutical form and the product concerned). 4. The change does not concern a sterile FPP. 5. Validation protocol is available or validation of the manufacturing process at the new site has been successfully carried out on at least three production-scale batches in accordance with the current protocol. Documents required: 1. Evidence that the proposed site has been properly authorized in the last three years. 2. Date and scope of last inspection. 3. Where applicable, for semi solid and liquid

None. **d. Filing Documentation** Changes being effected supplement; annual report (long term stability test data).	validation data including microscopic imaging of particle size distribution and morphology or any other appropriate imaging technique. **7.** i) If the new manufacturing site uses the active substance as a starting material — A declaration by the Qualified Person (QP) at the site responsible for batch release that the active substance is manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials as adopted by the Union. ii) In addition, if the new manufacturing site is located within the EU/EEA and uses the active substance as a starting material — A declaration by the Qualified Person (QP) of the new manufacturing site that the active substance used is manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials as adopted by the Union. **8.** Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 6B format for veterinary products, as appropriate). **9.** If the manufacturing site and the primary packaging site are different, conditions of transport and bulk storage should be specified and validated. B.II.b.2 Change to importer, batch release arrangements and quality control testing of the finished product. (IA) a) Replacement or addition of a site where batch control/testing takes place. Conditions: 2. The site is appropriately authorised. 3. The product is not a biological/immunological medicinal product. 4. Method transfer from the old to the new site or new test laboratory has been successfully completed. 5. At least one batch control/testing site remains within the EU/EEA or in a country where an operational and suitably scoped GMP mutual recognition agreement (MRA) exists between the country concerned and the EU, that is able to carry out product testing for the purpose of batch release within the EU/EEA.	formulations in which the API is present in non dissolved form, appropriate validation data including microscopic imaging of particle size distribution & morphology. 4. (P.2)For solid dosage forms, data on comparative dissolution tests in the routine release medium, with demonstration of similarity of dissolution profiles with those of the biobatch, performed on one production-scale batch each from current and proposed manufacturing sites and comparison with the biobatch results, with commitment to generate dissolution profiles on two more production-scale batches. 5. (P.3.5) Process validation reports or validation protocol (scheme) for three batches of the proposed batch size, which includes comparative dissolution against the biobatch results with f2 calculation as necessary. 6. (P.5.1) Copies of release and shelf-life specifications. 7. (P.5.4) Batch analysis data on one production-scale batch from the proposed site and comparative data on the last three batches from the previous site. 8. (P.8.2) Updated post-acceptance stability protocol and stability commitment to place the first production-scale batch of the FPP produced at the new site into the long-term stability programme (bracketing and matrixing for multiple strengths and packaging components could be applied, if scientifically justified). 9. (R.1) Executed production documents for one batch of

	Documentation 1. For a site within the EU/EEA: Attach copy of manufacturing authorisation(s) or where no manufacturing authorisation exists a certificate of GMP compliance issued within the last 3 years by the relevant competent authority. 2. For a manufacturing site outside the EEA where an operational GMP mutual recognition agreement (MRA) exists between the country concerned and the EU: a GMP certificate, issued within the last 3 years by the relevant competent authority. Where no such agreement exists a GMP certificate issued within the last 3 years by a EU/EEA competent authority. 5. Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 6B format for veterinary products, as appropriate), including revised product information as appropriate.	the FPP manufactured at the new site. 29 Replacement or addition of a site involving batch control testing. Conditions to be fulfilled 1. Site is appropriately authorized by the NMRA and satisfactorily inspected either by WHO or an SRA. 2. Transfer of methods from the current testing site to the proposed testing site has been successfully completed. Documentation required 1. Clear identification of the currently accepted and proposed quality control sites on the letter accompanying the application. 2. Documented evidence that the site is appropriately authorized by the NMRA & satisfactorily inspected by HWO or SRA. 3. (P.5.3) Documented evidence of successful transfer of analytical procedures from the current to proposed site.

Proceedings: Registration Board was briefed regarding the data submitted by firm as per WHO TRS 981,2013 (47th report, Annex 3) and SOP for approval of post-registration variations approved in 283rd DRB meeting. Board was also apprised that firm has changed sources of APIs for following products and has submitted stability data of the products with changed source from both current & new site. The details of the source change and stability data have been summarized in following table:

Brand name	**API**	**API Source of Stability Batches till shelf life (Current Site)**	**API Source (In-use at Current Site**	**API Source (New Site)**	**Stability data with the in-use API source**	
					Current site (On-going commercial)	**New site**
Leflox Tablet	Levofloxacin	M/s Gencare Pharmaceuticals Pvt. Ltd. - India	M/s Zhejiang East-Asia Pharmaceutical Co., Ltd. – China	M/s Zhejiang East-Asia Pharmaceutical Co., Ltd. – China	0, 3, 6, 9, 12, 18, 24	0, 3

Moreover, firm has also submitted 3-month stability studies data of two batches (10,000 units each) for applied products from new site.

1.	Name, address of applicant.	M/s Getz Pharma (Pvt.) Ltd. Plot No. 01, Sector 25, Korangi Industrial Area, Karachi Pakistan
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Ltd. Plot No. 01, Sector 25, 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.: 21990 and 11-08-2021
	Details of fee submitted	PKR 30,000/-: 15-06-2021
	The proposed proprietary name / brand name	Leflox Tablets 250mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Levofloxacin USP… 250mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	10's
	Proposed unit price	Rs. 426.99/-
	The status in reference regulatory authorities	"LEVOFLOXACIN Tablets 250mg" Approved by Health US-FDA manufactured by TEVA.
	For generic drugs (me-too status)	LEFLOX TABLETS 250mg (Reg. No.: 026164) manufactured by M/s Getz Pharma (Pvt.) Limited, Plot no. 29 – 30, Sector 27 Korangi Industrial Area, Karachi
	Name and address of API manufacturer.	M/s Zhejiang East-Asia Pharmaceutical Co., Ltd., Coastal Industrial City, Pubagang town, Sanmen county, Zhejiang 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 drug substance related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, 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 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, 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	**Getz Pharma (Pvt) Limited Plot no. 29 – 30, sector 27**

	Comparative Dissolution Profile	**Korangi Industrial Area, Karachi** Pharmaceutical Equivalence Studies & Comparative Dissolution Profile studies of Leflox Tablets 250mg against the reference product Levaquin Tablet 250mg, in three dissolution mediums has been submitted wherein more than 85% of drug is released in 15 minutes. **Getz Pharma (Pvt) Limited** **Plot No. 01, Sector 25 Korangi Industrial Area, Karachi** Firm has also submitted the Comparative Dissolution Profile studies of Leflox Tablets 250mg against the reference product Tavanic Tablet 250mg in Routine Release Medium wherein more than 85% of drug is released in 15 minutes..
	Analytical method validation/ verification of product	Firm has submitted verification studies of the drug substance and drug product.
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions from existing site and stability studies data of two batches at initial time interval (both accelerated and long term conditions) from new site.

STABILITY STUDY DATA (Plot No. 29-30, Sector 27, Korangi Industrial Area, Karachi)			
Manufacturer of APIs	M/s Gencare Pharmaceuticals Pvt. Ltd., Adargunchi, Karnataka, India.		
API Lot No.	C008-1412302, C008-1412303		
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	Accelerated: 6 months Real Time: 36 months		
Frequency	Accelerated: Initial, 3, 6 months Real Time: Initial, 3, 6, 9, 12, 18, 24 & 36 months		
Batch No.	280F08	281F08	282F08
Batch Size	1,050,000 Tablets	1,050,000 Tablets	1,050,000 Tablets
Manufacturing Date	08.05.2015	08.05.2015	08.05.2015
Date of initiation	20.06.2015	20.06.2015	20.06.2015
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 Estine (Ebastine) tablets 10mg & 20mg which was conducted on 06th May, 2019 and was presented in 289th meeting of Registration Board held on 14th -16th May, 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.	The firm has submitted the GMP Certificate of current drug substance manufacturer.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice attested by AD I&E DRAP, Karachi.

Batch No.	**Invoice No.**	**Date of approval by DRAP**
C008-1412302	PLCL/GPPL /2015/165	03.04.2015
C008-1412303		

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 attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets.
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 & 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)

STABILITY STUDY DATA (Plot No. 01, Sector 25 Korangi Industrial Area, Karachi)

Manufacturer of APIs	M/s Zhejiang East-Asia Pharmaceutical Co., Ltd., Costal Industrial City, Pubagang town, Sanmen county, Zhejiang province, P.R. China.		
API Lot No.	DC-004-2011007		
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: 0, 3 months Accelerated: 0, 3 months		
Frequency	Accelerated: Initial, 3, 6 months Real Time: Initial, 3, 6, 9, 12, 18, 24 & 36 months		
Batch No.	008ES01	008ES02	-
Batch Size	10,000 Tablets	10,000 Tablets	-
Manufacturing Date	28.05.2021	28.05.2021	-
Date of initiation	08.06.2021	08.06.2021	-
No. of Batches	02		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Getz Pharma (Pvt.) Limited situated at Plot No. 01, Sector 25 Korangi Industrial Area, Karachi 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 DML (No. Zhe20000312) issued by China Food and Drug Administration valid till October 07, 2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice attested by AD I&E 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 data of stability batches along with attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets.
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 & humidity monitoring	Firm has submitted record of digital data logger for temperature & humidity monitoring of stability chambers (real time and

Batch No.	**Invoice No.**	**Date of approval by DRAP**
DC-004-2011007	JC202010021-1	11.01.2021

	of stability chambers (real time and accelerated)	accelerated)
2.	Name, address of applicant.	M/s Getz Pharma (Pvt.) Ltd. Plot No. 01, Sector 25, Korangi Industrial Area, Karachi Pakistan
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Ltd. Plot No. 01, Sector 25, 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.: 21991 and 11-08-2021
	Details of fee submitted	PKR 30,000/-: 15-06-2021
	The proposed proprietary name / brand name	Leflox Tablets 500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Levofloxacin USP… 500mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	10's
	Proposed unit price	Rs. 445.91/-
	The status in reference regulatory authorities	"LEVOFLOXACIN Tablets 500mg" Approved by Health US-FDA manufactured by TEVA.
	For generic drugs (me-too status)	LEFLOX TABLETS 500mg (Reg. No.: 026163) manufactured by M/s Getz Pharma (Pvt.) Limited, Plot no. 29 – 30, Sector 27 Korangi Industrial Area, Karachi
	Name and address of API manufacturer.	M/s Zhejiang East-Asia Pharmaceutical Co., Ltd., Coastal Industrial City, Pubagang town, Sanmen county, Zhejiang 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 drug substance related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, 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 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, 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	**Getz Pharma (Pvt) Limited Plot no. 29 – 30, Sector 27, Korangi Industrial Area, Karachi** Pharmaceutical Equivalence Studies & Comparative Dissolution Profile studies of Leflox Tablets 500mg against the reference product of Levaquin Tablet 250mg, in three dissolution mediums has been submitted wherein more than 85% of drug is released in 15 minutes. **Getz Pharma (Pvt) Limited** **Plot No. 01, Sector 25, Korangi Industrial Area, Karachi** Firm has also submitted additionally the Comparative Dissolution Profile studies of Leflox Tablets 500mg against the reference product of Tavanic Tablet 500mg in Routine Release Medium wherein more than 85% of drug is released in 15 minutes.		
	Analytical method validation/ verification of product	Firm has submitted verification studies of the drug substance and drug product.		
	Stability studies	Firm has submitted stability studies data of three batches at both accelerated and long term conditions from existing site and stability studies data of two batches at initial time interval (both accelerated and long term conditions) from new site.		
STABILITY STUDY DATA (Plot No. 29-30, Sector 27, Korangi Industrial Area, Karachi)				
Manufacturer of APIs		M/s Gencare Pharmaceuticals Pvt. Ltd., Adargunchi, Karnataka, India.		
API Lot No.		C008-1412303, C008-1501301		
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		Accelerated: 6 months Real Time: 36 months		
Frequency		Accelerated: Initial, 3, 6 months Real Time: Initial, 3, 6, 9, 12, 18, 24 & 36 months		
Batch No.		351F09	352F09	353F09
Batch Size		562,200 Tablets	562,200 Tablets	562,200 Tablets
Manufacturing Date		13.05.2015	13.05.2015	13.05.2015
Date of initiation		10.07.2015	10.07.2015	10.07.2015
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 Estine (Ebastine) tablets 10mg & 20mg which was conducted on 06th May, 2019 and was presented in 289th meeting of Registration Board held on 14th -16th May, 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	The firm has submitted the GMP Certificate of current drug substance manufacturer.		

	country of origin.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice attested by AD I&E DRAP, Karachi. **Batch No.** / **Invoice No.** / **Date of approval by DRAP** C008-1412303, C008-1501301 / PLCL/GPPL /2015/165 / 03.04.2015
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 attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets.
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 & 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)

STABILITY STUDY DATA (Plot No. 01, Sector 25 Korangi Industrial Area, Karachi)

Manufacturer of APIs	M/s Zhejiang East-Asia Pharmaceutical Co., Ltd., Costal Industrial City, Pubagang town, Sanmen county, Zhejiang province, P.R. China.		
API Lot No.	DC-004-2011007		
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: 0, 3 months Accelerated: 0, 3 months		
Frequency	Accelerated: Initial, 3, 6 months Real Time: Initial, 3, 6, 9, 12, 18, 24 & 36 months		
Batch No.	014ES01	014ES02	-
Batch Size	10,000 Tablets	10,000 Tablets	-
Manufacturing Date	31.05.2021	31.05.2021	-
Date of initiation	08.06.2021	08.06.2021	-
No. of Batches	02		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

#	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Getz Pharma (Pvt.) Limited situated at Plot No. 01, Sector 25 Korangi Industrial Area, Karachi 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 DML (No. Zhe20000312) issued by China Food and Drug Administration valid till October 07, 2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice attested by AD I&E DRAP, Karachi. **Batch No.** / **Invoice No.** / **Date of approval by DRAP** DC-004-2011007 / JC202010021-1 / 11.01.2021
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 data of stability batches along with attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets.
5.	Compliance Record of HPLC	Firm has submitted compliance certificate of HPLC software and

	software 21CFR & audit trail reports on product testing.	audit trail reports on product testing..
6.	Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time & accelerated)	Firm has submitted record of digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)

Remarks of the Evaluator:

The firm has submitted the following documents as per WHO TRS 981, 2013 (47th report, Annex 3) and SOP for approval of post-registration variations approved in 283rd DRB meeting:

- Stability Data of 3 batches till shelf life manufactured at their existing facility located at Plot No. 29 – 30, Sector 27, Korangi Industrial Area.
- Stability Data of 2 stability batches (at initial time point) from new facility located at Plot No. 01, Sector 25, Korangi Industrial Area as per Guidance Document for Submission of Application on Form 5-F (CTD) for registration of pharmaceutical drug products for human use issued in October.
- Comparative Dissolution Profile and Pharmaceutical Equivalence studies of the product with the innovator from existing manufacturing facility & also submitted Comparative Dissolution Profile against innovator from new manufacturing facility.
- Comparative batch analysis data on two batches from the new facility and comparative data on the last three batches from the existing facility.
- Executed Production document of stability batch.
- Process Validation Protocol from new site.
- Undertakings in accordance with SOP for approval of post-registration variations by DRAP.
- Analytical Method Verification / validation studies of API & Finished product.
- Valid GMP Certificate of the API manufacturer.
- Data of pre-validation batch / pilot scale batch of Leflox Tablets 250mg (Batch No. 008SE01, Batch Size: 60,000 Tablets).

Decision of M-312:

Deferred the case w.r.t following products for submission of requisite fee for renewal i.e., applied after due date.

S. No.	Reg. No.	Product Name
1.	026164	Leflox Tablets Each tablet contains:- Levofloxacin……..……...250mg
2.	026163	Leflox 500mg Tablets Each tablet contains:- Levofloxacin 500mg

The firm has now submitted copy differential fee of Rs.15000/- each (for renewal of registration) and same has been verified from https://fee.dra.gov.pk/.

S.#	Reg.#	Product Name & Composition	Invoice No., Fees & Date
1.	026164	Leflox Tablets Each tablet contains:- Levofloxacin……...250mg	Invoice# 9028271867 Fees: Rs.15000/- Date: 21-09-2021
2.	026163	Leflox 500mg Tablets Each tablet contains:- Levofloxacin 500mg	Invoice# 85987709059 Fees: Rs.15000/- Date: 21-09-2021

Proceedings of M-313:

The Board was further informed that above-mentioned renewal applications of M/s Getz Pharma (Pvt) Ltd, 29-30, Sector 27, Korangi Industrial Area, Karachi (DML No. 000284) are also included in agenda of RRR section under Case No.1.

Decision: Registration Board decided as under:

i. Cancelled registration of following products from the name of M/s Getz Pharma (Pvt) Ltd, 29-30, Sector 27, Korangi Industrial Area, Karachi (DML No. 000284).

S. No.	Reg. No.	Product Name & Composition
1.	**026164**	**Leflox Tablets** **Each tablet contains:-**

		Levofloxacin……..250mg
2.	**026163**	**Leflox 500mg Tablets Each tablet contains:- Levofloxacin 500mg**

ii. Approved registration of following products in the name of M/s Getz Pharma (Pvt) Ltd, Plot No.01, Sector 25, Korangi Industrial Area, Karachi (DML No. 000933) with same registration numbers in the light of legal opinion furnished by Legal Affairs Division, DRAP vide letter F.No. 11-1/2018/DD(LA)-Vol-I dated 05-10-2021.

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.

c) Furthermore, keeping in view the real time stability data (performed at M/s Getz; DML 000284) and data submitted (by M/s Getz; DML 000933) as per WHO TRS 981,2013 (47th report, Annex 3), registration letter will be issued with shelf life of 36 Months as done in previous cases.

S. No.	Reg. No.	Product Name & Composition
1.	**026164**	**Leflox Tablets 250mg Each film coated tablet contains:- Levofloxacin……..……...250mg (USP Specifications)**
2.	**026163**	**Leflox Tablets 500mg Each film coated tablet contains:- Levofloxacin……...500mg (USP Specifications)**

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.2. Requests/ Intimations of Various Firms for Withdrawal/ Discontinuation/ Cancellation of Registration of their Registered Drugs

Request For De- Registration of Products By M/s Novartis Pharma (Pakistan) Limited, 15 West Wharf, Dockyard Road, Karachi.

S/N	Reg. No.	Brand name and composition	Justification	Alternate Brands	Date of Reg. & Last Renewal Status
I	II	III	IV	V	VI
1.	023316	Butal 400mg Tablet Each tablet contains: Ethambutol…….400mg	Due to business non-viability	1. Abbutol by M/s Abbott 2. Ethambutol by M/s. Alina Combine.	02-02-1999
2.	023054	Clorotir Capsules Each capsule contains: Cefaclor……500mg	Due to business non-viability	1. Cefanol by M/s Abbott 2. Cedor by M/s AGP. 3. Alcef by M/s. Alina Combine.	15-03-1999
3.	014670	Dotur Capsule 100mg Each capsule contains: Doxycycline (as dihydrochloride)…….100mg	Due to business non-viability	1. Doxyn by M/s Atco 2. Hyclodox by M/s Danas 3. Doxy Day by M/s Davis.	31-03-2001
4.	032638	Elgin Tablets 500ug Each tablet contains: Mecobalamin……..0.5mg	Due to business non-viability	1. Balco by M/s AGP 2. Mecomin by M/s Akhai.	**Reg. date:** 13-08-2004 **Transfer of**

				3. Robalin by M/s Akson	**Reg** from M/s Amson Vaccines & Pharma (Pvt) Ltd., Islamabad to M/s Novartis Pharma (Pakistan) Limited, Karachi: 12-06-2008
5.	004714	Parlodel 2.5mg Tablets Each tablet contains: Bromocriptine Mesylate……2.5mg (Manufacturer Specifications)	Due to business non-viability	1. Brolib by M/s Libra 2. Bromit by M/s Martin Dow. 3. Bromotin by M/s Caraway.	22-01-2020
6.	083006	Nocid 40mg/5ml Suspension Each 5 ml of reconstituted suspension contains: Famotidine …… 40 mg (Manufacture Specification)	Due to business non-viability	1. Acicon AD by M/s Barret Hodgson 2. Nocer by M/s Bryon 3. Nocid by M/s Novartis.	**Reg. date:** 14-11-2016
7.	070691	Tamsuna Capsule 0.2mg Each capsule contains: Tamsulosin HCl …….0.2 mg (Manufacturer's Specification)	Due to business non-viability	1. Maxiflo by M/s. Ferozsons. 2. Tamsolin by M/s Getz. 3. Tamsol by M/s Global	**Reg. date:** 18-08-2011
8.	070692	Tamsuna Capsule 0.4mg Each capsule contains: Tamsulosin HCl …….0.4 mg (Manufacturer's Specification)	Due to business non-viability	1. Prostreat by M/s Asian Continental 2. Prostop by M/s Aulton. 3. Tamusin by M/s Adcare Pharma.	**Reg. date:** 18-08-2011
9.	070693	Fe Aid Tablet Each chewable tablet contains: Iron III Hydroxide Polymaltose Complex eq. to Elemental Iron……....100 mg (Manufacturer's Specification)	Due to business non-viability	1. Fersip by M/s Scotman 2. Ipcom by M/s Searle. 3. Iroton by M/s Shaigan.	**Reg. date:** 18-08-2011
10.	070694	Fe Aid Syrup Each 5ml contains: Iron III Hydroxide Polymaltose Complex eq. to Elemental Iron……50mg (Manufacturer's Specification)	Due to business non-viability	1. Polon by M/s. Adamjee. 2. Rubifer by M/s AGP. 3. Hemitose by M/s Akson.	**Reg. date:** 18-08-2011
11.	070695	Fe Aid Drops Each ml contains: Iron III Hydroxide Polymaltose Complex eq. to Elemental Iron……..50 mg (Manufacturer's Specification)	Due to business non-viability	1. Rubifer by M/s AGP. 2. RBC by M/s Genix 3. Ferlife by M/s. Asian Continental	**Reg. date:** 18-08-2011
12.	070696	Fe Aid Plus Tablet Each chewable tablet contains: Iron III Hydroxide	Due to business non-viability	1. Polon by M/s. Adamjee. 2. Addfer-F by M/s	**Reg. date:** 18-08-2011

		Polymaltose Complex eq. to Elemental Iron…..100 mg Folic Acid ……...0.35 mg (Manufacturer's Specification)		Atco. 3. Polyfer FA by M/s Barret hodgson.	
13.	030398	Noktan Tablets 25mg Each tablet contains:- Losartan Potassium ….25mg	Due to business non-viability	1. Lostress by M/s Atco 2. Sozaar by M/s Alliance 3. Parlak by M/s Ambrosia	**Reg. date:** 30-06-2003
14.	030399	Noktan Tablets 50mg Each tablet contains:- Losartan Potassium …50mg	Due to business non-viability	1. Losium by M/s Madera 2. Tilosar by M/s Medicaids 3. Medizar by M/s Mediceena	**Reg. date:** 30-06-2003
15.	048831	Risperidone-Sandoz 1mg Tablet Each film coated tablet contains:- Risperidone…….1mg (Manufacturer's Specification)	Due to business non-viability	1. Risp by M/s Adamjee 2. Choir by M/s AGP 3. Neoris by M/s Amarant	**Reg. date:** 22-07-2008 **Last Renewal:** 05-07-2018
16.	048832	Risperidone-Sandoz 2mg Tablet Each film coated tablet contains:- Risperidone…….2mg (Manufacturer's Specification)	Due to business non-viability	y M/s Adamjee by M/s AGP one by M/s Akson	**Reg. date:** 22-07-2008 **Last Renewal:** 05-07-2018
17.	048833	Risperidone-Sandoz 3mg Tablet Each film coated tablet contains:- Risperidone…….3mg (Manufacturer's Specification)	Due to business non-viability	1. Risp by M/s Adamjee 2. Choir by M/s AGP 3. Neoris by M/s Amarant	**Reg. date:** 22-07-2008 **Last Renewal:** 05-07-2018
18.	048834	Risperidone-Sandoz 4mg Tablet Each film coated tablet contains:- Risperidone……...4mg (Manufacturer's Specification)	Due to business non-viability	1. Risp by M/s Adamjee 2. Choir by M/s AGP 3. Neoris by M/s Amarant	**Reg. date:** 22-07-2008 **Last Renewal:** 05-07-2018
19.	076539	Zumatram P Tablet Each film coated tablet contains: Tramadol HCl …...37.5mg Paracetamol ……..325mg (Manufacturer Specification)	Due to business non-viability	1. Campex-P by M/s Akhai 2. Tdol-P by M/s Alina Combine 3. Acetra by M/s Amarant	**Reg. date:** 03-10-2014
20.	076540	Zumatram 100mg Tablet Each prolonged release tablet contains: Tramadol HCl ……100 mg (Manufacturer Specification)	Due to business non-viability	1. Campex by M/s Akhai 2. Calfina by M/s AGP 3. Amadol by M/s Amarant	**Reg. date:** 03-10-2014
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 not provided in some cases) 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.

S/N	Reg. No.	Brand name and composition	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….25mg	➢ 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.	1. Cortec Plus by M/s Nabiqasim 2. Co-Renitec by M/s OBS 3. Cardace-H by M/s Zafa	**Reg. date:** 26-02-1987 **Transfer of Reg.** From M/s Bristol Myers Squibb (Pvt.0 Ltd. to GSK Pakistan Ltd.**:** 01-10-2010 **Last Renewal:** 18-09-2020
2.	013816	Monopril 10mg Tablets Each tablet contains: Fosinopril Sodium…10mg		1. Aksopril by M/s Akson Pharma	**Reg. date:** 17-11-1992 **Transfer of Reg** From M/s Bristol Myers Squibb (Pvt.0 Ltd. to GSK Pakistan Ltd.**:** 01-10-2010 **Last Renewal:** 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.			

Request For De- Registration of Local Products By M/s GlaxoSmithKline Pakistan Limited, F-268, S.I.T.E, Karachi.

S/N	Reg. No.	Brand name and composition	Justification	Alternate Brands	Date of Reg. & Last Renewal Status
I	II	III	IV	V	VI
1.	075850	Coarbid 80/480mg Tablets Each tablet contains:- Artemether …….…80mg Lumefantrine …….480mg (Manufacturer's Specification)	➢ 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	1. Defal of M/s Abbott. 2. MalEra of M/s Barret Hodgson 3. Qmetem of M/s Bosch	**Reg. date:** 10-04-2013 **Last Renewal:** 15-02-2018

			there is no demand of this product in local market.		
2.	013321	Nemazole Suspension Each 5ml contains: Mebendazole…….100mg	➢ 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.		**Reg. date:** 25-05-1992 **Transfer of Reg** From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi**:** 30-08-2003 **Last Renewal:** 20-07-2018
3.	017306	Nemazole-500 Chewable Tablets Each tablet contains: Mebendazole…….500mg		1. Vermox of M/s Aspin 2. Vermin of M/s Adamjee 3. Vermol of M/s Woodwards	**Reg. date:** 21-06-1995 **Transfer of Reg** From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi**:** 30-08-2003 **Last Renewal:** 20-07-2018
4.	013320	Neamzole Tablets Each tablet contains: Mebendazole…….100mg			**Reg. date:** 25-05-1992 **Transfer of Reg** From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi**:** 30-08-2003 **Last Renewal:** 20-07-2018
5.	000219	Orbenin Syrup 125mg/ml		1. Aksopril by M/s Akson Pharma	**Reg. date:** 16-04-1976 **Transfer of Reg** From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi**:** 30-08-2003 **Last Renewal:** 20-07-2018
6.	000217	Penbritin Paediatric Drops 100mg/ml		1. Omnipen of M/s Pfizer	**Reg. date:** 16-04-1976

				2. Standacillin by M/s Novartis. 3. Arpicillin by M/s Sanofi.	**Transfer of Reg** From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi**:** 30-08-2003 **Last Renewal:** 03-08-2018
7.	000216	Penbritin Syrup 125mg/5ml	➢ 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.		**Reg. date:** 16-04-1976 **Transfer of Reg** From M/s Glaxo Wellcome to M/s GSK Pakistan Ltd., Karachi**:** 30-08-2003 **Last Renewal:** 03-08-2020
8.	024305	Zeatin Tablets Each tablet contains:- Cetirizine Dihydrochloride…….10mg		1. Zyrtec by M/s Gsk 2. Rigix by M/s AGP 3. Gixer by M/s Barret Hodgson.	**Reg. date:** 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:** 24-11-2017
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 License Withdrawal of Locally Registered Products By M/s SANOFI, Karachi					
S/N	**Reg. No.**	**Brand name and composition**	**Justification**	**Alternate Brands**	**Date of Reg. & Last Renewal Status**
I	**II**	**III**	**IV**	**V**	**VI**
1.	010805	Rulid Tablets 100mg Each tablet contains: Rexithromycin……100mg	Product is not in demand and better	1. Plusate Tablet 100mg by M/s Sami 2. Roxy Tablet 100mg	**Reg. date:** 27-03-1990

			molecules are available for patient's use. Furthermore, Rulid Tablet 150mg is freely available in the market to fulfil patient's needs.	by M/s Paramount. 3. Strike Tablet 100mg by M/s Tagma Pharma.	**Last Renewal:** 03-05-2016
2.	015352	Rulid 300mg Tablets Each tablet contains: Rexithromycin……300mg		1. Plusate Tablet 300mg by M/s Sami 2. Roxy Tablet 300mg by M/s Paramount. 3. Strike Tablet 300mg by M/s Tagma Pharma	**Reg. date:** 22-06-1994 **Last Renewal:** 03-05-2016
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.			

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	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.	**Reg. date:** 30-11-2006 **Last Renewal:** 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 **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.3. **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.**

Registration Board, in its 296th meeting held on 08th-10th September, 2020 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"*** as per following details:

Proceedings of M-296:

Registration Board, in its 288th meeting held on 14th -15th February, 2019 considered the case regarding issuance of show cause notice to registration holders of Diclofenac Potassium 75 and 100mg (Ref. M-258) and current status of court cases filed by different firms against the decision of Registration Board, taken vide its 258th meeting.

Proceedings of M-288:

Registration Board, in its 248th meeting considered the request of M/s Cibex (Pvt.) Ltd Plot No. F-405, S.I.T.E, Karachi wherein it was informed by the firm that have developed their facility for manufacturing of Tablet (General), Capsule (General), Sachet (General), Tablet (General Antibiotics),

Liquid Manufacturing, Capsule (General Antibiotics), Dry Syrup (General Antibiotics), Ointment-I (Steriods) and Ointment-II (Non Steriods) located at Plot No. F-405, S.I.T.E, Karachi vide Drug Manufacturing License No.000784.

The firm has requested for transfer of their following registered drugs from M/s Macter International Ltd, Karachi to their name as per following details: -

Sr. No.	Reg. No.	Brand Name(s)	Formulation / Generic Name	Date of Registration	Remarks
1.	027108	Famobex Suspension	Each 5ml contains:- Famotidine….10mg	13-06-2001	The applied formulation is not approved in SRA's
2.	039198	Catafen Tablets 100mg	Each sugar coated tablet contains:- Diclofenac Potassium…….100mg	26-05-2005	Formalities required as per Form -5 are complete

Registration Board in its 248th meeting approved the product at Sr.No.2 and deferred the product at Sr.No.1 for review of formulation.

For product at Sr.No.1 the firm has submitted that the same formulation is freely available, manufactured and marketed by multiple firms in Pakistan. These products are old registered products and were registered prior from the implementation of SRA regime. DRAP has not taken any action to withdraw this product from the market or stop its manufacturing. DRAP has also awarded price increase for same product (Al-Famot) to Ali Industries vide SRO 908(I)/2017 dated 07-09-2017, which demonstrate DRAP's intention to patronize selected companies which unfortunately is discriminating. W.r.t. product at Sr.No.2, the firm has stated that multiple companies are still manufacturing the 75mg and 100mg strength of this molecule without any hindrance from DRAP. Therefore, non issuance of registration is unconstitutional and illegal. They have requested to grant them registration of above products.

Furthermore, the firm has submitted that "if DRAP issues registration letters of above mentioned two products, we are ready to withdraw the suit (CP Suit No.1545/2017, Cibex vs DRAP & others) filed by us against DRAP and also undertake to stop manufacturing and marketing these two products if other companies are compelled by DRAP to withdraw these products from market."

The case was deferred in 14th meeting of PRVC for deliberation in next meeting. Later on the case was reconsidered in 19th PRVC with following decision taken:

Decision of 19th PRVC:

The Committee deferred the case for presentation before registration board in next meeting with complete background, record and updated status of WP No 1695/2017 filed in Islamabad High Court Islamabad by M/s. Quaper Pharma V/S Federation of Pakistan, in the case of Diclofenec Potassium 100 mg Tablets.

Background

W.r.t above mentioned two formulations, the Registration Board has already taken following decisions:

Sr. No.	Formulation	Ref. Meeting No. of Reg. Board	Decision/Remarks
1.	Famotidine 10mg/5ml Suspension	M-250	***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.
2.	Diclofenac	M-258	**Decision:**

	Potassium 75mg & 100mg		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.

In this regard, manufactures of Diclofenac Potassium 75mg & 100mg Tablets have already been issued show cause notice including following firms:

S. No	Reg. No.	Firm Name	Name of drug(s) & Composition
1.	021634	M/s Global Pharmaceuticals, Plot no.204-205, Industrial Triangle, Kahuta Road, Islamabad.	Artinil-K Tablets 75mg Each tablet contains: Diclofenac Potassium……..75mg
2.	066670	M/s. Medizan Labs. (Pvt) Ltd. P.No. 313, Industrial Triangle Kahuta Road, Islamabad	Qrelif-75 Tablets Each tablet contains: Diclofenac Potassium…….75mg
3.	027876	M/s. Valor Pharmaceuticals, 124/A Kahuta Road, Industrial Triangle Zone, Islamabad.	Vaclo-Pot Tablets Each tablet contains: Diclofenac Potassium…….75mg
4.	028340	M/s. Robins Pharmaceuticals Industries, 43, Industrial Triangle, Kahutta Road, Islamabad	Dinak Tablets Each tablet contains: Diclofenac Potassium…….75mg
5.	031800	Technovision Pharmaceuticals 295-Industrial Triangle, Kahuta Road.	Ketagesic-75 Tablets Each tablet contains: Diclofenac Potassium…….75mg
6.	037415	Makson Pharmaceuticals Plot No.80-B, Street No.6I-10/3, Industrial Area Islamabad	Makaid-K 75Mg Tablets Each tablet contains: Diclofenac Potassium…….75mg
7.	056845	Webros Pharmaceuticals, Plot# 1, Street# 10, RCCI Industrial Estate, Rawat, Islamabad	Deltaflam Tablets 75mg. Each Tablet Contains :- Diclofenac Potassium.....75mg.
8.	038437	Pearl Pharmaceuticals, Plot No.204, Street No.1, I-10/3, Islamabad	Phlodic-K Each Tablet Contains :- Diclofenac Potassium.....75mg.
9.	024333	Candid Pharmaceutical, Opposite Pasrur Suagr Mills Sialkot Road, Pasru	Kalfen Tablets Each tablet contains:- Diclofenac Potassium.....75mg
10.	047860	M/s. Wise Pharmaceuticals, Plot no.3-A, S-1, RCCI Industrial Estate, Rawat, Islamabad.	Achex-75mg Tablets Each film coated tablet contains: Diclofenac Potassium.....75mg
11.	049385	M/s shawan Pharmaceuticals, Plot no.37, road NS-1, National Industrial Zone Rawat Islamabad	Lofen Tablets Each tablet contains: Diclofenac Potassium.....75mg
12.	043655	Miracle Pharmaceuticals (Pvt.) Ltd. Pharmaceuticals (Pvt) Ltd	Marinac-P 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
13.	043987	M/s Neomedix Pharmaceuticals, Islamabad	Neofenik- 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
14.	037574	M/s Vision Pharmaceuticals, Islamabad	Deflam 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
15.	038553	M/s Glitz Pharmaceuticals, Islamabad	Glif-K 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
16.	050019	M/s Caraway Pharmaceuticals, Islamabad	Carafenac-P 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg

17.	050107	M/s Harrison Pharmaceuticals, Islamabad	Diclokam-K 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
18.	050953	M/s Leads Pharma, Islamabad	Diclosoft-K 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
19.	052552	M/s Panacea Pharmaceuticals, Islamabad	Tasilex 75 Tablets Each tablet contains:- Diclofenac Potassium 75mg
20.	052727	M/s Paramount Pharmaceuticals, Islamabad	Ronset SRTablets Each tablet contains:- Diclofenac Potassium 75mg

Status of WP No 1695/2017

M/s. Quaper Pharmaceuticals (Pvt) Limited, Sargodha has filed a Writ Petition in Islamabad High Court Islamabad v/s Federation of Pakistan, Drugs Registration Board etc against issuance of show cause notice in the case of Diclofenec Potassium 75mg Tablets. The case was heard on 30-05-2017and adjourned.

Decision of M-288: Registration Board decided that all registration holders of "Diclofenac Potassium 75mg & 100mg" shall be called for personal hearing.

Current Status of WP No 1695/2017 (Ref. M-295):

The Islamabad High Court, Islamabad dismissed the application of M/s. Quper Pharma, Sargodha vide its orders dated 29-01-2020 being without merit. Registration Board in its 295th meeting deliberated on the matter in details and decided to give an opportunity of personal hearing as per Drug Act, 1976 and Rules framed there under to all the firms who have registration of Diclofenac Potassium 75mg & 100mg in forthcoming meeting of Registration Board.

Decision taken by DRAP's Authority in its 70th meeting held on 05-09-2019:

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.

Draft List of Registered Products Containing Diclofenac Potassium 75mg & 100mg

Sr.No.	Reg. No.	Brand Name & Composition	Reg. Holder
1.	023973	Fen-K SR Tablet 100mg Diclofenac Potassium…100mg	Pakheim International Pharma (Pvt) Ltd., 28 Km Ferozepur Road Lahore.
2.	030960	Artimov-K Tablets 100mg Diclofenac Potassium …..100mg	Barrett Hodgson Pakistan (Pvt) Ltd., F/423 SITE Karachi
3.	031178	Mediflam SR 100mg Tablets Diclofenac Potassium……100mg	Mediceena Pharma (Pvt) Ltd., 27 Km Raiwind Road Lahore
4.	038450	Kaldic Tablet Each tablet contains:- Diclofenac Potassium 100mg	Mass Pharma (Pvt) Ltd., 17 Km Ferozpur Road Lahore., Lahore
5.	039198	Catafen 100 Tablets Diclofenac Potassium…..100mg	Macter International, Karachi
6.	039800	Noafilm Tablet 100mg DiclofenacPotassium…...100mg	Noa Hemis Pharmaceuticals, Plot No. 154 Sector23 Korangi Industrial Area Karachi
7.	042985	Movom-P Capsule 100mg DiclofenacPotassium (enteric coated granules)…100mg	Nenza Pharmaceuticals (Pvt) Ltd., 33-A Hayatabad Industrial Estate Peshawar
8.	047294	Dic-P 100mg Tablets Each tablet contains Diclofenac Potassium……100mg	Uni-Tech Pharmaceuticals (Pvt) Ltd., Plot No. 4/116 Sector 21 Korangi Industrial Area Karachi.
9.	052727	Ronset SR Tablets. Diclofenac Potassium……100mg	Paramount Pharmaceuticals, 36 Industrial Triangle, Kahuta Road Islamabad

10.	053260	Sustiva 100mg Tablet Diclofenac Potassium .. ……100mg	Mediate Pharmaceutical (Pvt) Ltd., Plot No. 150-151 Sector 24 Korangi Industrial Area Karachi
11.	054325	Fapa 100mg SR Tablet Diclofenac Potassium…….100mg	Caylex Pharmaceuticals (Pvt) Ltd., 27-Km Mian Raiwind Road Lahore.
12.	054918	Artinil-K SR 100mg Tablet Each tablet contains:- Diclofenac Potassium 100mg	Global Pharmaceuticals, Plot No 204-205 Kahuta Triangle Industrial Area Islamabad.
13.	013758	Diclokon-100 Sugar Coated Tablet Each tablet contains:- Diclofenac…… 100mg	Pharmakon Karachi
14.	055109	Dyfe-P 100mg SR Tablet DiclofenacPotassium……100mg	Safe Pharmaceuticals (Pvt) Ltd., Plot No C-I, 20, Sector 6-B, North Karachi Industrial Area, Karachi
15.	058147	Zulfenec –P 100mg Tablet Diclofenac Potassium…….100 mg	Adamjee Pharmaceuticals (Pvt) Ltd., Plot No. 39 Sector 15 Korangi Industries Area Karachi.
16.	058263	Velflex 100mg Tablet Diclofenac Potassium ……100 mg	Ray Pharma (Pvt) Ltd., S-58 S.I.T.E. Karachi, Karachi
17.	060292	Difene 100mg SR Capsule Diclofenac Potassium Enteric Coated Pellets eq. to Diclofenac Potassium…….100mg	Aries Pharmaceuticals (Pvt) Ltd., 1-W Industrial Estate Hayatabad Peshawar.
18.	060366	Harrifan-K 100mg Tablet Diclofenac Potassium….100mg	Harrison Pharmaceuticals, 10-Km Lahore Road Sargodha., Sargodha
19.	063176	Mobil-K 100mg Tablets Each tablet contains:- Diclofenac Potassium 100mg	Davis Pharmaceutical Laboratories , Plot No. 121 Industrial Triangle Kahuta Road Islamabad.
20.	064026	DP-Med 100mg Tablet Diclofenac Potassium.…100mg	Medicraft Pharmaceuticals (Pvt) Ltd., 126-B Industrial Estate Hayatabad, Peshawar
21.	064198	Diclosaf-P SR 100mg Tablets Diclofenac Potassium…….100mg	SAAAF Pharmaceutical Industries , Plot No. 15 Nowshera Industial Estate Risalpur
22.	064842	Declam Tablet 100mg Diclofenac Potassium……100mg	NovaMed Pharmaceuticals (Pvt) Ltd., 28-Km Ferozepur Road Lahore,
23.	065135	Ronac Tablet Each tablet contains:- Diclofenac Potassium 100mg	Rogen Pharmaceuticals, Plot No. 30 S-4 National Industrial Zone Rawat Islamabad
24.	065546	Theradic-P Tablet 100mg Diclofenac Potassium….100mg	Theramed Pharmaceuticals (Pvt) Ltd., 45-Km Multan Road Lahore
25.	073273	Anti-Pain 100mg Capsule Diclofenac Potassium Pellets eq. to Diclofenac Potassium……100mg	Medicraft Pharmaceuticals (Pvt) Ltd., 126-B Industrial Estate Hayatabad, Peshawar.
26.	021634	Artinil-K 75mg Tablet Diclofenac Potassium..75mg	Global Pharmaceuticals, Plot No 204-205 Kahuta Triangle Industrial Area Islamabad
27.	022543	Maxit 75mg Tablet Diclofenac Potassium… 75 mg	Hilton Pharma (Pvt) Ltd., Plot No. 13 & 14 Sector 15 Korangi Industrial Area Karachi
28.	023811	Ardi-K Tablet Diclofenac Potassium…..75mg	English Pharmaceutical Industries, Indus Link Katarband Road Thokar Niaz Beg, Multan Road Lahore.
29.	023822	Klic-F tablet Diclofenac Potassium……75mg	Tabros Pharma (Pvt) Ltd., Plot No. L-20/B Karachi Industrial Area Sector-22 Federal

			B Area Karachi.
30.	024049	Rheumatin-K Tablet Diclofenac Potassium…75mg	Siza International (Pvt) Ltd., 18-Km Main Ferozepur Road Lahore
31.	024273	Antiflam Tabelts Each tablet contains:- Diclofenac Potassium…..75mg	Wilshire Laboratories (Pvt) Ltd ., 124/1 Industial Estate Kot Lakhpat Lahore.
32.	024333	Kalfen Tablet 75mg Diclofenac Potassium...75mg	Candid Pharmaceuticals, Opp Pasrur Sugar Mills Sialkot Road, Pasrur
33.	028340	Biscot Tablet Diclofenac Potassium……..75mg	Robins Pharmaceutical Industries, 43, Industrial Triangle, Kahuta Road Islamabad.
34.	028866	Inflaban 75 Tablet Diclofenac Potassium……..….75mg	Medera Pharmaceuticals (Pvt) Ltd., 249-A Industrial Triangle Kahuta Road Islamabad
35.	030959	Artimov-K Tablets 75mg Diclofenac Potassium …..75mg	Barrett Hodgson Pakistan (Pvt) Ltd., F/423 SITE Karachi
36.	031128	Beflam Tablets 75mg Diclofenac Potassium ….75mg	Batala Pharmaceuticals, 23/B Small Industrial Estate No. 2 Near Wapda Town, Khiali Bypass Gujranwala
37.	031800	Ketagesic-75 Tablet Diclofenac Potassium…….75mg	Hygeia Pharmaceuticals, Plot No. 295 Industrial Triangle Kahuta Road Islamabad.
38.	032086	Tonek Tablet 75mg Diclofenac Potassium …75mg	Polyfine Chempharma, 51 Industrial Estate Hayatabad Peshawar
39.	032102	Dicfin 75mg Tablets Each tablet contains:- Diclofenac Potassium 75mg	Dr. Raza Pharma, Road B-4 P.No 44-C Industrial Estate, Jamrud Road, Peshawar
40.	035988	Quikrel 75mg Tablet Each tablet contains:- Diclofenac Potassium 75mg	Z-Jans Pharmaceutical (Pvt) Ltd., 148-A Industrial Estate Hayatabad Peshawar.
41.	036326	Aldal Tablets Diclofenac Potassium…75mg	Alson Pharmaceutical, 169, Road No. 7-B, Industrial Estate Hayatabad Peshawar
42.	036727	Confenac-K Tablets Diclofenac Potassium…….75mg	Convell Laboratories, Saidu Sharif Swat
43.	036772	Pofen 75mg Tablets Diclofenac Potassium……..75mg	Fozan Pharmaceticals Industries (Pvt) Ltd., 36-A Hayatabad Industrial Estate Peshawar
44.	036815	Dic-P 75mg Tablets Diclofenic Potassium…….75mg	Shaheen Pharmaceuticals, 3-Km Murghzar Road Saidu Sharif Swat
45.	037197	Ardic K Tablets Diclofenac Potassium……75mg	Wilshire Laboratories (Pvt) Ltd ., 124/1 Industial Estate Kot Lakhpat Lahore.
46.	037415	Makaid-K 75mg Tablets Diclofenac Potassium…75mg	Makson Pharmaceuticals, Plot No. 80-B, Street No.61, 10/3, Industrial Area, Islamabad
47.	037574	Diclovis-K 75Mg Tablets Each tablet contains Diclofenac Potassium……..75mg	Vision Pharmaceuticals, Plot No. 22-23 Industrial Triangle Kahuta Road Islamabad
48.	037849	Phenpal Capsule Each capsule contains:- Diclofenac Potassium 75mg	Alson Pharmaceutical, 169, Road No. 7-B, Industrial Estate Hayatabad Peshawar.
49.	037887	Diclovel Tablets Diclofenac Potassium…..75mg	Convell Laboratories, Saidu Sharif Swat
50.	037975	Dicomak 75mg Tablets Diclofenac Potassium…75mg	Makson Pharmaceuticals, Islamabad

51.	038016	Dicloned-k 75mg tablet Diclofenac Potassium USP……..75mg	Nenza Pharmaceuticals (Pvt) Ltd., 33-A Hayatabad Industrial Estate Peshawar
52.	038169	Synoflam- 75Mg Tablets Diclofenac PotassiumUSP…..75mg	Fedro Pharmaceutical Labs (Pvt) Ltd., 149-Industrial Estate Jamrud Road Peshawar
53.	038342	Irozee-F Tablet Each tablet contains:- Diclofenac Potassium 75mg	Z-Janz Pharmaceuticals, Peshawar.
54.	038437	Phlodic-K Tablet Each tablet contains:- Diclofenac Potassium 75mg	Pearl Pharmaceuticals, Plot No 204 Street No. 1 I-10/3 Industrial Area Islamabad
55.	038553	Glift-K 75mg Tablet Each tablet contains:- Diclofenac Potassium 75mg	Glitz Pharma, Plot No 265 Industrial Triangle Kahuta Road Islamadad
56.	040186	Ura 400mg Tablet DiclofenacPotassium…….75mg	Rasco Pharma (Pvt) Ltd., 5.5 Km Raiwind Road Ali Razabad Lahore
57.	041483	Getab tablet Diclofenic Potassium…… 75mg	Hicon Pharmaceuticals, 131-Industrial Estate Hayatabad Peshawar
58.	041945	Mobil K 75mg Tablet Diclofenac Potassium…….75 mg	Davis Pharmaceutical Laboratories , Plot No. 121 Industrial Triangle Kahuta Road Islamabad
59.	042123	Noafilm-75 Tablet 75mg Diclofenac Potassium……75mg (Anti-rheumaticsystemic)	Noa Hemis Pharmaceuticals, Plot No. 154 Sector 23 Korangi Industrial Area Karachi
60.	042483	Medic-P 75mg Tablets Diclofenac Potassium…..…75mg	Medicure Laboratories, Plot No. F./109 Behind Karachi Polytechnic Hub River Road SITE Karachi
61.	042984	Movom-P cap 75mg Diclofenac Potassium (enteric coated granules)…75mg	Nenza Pharmaceuticals (Pvt) Ltd., 33-A Hayatabad Industrial Estate Peshawar. , Peshawar
62.	043605	Declam Tablets 75mg Diclofenac Potassium(B.P)……75mg	NovaMed Pharmaceuticals (Pvt) Ltd., 28-Km Ferozepur Road Lahore
63.	043655	Marinac-P 75 tablet Each tablet contains:- Diclofenac Potassium 75mg	Miracle Pharmaceuticals (Pvt) Ltd., Plot No-8 Street No-5 National Industrial Zone Rawat, Islamabad
64.	043908	Digam Tablets 75mg Diclofenac Potassium……75mg.	Navegal Laboratories, Plot No. 41/1-A-2 Phase-I Industrial Estate Hattar Peshawar
65.	046175	Reform Capsules 75mg. Diclofenac Potassium…….75mg	Silver Oak Corporation, 16/1, Phase IV, Industrial Area, Hattar
66.	046202	Kaymax Tablet Diclofenac Potassium…….75mg. (B.P)	Quaper (Pvt) Ltd., 26-A S.I.E. Lahore Road Sargodha.
67.	046215	Brisc Tablets 75mg. Diclofenac Potassium……75mg. (B.P)	Envoy Pharmaceuticals (Pvt) Ltd., 27-Km Multan Road Maraka Lahore
68.	046319	Diclopot 75mg tablet Diclofenac Potassium……..75mg.	Zesion Pharmaceuticals, 293, Industrial Triangle, Kahuta Road, Islamabad
69.	046893	Feflam-75 Tablets. Diclofenac Potassium …75mg.	Festal Laboratories, Jinnah Industries Link Kattar Band Road Thokar Niaz Baig Lahore
70.	047860	Achex Tablet Each tablet contains:- Diclofenac Potassium 75mg	Wise Pharmaceuticals, Plot No. 3-A Street S-1 National Industrial Zone, Rawat Islamabad

71.	048383	Deflam Tablet 75mg Diclofenac Potassium ……75mg. (B.P)	CCL Pharmaceuticals (Pvt) Ltd., 62 Industrial Estate Kot Lakhpat Lahore
72.	049013	Caveron Tablet 75mg Each tablet contains:- Diclofenac Potassium 75mg	FYNK Pharmaceuticals, 19-Km Ferozepur Road G.T. Road Kala shah Kaku Lahore.
73.	049385	Lofen 75mg Tablet Diclofenac Potassium……..75mg. (B.P Specs)	Shawan Pharmaceuticals, Plot No. 37 Road NS-1 National Industrial Zone Rawat Rawalpindi
74.	049839	D-K Tablet 75mg Diclofenac Potassium ……75mg. (USP Specs)	Ferroza International Pharmaceuticals (Pvt) Ltd., 33-Km Ferozepur Road Lahore
75.	050019	Carafenac-P Tablets 75mg. Diclofenac Potassium ……..75mg. (USP Specs)	Caraway Pharmaceuticals, Plot No. 12 Street No. N-3 National Industrial Zone (RCCI) Rawat Islamabad
76.	050107	Diclokam-K Tablets 75mg. Diclofenac Potassium …….75mg. (USP Specs)	Harrison Pharmaceuticals, 10-Km Lahore Road Sargodha
77.	050330	Kemipan Plus Tablet Diclofenac Potassium……75mg	Alkemy Pharmaceutical Laboratories (Pvt) Ltd., P-9 SITE Hyderabad
78.	050953	Diclosoft- K Tablets 75mg. Diclofenac Potassium…….75mg. (B.P Specs)	Leads Pharma (Pvt) Ltd., Plot No. 81-A Street No. 6 I-10/3 Islamabad
79.	051172	Engrol 75mg Capsules. Diclofenac Potassium…….75mg. (BP Specs)	English Pharmaceutical Industries, Indus Link Katarband Road Thokar Niaz Beg, Multan Road Lahore
80.	052438	Dicsium Tablets. Diclofenac Potassium……..75mg. (B.P Specs)	Evergreen Pharmaceuticals , 69-70/B Main Glaxo Town Industrial Estate 20Km Ferozepur Road Lahore
81.	052552	Tasilex Tablets 75mg Diclofenac Potassium…….75mg.	Panacea Pharmaceuticals, Plot No.4 Street No.S-6 National Industrial Zone Rawat Islamabad
82.	052707	Unifin Tablet 75mg Each tablet contains:- Diclofenac Potassium 75mg	Unison Chemical Works, 15 Km Raiwind Road Lahore
83.	052803	Tasium Capsule 75mg. Diclofenac Potassium (as enteric coated Pellets)……75mg.	Panacea Pharmaceuticals, Plot No.4 Street No.S-6 National Industrial Zone Rawat Islamabad
84.	054195	Frendic-P Tablet 75mg Diclofenac Potassium…….75mg (USP Specs)	Friends Pharma (Pvt) Ltd., 31-Km Ferozepur Road Lahore
85.	054273	Muskel 75mg Tablets Diclofenac Potassium……..75mg (USP Specs)	Hamaz Pharma, Multan
86.	054527	Difene 75mg Capsule Diclofenac Potassium enteric coated pellets eq. to …….75mg	Aries Pharmaceuticals (Pvt) Ltd., 1-W Industrial Estate Hayatabad Peshawar
87.	054665	Dipot-K Tablet Each tablet contains:- Diclofenac Potassium 75mg	Tas Pharma (Pvt) Ltd., 209 Sehala Triangle Kahuta Road Islamabad
88.	054702	D-Fine P 75mg Tablet Diclofenac Potassium ……75mg	Alliance Pharmaceuticals (Pvt) Ltd., 112-A Hayatabad Industrial Estate Peshawar
89.	055108	Dyfe-P 75mg Tablet Diclofenac Potassium…75mg	Safe Pharmaceuticals (Pvt) Ltd., Plot No C-I, 20, Sector 6-B, North Karachi Industrial Area, Karachi

90.	055997	Qufen -K 75mg Tablet Diclofenac Potassium……..….75mg	High-Q Pharmaceuticals, Plot No. 224 Sector 23 Korangi Industrial Area Karachi.
91.	056183	Potafin Tablet Each tablet contains:- Diclofenac Potassium 75mg	Goodman Laboratories, Plot No.5 St: No. S-5 National Industrial Zone Rawat Islamabad
92.	056250	Dipolive 75mg Tablet Each tablet contains:- Diclofenac Potassium 75mg	Olive Laboratories, Plot No.52-S-6 National Industrial Zone Rawat Rawalpindi
93.	056377	Dlf-K Tablet Each tablet contains:- Diclofenac Potassium 75mg	Crown Pharmaceuticals, 286 Kahuta Industrial Triangle Islamabad
94.	056529	Pofac 75mg tablet Diclofenac Potassium……75mg	Wnsfield Pharmaceuticals, Plot No. 122 Block-A Phase-V Industrial Estate Hattar
95.	056701	Volden Fort K 75mg Tablet Each tablet contains:- Diclofenac Potassium 75mg	Rotex Pharma (Pvt) Ltd., Plot No. 206-207 Industrial Triangle Khuta Road Islamabad
96.	056720	Dilo-K 75mg Capsule Diclofenac Potassium75mg	Farm Aid Group, Plot No. 3/2 Hattar Industrial Area Hattar
97.	056845	Detaflam Tablet 75mg Diclofenac Potassium.....75mg.	Webros Pharmaceuticals, Plot No. 1 Street No. 10 National Industrial Zone Rawat Islamabad
98.	056977	Olitass Capsule Each capsule contains:- Diclofenac Potassium 75mg	Olive Laboratories, Plot No.52-S-6 National Industrial Zone Rawat Rawalpindi
99.	057517	Lyon Tablet Diclofenac Potassium…75mg.	Alfalah Pharma (Pvt) Ltd., 12-Km, Sheikhupura Road, Lahore.
100.	057612	Detran-P 75mg Tablet Diclofenac Potassium…..75mg	Sunshine Pharmaceuticals, Emanabad, G.T. Road, Gujranwala
101.	057662	K-Lam Tablets 75mg Diclofenac Potassium …..75mg	DrugPharm (Pvt) Ltd., 28-Km, Sheikhupura Road, Lahore
102.	057784	Fareop 75 mg Tablet Diclofenac Potasium……75mg	Lexicon Pharmaceuticals Pvt. Ltd. Karachi
103.	057985	Painogin 75mg Tablet DiclofenacPotassium…...75mg	Zanctok Pharmaceutical Laboratories, F/5 SITE Hyderabad
104.	058146	Zulfenec –P 75mg Tablet Diclofenac Potassium……..75 mg	Adamjee Pharmaceuticals (Pvt) Ltd., Plot No. 39 Sector 15 Korangi Industries Area Karachi.
105.	058262	Velflex 75 mg tablet Diclofenac Potassium …….75 mg	Ray Pharma (Pvt) Ltd., S-58 S.I.T.E. Karachi
106.	058318	Hasten 75mg Tablet Diclofenac Potassium…..…...75 mg	Klifton Pharma Jomshoro
107.	058404	Corom-P 75mg Tablet Diclofenac Potassium ……...75 mg	Zephyr Pharmatec (Pvt) Ltd., Plot No. A-39 S.I.T.E. II Super Highway Karachi
108.	058420	Eplopot Tablet Diclofenac Potassium …..75 mg	E-Pharm Laboratories, A-40 S.I.T.E Super Highway North Karachi
109.	059535	D-Fenac Tablets Each tablet contains Diclofenac Potassium…….75mg	Medley Pharmaceuticals, 41/A Punjab Small Industries Estate Jhang Bahtar Road Wah Cantt
110.	059625	Nostif-K Tablet Diclofenac Potassium…..75mg	Axis Pharmaceuticals , 3-B Value Addition City 1.5 Km Khurrianwala – Sahanwala Road Faisalabad
111.	059883	Zofen-K Tablets 75mg Each tablet contains:- Diclofenac Potassium…75mg	Harmann Pharmaceutical Laboratories (Pvt) Ltd., 16-Km Multan Road Lahore

112.	059971	Reuqin-75mg Tablet Diclofenac Potassium….75mg	Qintar Pharmaceuticals, 14-A Small Industrial Estate Lahore Road Sargodha
113.	060445	Relic Tablet 75mg Diclofenac Potassium…..75mg	Brand Pharma International,, K-105, Super Highway, Phase-II, S.I.T.E,Karachi,
114.	060923	Flexura 75mg Tablet Diclofenac Potassium…….…75mg	Fassgen Pharmaceuticals, Plot No. 67/1 Block-A Phase-III Industrial Estate Hattar
115.	060965	Diclowan-P 75mg Tablet Diclofenac Potassium…75mg	Swan Pharmaceutical (Pvt) Ltd., 11-E Industrial Triangle Kahuta Road Islamabad
116.	061515	Blif-B Tablet Each tablet contains:- Diclofenac potassium … 75 mg	Brand Pharma International,, K-105, Super Highway, Phase-II, S.I.T.E, Karachi,
117.	061574	Dicsod-K Tablet Each tablet contains:- Diclofenac potassium … 75 mg	Medicaids (Pvt) Ltd., Plot No 10 Sector 37 Korangi Industrial Area Karachi
118.	062476	Kaynac Capsule 75mg Diclofenac Potassium Pellets Eq. to Diclofenac Potassium …75mg	Hoover Pharmaceuticals (Pvt) Ltd., Plot No.16 Zain Park Industrial Area Saggain By Pass Road Lahore
119.	062591	Diclotal K Tablet 75mg Diclofenac Potassium….75mg	Berlex Lab. International, 10-Km Nangshah Chowk Karachi Road Multan
120.	062636	Diclofil P Tablet Diclofenac Potassium….75mg	Murfy Pharmaceuticals (Pvt) Ltd., 8-Km Raiwind Road Lahore
121.	062985	Diclosaf-P 75mg Tablets Diclofenac Potassium…..75mg	SAAAF Pharmaceutical Industries , Plot No. 15 Nowshera Industial Estate Risalpur
122.	063038	Arthopot Capsule Diclofenac Potassium…..75mg	Gillman Pharmaceuticals, Plot No. 41/2-A Phase-I & II Industrial Estate Hattar.
123.	063262	Diclotus-K Tablet Each tablet contains:- Diclofenac Potassium 75mg	Lotus Pharmaceutials (Pvt) Ltd. , Plot No.118-A Street No. 8, I-10/3 Industrial Area Islamabad
124.	064022	Anti-Pain 75mg Capsule Diclofenac Potassium Pellets equivalent to Diclofenac Potassium……..75mg	Medicraft Pharmaceuticals (Pvt) Ltd., 126-B Industrial Estate Hayatabad, Peshawar
125.	064588	Daikin Tablets 75mg Diclofenac potassium….75mg	3S Pharmaceuticals (Pvt) Ltd,, 5km Off Raiwind Manga Road, Lahore,
126.	064791	Pointer 75 Capsule Diclofenac Potassium (Pellets)…..75mg	M/s Shrooq Pharmaceuticals (Pvt) Ltd,, 21 Km Ferozpur Road,
127.	065126	Relpain Tablet Each tablet contains:- Diclofenac Potassium 75mg	Well & Well Pharma (Pvt) Ltd., Plot No.7 Street S-8 National Industrial Zone RCCI Rawat Islamabad
128.	065134	Ronac Tablet Each tablet contains:- Diclofenac Potassium 75mg	Rogen Pharmaceuticals, Plot No. 30 S-4 National Industrial Zone Rawat Islamabad
129.	065195	Biodic-P Tablet Each tablet contains:- Diclofenac Potassium 75mg	Biorex Pharmaceuticals, Plot No.292 Industrial Triangle Kahuta Road Islamabad
130.	065234	Linofenac-P 75mg Tablet Each tablet contains:- Diclofenac Potassium 75mg	Linear Pharma, Plot No. 18 S. No. S-4 National Industrial Zone (RCCI) Rawat Islamabad
131.	066480	Frisky Tablet Each tablet contains:- Diclofenac Potassium 75mg	Crest Pharmaceuticals, Plot No. 43 Industrial Triangle Kahuta Road Islamabad
132.	066670	Qrelif-75 Tablets Diclofenac Potassium…75 mg	Medizan Laboratories (Pvt) Ltd., Plot No 313 Industrial Triangle Kahuta Road Islamabad

133.	066886	Regopyrin Tablet 75mg Diclofenac Potassium …..75 mg	Regent Laboratories, C-20 SITE Super Highway Karachi.
134.	068239	Naveflam Capsules 75mg. Diclofenac Potassium….75mg	Navegal Laboratories, Plot No. 41/1-A-2 Phase-I Industrial Estate Hattar
135.	068326	Dolwel 75mg Tablet Diclofenac Potassium……75mg	WelMark Pharmaceuticals, Plot No. 122 Block-B Phase-V Industrial Estate Hattar.
136.	068362	Rxoflam Tablets 75mg. Diclofenac Potassium……75mg	Healer Laboratories (Pvt) Ltd., 96/102-C SIE Kohat Road Peshawar
137.	068456	Volmed-K Capsule Diclofenac Potassium……75mg	Meditech Pharmaceuticals, 15-D Industrial Estate, Jamrud Road, Peshawar,
138.	069004	Kenac Tablet 75mg Diclofenac Potassium ….75mg	Medisave Pharmaceuticals, Plot No.578-579 Sundar Industrial Estate Lahore
139.	069281	Zainex 75mg tablet Diclofenac Potassium…….75mg	Sapient Pharma, 123-S Industrial Area Kot Lakhpat Lahore
140.	069285	Denum K Tablets Diclofenac Potassium……..75mg	Irza Pharma (Pvt) Ltd., 10.2-Km Lahore Sheikhupura Road P.O Kot Abdul Malik District Sheikhupura
141.	073586	Defenac 75mg Capsule Each capsule contains Diclofenac Potassium: 75mg	Mediate Pharmaceutical (Pvt) Ltd., Plot No. 150-151 Sector 24 Korangi Industrial Area Karachi
142.	074198	Peflam Tablet Diclofenac Potassium……75mg	Arsons Pharmaceutical Industries (Pvt) Ltd., 22-Km Multan Road Off 2.5-KM Defence Road, Lahore
143.	074501	Caldic 75mgTablet Diclofenac Potassium….75mg	Caliph Pharmaceuticals (Pvt) Ltd., Plot No. 17 Industrial Estate Risalpur
144.	074597	Nexfen Tablets 75 mg. Diclofenac Potassium…..75 mg	Libra (Pvt) Ltd., 77 Industrial Estate Hayatabad Peshawar
145.	076892	Dicgesic-K Tablets 75 mg Each film coated tablet contains Diclofenac Potassium: 75mg	Alen Pharmaceuticals (Pvt) Ltd., 138 Nowshera Industrial Estate, Risalpur
146.	078831	VALRON-P 75 Tablets Each film coated tablet contains Diclofenac Potassium: 75mg	Venus Pharma, 23 Km Multan Road Lahore
147.	077028	Basocap -75mg Capsule Each capsule contains Diclofenac Potassium (Pellets): 75mg	Basel Pharmaceuticals, 227-Phase-II Multan Industrial Estate Multan
148.	021577	Keygesic Tablet 75mg Each tablet contains Diclofenac Potassium: 75mg	Benson Pharmaceuticals, Plot No.119 Street No.8, I-10/3 Industrial Area Islamabad

List of Registered Products Containing Famotidine 10mg/5ml

S/N	Reg. No.	Brand Name & Composition	Manufacturer
1.	024255	Acicon Suspension Each 5ml contains:- Famotidine USP…..10mg	Barrett Hodgson Pakistan (Pvt) Ltd, F/423, SITE, Karachi
2.	025037	Peptiban Suspension Famotidine.....10mg	Werrick Pharmaceuticals, 216-217, I-10/3, Industrial Area, Islamabad.,
3.	025149	Fadiphine Suspension Famotidine.....10mg	Global Pharmaceuticals, Plot No 204-205, Kahuta Triangle, Industrial Area, Islamabad
4.	025469	Capcid Suspension Each 5Ml Contains:- Famotidine.....10mg	Bloom Pharmaceuticals (Pvt) Ltd, Plot No30, Hattar Ind Estate, Phase I & II, Hattar
5.	025565	Reducid Suspension Famotidine.....10mg	Platinum Pharmaceuticals (Pvt) Ltd, A-20, North Western Industrial Zone, Bin Qasim, Karachi

6.	025568	Ulcenil Suspneion Each 5Ml Contains:- Famotidine....10mg	Siza International (Pvt) Ltd, 18 KM, Main Ferozepur Road, Lahore-53000, , , ,
7.	027108	Famobex Suspension Each 5Ml Contains:- Famotidine…..10.000mg	Macter International (Pvt) Ltd,, F-216, S.I.T.E, Karachi
8.	027115	Famorex Suspension Each 5Ml Contains:- Famotidine……..10mg	Mediceena Pharma (Pvt) Ltd, , 27-K.M, Raiwind Road, Lahore
9.	027709	Zepsin Suspension Famotidine……..10mg	Cirin Pharmaceuticals,, 32/2A, Phase III, Industrial Estate, Hattar. Manufactured by M/s. Bloom Pharmaceutical, Hattar.
10.	027723	Peprax Suspension Famotidine….10mg	Umersons Laboratories,, 467, Industrial Area, Sector I/9, Islamabad
11.	028254	Famoscot Oral Suspension 10mg Famotidine……10 mg	Scotmann Pharmaceuticals, 5D, I-10/3 Industrial Area, Islamabad
12.	030082	Nulcer Suspension Famotidine …….10mg	Brookes Pharmaceutical Labs, (Pak) Ltd,, 58/15, Korangi Industrial Area, Karachi
13.	030124	Recid Syp Famotidine…..10mg	Regent Laboratories,, Plot No. C-20 S.I.T.E,,Karachi
14.	030273	Cantil Suspension Famotidine……10mg	Helicon Pharmaceutek, Pakistan (Pvt) Ltd,, Model Town Road, Faisalabad,
15.	031233	Peprid Suspension Famotidine …….10mg	Helix Pharma (Pvt) Ltd,, A/56, S.I.T.E.,, , Karachi,
16.	031646	Capcid Suspension Famotidine…….10mg	Olive Laboratories,, Plot # 52-S6, National Industrial Zone ,
17.	031771	Fadin Suspension Famotidine ……10mg	Zeb Laboratories, (Pvt) Ltd,, Link Rai-Wind Road, Nisar Abad
18.	033340	Fagastril Syrup Famotidine…….10mg	Gray's Pharma, Islamabd,
19.	033684	Acidrol Suspension Famotidine ……10mg	Medisearch Pharmacal, Lahore.
20.	033704	Neofam Suspension Famotidine……..10mg	Neomedix , Plot No.5, N-5 National Industrial Zone Rawat (Islamabad), ,
21.	033996	Pepton Suspension Famotidine…..10mg	Paramount Pharma,Islamabad, 36,Industrial Triangle Kahuta Road, Islamabad,
22.	034789	Gastridine Suspension Famotidine……..10mg	Unicorn Pharma , E-30, Sector 15, Korangi Industrial Area, Karachi
23.	035275	Ge Pep Suspension Each 5ml contains:- Famotidine 10mg	Akson Pharmaceuticals Co. (Pvt.) Ltd.
24.	037994	Famotop Suspension Famotidine…….10mg	Xenon Pahrma, Lahore.
25.	038876	Neutidin Suspension 10mg/5ml Famotidine…….10mg	Neutro Pharma (Pvt) Ltd, 9.5Km,SheikhupuraLahore,
26.	040312	Fomen Suspension 10mg Famotidine…..10mg	Shrooq Pharmaceutical (Pvt) Ltd, 21-KM, Feroze Pur Road, Lahore
27.	040816	Fambria Suspension Famotidine... 10mg	Ambrosia Pharmaceuticals,, Plot No.18, St. No.9, National Industrial Zone, Rawat, Islamabad.,
28.	041444	Famo Rains Suspension Famotidine ……10 mg	MAC AND RAINS Pharmaceuticals (Pvt) Ltd, Lahore

29.	041472	Hifame Suspension Famotidine …… 10mg	Hicon Pharmaceuticals, 131 Industrial Estate Hayatabad, Peshawar.,
30.	041619	Servipep Susp. Famotidine…….10mg	Polyfine Chemical Pharmaceuticals, 51 Industrial Estate, Jamrud Road, Peshawar
31.	042764	Fastine Suspension Famotidine ……..10mg	Trigon Pharmaceutical (Pvt) Limited, 18 Km Raiwind Road, Lahore
32.	042966	Nocer 10 Suspension Famotidine……..10mg	Bryon Pharma (Pvt) Ltd,, 48 Hayatabad, Indus. Estate, Peshawar.
33.	043409	Sypep Suspension Famotidine……10 mg	Alsons Pharmaceuticals, 169-Hayatabad Industrial Estate, Peshawar.
34.	043731	Ulcare.Suspension.10mg. Famotidine……10mg	Z-JANS Pharmaceuticals,, 148-A, Industrial Estate, Hayyatabad, Peshawar,
35.	044794	Famofit Suspension Famotidine ……..…10mg	M/s Synchro Pharmaceuticals, 77-Industrial Estate, Kot Lakhpat Lahore.,
36.	045470	Pharmotidin Suspension Famotidine. …….. 10 mg	Epharm Labs, Karachi,
37.	046936	H2foz Suspension Famotidine ……..10mg	Fozan Pharmaceuticals (Pvt) Ltd, 36-A, industrial Estate, Hayatabad, Peshawar,
38.	047354	Zebid Suspension Famotidine……10mg	Atco Laboratories Limited, , B-18, SITE, Karachi.,
39.	047829	Famonil Suspension 60ml Famotidine……..10mg	Hisun Pharmaceuticals, Plot.No.37 Road No, R-2, Industrial Estate Gadoon, Swabi
40.	052452	Fam-PH Suspension. Famotidine……..10mg	Evergreen Pharmaceuticals,, Sundar Industrial Estate, Lahore.,
41.	054223	Myolif Suspension Famotidine……..10mg	Life Pharmaceutical Company, 24-III, Industrial Estate, Multan
42.	054287	Stomachcare Susp Each 5ml contains:- Famotidine 10mg	Jawa Pharmaceuticals (Pvt.) Ltd.,
43.	054455	Famosin Suspnesion Famotidine 10mg	Irza Pharma (Pvt) Ltd, 10/2 Km Sheikhupura Road, P.O. Kot Abdul Malik, Sheikhupura.
44.	054613	Efdine Suspension Famotidine……..10mg	Meditech Pharmaceuticals,, 15-D Industrial Estate, Jamrud Road, Peshawar,
45.	054717	Afomit Susp Famotidine ……..10mg	Alliance Pharmaceuticals (Pvt) Ltd, 112-A, Industrial Estate, Hayatabad, Peshawar.,
46.	055103	Famdin Suspension Famotidine……10mg	Pakistan Pharmaceuticals Products, Karachi,
47.	055282	Almadine Suspension 10mg/5ml Famotidine…10mg	Selomore Pharmaceuticals (Pvt) Ltd.,35 KM, Multan Raod, lahore
48.	056653	Nogacid Suspension Famotidine…….10mg	LowittPharmaceutical(Pvt)Ltd, Plot.No.24 Industrial Estate,Peshawar.,
49.	057740	Famtaza Dry Suspension Famotidine…..…….....10mg	ZafaPharmaceuticals,, Karachi,
50.	058116	Atodine Suspension 10mg/5ml Famotidine ……..10 mg	Macquins International, Karachi,
51.	058152	Trump 10mg/5ml Suspension Famotidine……..10 mg	Adamjee Pharmaceuticals, Karachi
52.	059498	Fedcid Suspension Each 5ml contains:- Famotidine 10mg	Fedro Pharmac (Pvt.) Ltd., Peshawar

53.	059540	Motidin Suspension Famotidine….10mg	Medley Pharmaceutical,, 41-A P.S.I.E Jhang Bahtar Road, Wah Cantt,
54.	059885	Gestrodine Suspension Each 5ml contains:- Famotidine…….10mg	Harmann Pharmaceutical Labs (Pvt) Ltd,, 16 -Km Multan Road, Lahore.,
55.	059947	Gaster Suspension Famotidin ……. 10mg	Hamaz Pharmaceuticals (Pvt) Ltd,, 22 Km Lutafabad Road, Multan.,
56.	060333	Famodex Suspension Famotidine …… 10mg	Ameer Pharma (Pvt) Ltd, , 23-KM, Sheikhupura Road,Lahore.,
57.	061150	Flut Suspension Famotidine……..……10mg	Zephyr, Karachi,
58.	061758	Kohiton Suspension Famotidine……..10mg	KohsPharmaceuticals,, P8,SITE,Phyderabad,
59.	062698	NO-UL Suspension Famotidine ……10mg	Fynk Pharmaceuticals,, 19 K.M. G.T. Road, Kala Shah Kaku, Lahore.,
60.	063004	Famoday Suspension Each 5ml contains:- Famotidine 10mg	Max Pharmaceuticals,
61.	063081	Pepcimed Suspension 10mg/5ml Famotidine…….10mg	MedicraftPharmaceuticals(Pvt)Ltd, 126-B, Industrial Estate, Jamrud Road, Peshawar.,
62.	064293	S.Famers 10mg Syrup Famotidine……..10mg	SayyedPharmaceuticals(Pvt)Ltd.,, Plot No.67/2 Phase 3, Industrial Estate, Hattar,
63.	064891	Famoprime Suspension 10mg Famotidine ……10mg	Prime Labs (Pvt) Ltd, 9.5 Km Sheikhupura Road, Lahore.,
64.	065555	Therafame Suspension 10mg/5ml Famotidine…..10mg	Theramed Pharmaceutical, , 331-J-1 Johar Town Lahore,
65.	065677	Famid 10mg Suspension Famotidine……10mg	Wilshire Laboratories,, 124/A, Kotlakhpat, Indus. Area, Township Scheme, Lahore.,
66.	065956	Famotop Suspension Famotidine…… 10mg	Xenon Pharmaceuticals (Pvt) Ltd, , 9.5 KM Sheikhupura Road, Lahore,
67.	066298	Maripep Each 5ml contains:- Famotidine.. 10mg	Miracle Pharmaceuticals (Pvt.) Ltd., Islamabad,
68.	067940	Gdicd Suspension Famotidine…10mg	Unison Chemical Works, Lahore,
69.	069070	Femcare Suspension Famotidine ……10mg	Care Pharmaceuticals, 8-KM Thokar, Raiwind Road, Lahore.,
70.	069396	Famtac Suspension Famotidine…10mg	Rasco Pharma,, 5.5 KM Raiwind Road Ali Razabad, Lahore,
71.	070711	Acicon 10mg/5ml Dry Suspension Famotidine …….10 mg	Barret Hodgson,, Karachi,
72.	071168	Famotidine 10mg/5ml Suspension Famotidine …… 10mg	Lawrence Pharma (Pvt.) Ltd, , 10.5Km Sheikhupura Road, Lahore.,
73.	075050	Dinex Suspension Each 5 ml contians:- Famotidine … 10 mg	Gulf Pharmaceuticals, Plot No.4, St.No.S-6, National Industrial Zone, Rawat,
74.	075259	Modin Suspension Famotidine: 10mg	Metro Pharmaceuticals, Plot No. 14 St. No. SS-2 National Industrial Zone (RCCI) Rawat Islamabad, Islamabad
75.	077070	Feptid Oral Suspension Famotidine: 10mg	Axis Pharmaceuticals , 3-B Value Addition City 1.5 Km Khurrianwala – Sahanwala Road Faisalabad

76.	077441	Famonyx 10 Suspension Famotidine: 10mg	Onyx Pharamaceuticals Industries, 30-A SIE Mansehra, Mansehra,
77.	078725	Al-Famot Oral Liquid Suspension 60ml Famotidine: 10mg	Ali Industries, Plot No.239/C Sundar Industrial Estate Raiwind Road Lahore.,

Proceedings of 296th Meeting:

The Board discussed the case at length that the above formulations are registered since long. As per available record and reviewing of information available at websites of RRAs, no data regarding their safety and efficacy is available in such strengths/dosage forms, so continuity of these formulations is not justifiable. Furthermore, scrutiny of data revealed that there also exists a number of formulations, which were never approved in the strengths currently registered in the country, while, others have strengths identical to that approved by reference regulatory authorities but have different dosage forms.

Board emphasized the significance of recognition of RRAs as adopted by it since long. RRAs includes robust regulatory authorities of world like US-FDA, EMA, Health Canada, TGA Australia etc. etc. The concept of reliance on decisions of reference regulatory authorities assure the safety, efficacy, and quality of medicines. This reliance enables to have evidence for robust and accurate decision-making, considering that the products registered and sold in the countries of reference regulatory authorities fulfil the harmonized standards of safety, efficacy and quality as adopted by WHO, ICH, etc. This reliance also enables the national regulatory authority for post marketing surveillance particularly related to safety and efficacy issues. Reference regulatory authorities have stronger reporting and information sharing system, which can be used by national regulatory authorities as a useful tool for surveillance, new available treatments and new indications or contraindications.

It was also discussed that certain formulations were previously approved by reference regulatory authorities but later on withdrawn due to following reasons:

- Commercial/ marketing issues.
- Safety concerns.

In this context, all members endorsed the above stated facts and shared their views on the subject matter, which have been consolidated as under:

- Policies/ practices adopted by different countries regarding such formulations were discussed and it was concluded that it is reasonable to continue with such formulations in those countries, which have a well-developed regulatory system for reporting of adverse events and addressing of safety issues. While, there also exists examples of countries where a number such formulations have been withdrawn. However, in current health care system working in our country, safety cannot be established as ADRs reporting system is not well anchored.
- Once a product is discontinued in reference regulatory authorities due to safety reasons, the information regarding its label/ patient information leaflet (PIL), medical literature, clinical use, route of administration, dosage, storage conditions of finished products and type of container closure system/packaging material etc will not be available as a reference/ standard to be adopted by a local manufacturer, which is required as per conditions of registration.
- If a product has no evidence of availability/ approval in the Reference Regulatory Authorities or it was available in the past but now withdrawn due to marketing/ commercial etc. issues and not because of safety reasons.
- Therefore, there is a need to resolve the issue by taking administrative measures/ decision. Furthermore, all such cases need to be evaluated/ decided on case to case basis considering scientific grounds, therapeutic equivalencies and pharmacodynamic aspects provided that the strength remains same as available/ approved in reference regulatory authorities. In this regard, a working group may be created having members from Registration Board with relevant specialty and stake holders.

Decision of M-296:

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.

DRAP Authority in its 125th meeting held on 03-11-2021 decided as under:

The Authority deferred the agenda item for detailed deliberations keeping in view the therapeutic categories etc. of such formulations.

Proceedings of M-313:

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.

Decision: **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.

Case No.4. Issuance of Registration Letter of Pyrexa 5mg & 10mg Tablets of M/s. Genome Pharmaceuticals, Hattar

Registration Board in its 289th meeting held on 14th to 16th May, 2019 considered the subject mentioned case as per following details:

Proceedings of M-289

Following two products of M/s. Genome Pharmaceuticals, Hattar were approved in 264th meeting of Registration Board as dispersible tablets but because of availability of these products in reference regulatory authorities in Orally Disintegrating/Orodispersible tablets the registration letter could not be issued. Now the firm has submitted duplicate dossiers with respect to these products with correct formulation i.e. Orodispersible tablets.

S/N	Name of Manufacturers	Name of Drugs with composition.	Approved MRP with reference of meeting	Demanded pack size & Price	Remarks
1.	M/s. Genome Pharmaceuticals, Hattar.	Pyrexa 5mg Dispersible Tablets Each tablet contains:- Olanzapine …..5mg (Antipsychotic) Genome Specs	Price Not fixed yet	10‘s As Per SRO	Product is available and approved by US FDA as orally disintegrating tablet, and also available and approved by MHRA as orodispersible tablet specifications may be given accordingly. Name has been changed to **―Olnaz‖** due to similarity with already registered products.
2.	M/s. Genome Pharmaceuticals, Hattar.	Pyrexa 10mg Dispersible Tablets Each tablet contains:- Olanzapine …..10mg (Anti psychotic) Manufacturer‘s Specs	Price has not been fixed yet	10‘s As Per SRO	Product is available and approved by US FDA as orally-disintegrating tablet, and also available and approved by MHRA as orodispersible tablet specifications may be given accordingly. Name has been changed to **―Olnaz‖** due to similarity with already registered products.

Decision of M-287: *Registration Board decided to defer the case for submission of fresh fee for both products.*

Now, the firm has submitted a fresh fees of Rs.20,000/- for each product dated 6.02.2019. (Deposit Slip # 084063 & 084062 respectively).

Decision of M-289:

Registration Board deferred the request of M/s. Genome Pharmaceuticals, Hattar for submission of generic/me-too status of Olanzapine orally disintegrating/ Orodispersible Tablet 5 mg & 10mg.

In line with the above-mentioned decision of M-289 the firm has now submitted generic/ Me-Too Status for **Olanzapine Orodispersible Tablet 10mg only** i.e., as under:

1. Psyclan10mg Mouth Dispersible Tablet (Reg # 039161) of M/s PharmEvo Limited, Karachi
2. Olzip-10mg Orodispersible Tablet (Reg # 100234) of M/s Aries Pharmaceuticals, Peshawar.

Decision: Registration Board deferred the case till resumption of Drug Manufacturing License of M/s Genome Pharmaceuticals (Pvt) Ltd., Hattar.

Case No.5. Cancellation of Regitration of Ceftriaxone Injections of M/s Shazal’s Pharmaceuticals, Hattar.

Registration Board in its 307th meeting held on 8th – 10th June, 2021 approved following products of M/s Shazal’s Pharmaceuticals Plot No.41/1-A, Phase-I, Industrial Estate, Hattar by way of contract manufacturing at M/s Welmark Pharmaceuticals, Plot #122 Phase 5, Block B, Industrial Estate, Hattar:

S/N	Name of Manufacturer	Brand name of drug with composition and FPP specifications	Demanded MRP, Pack Size	Decision
1.	M/s Shazal's Pharmaceuticals. Plot No.41/1-A, Phase-I, Industrial Estate, Hattar, By M/s Welmark Pharmaceuticals. Plot #122 Phase 5, Block B, Industrial Hattar	Silver Cef 1g IV Injection Each Vial Contains: Ceftriaxone as Sodium …1gm USP	As per policy of MoH.	**Approved.**
2.	M/s Shazal's Pharmaceuticals. Plot No.41/1-A, Phase-I, Industrial Estate, Hattar, By M/s Welmark Pharmaceuticals. Plot #122 Phase 5, Block B, Industrial Hattar	Silver Cef 500mg IV Injection Each Vial Contains: Ceftriaxone as Sodium..500mg USP	As per policy of MoH.	**Approved.**
3.	M/s Shazal's Pharmaceuticals. Plot No.41/1-A, Phase-I, Industrial Estate, Hattar, By M/s Welmark Pharmaceuticals. Plot #122 Phase 5, Block B, Industrial Hattar	Silver Cef 250mg IV Injection Each Vial Contains: Ceftriaxone as Sodium…250mg USP	As per policy of MoH.	**Approved.**

While processing for issuance of registration letters, it was identified that as per available computerized record and copy of registration letter submitted by M/s Shazal's, Hattar, the firm was already issued registration of Ceftriaxone IV Injections 250mg, 500mg & 1g vide letter dated **24-07-2007** on contract manufacturing from M/s Trigon Pharmaceuticals, Lahore (**valid for 1/one year**). Detail is as under:

S. No.	Reg. No.	Name of Drug(s) & Composition	Packing	MRP
1.	045452	Sonacef 250mg IV Injection Each vial contains: Ceftriaxone Sodium eq. to Ceftriaxone…….250mg (USP Specifications)	Vial	Rs.101/-
2.	045453	Sonacef 500mg IV Injection Each vial contains: Ceftriaxone Sodium eq. to Ceftriaxone ……..500mg (USP Specifications)	Vial	Rs.170/-
3.	045454	Sonacef 1g IV Injection Each vial contains: Ceftriaxone Sodium eq. to Ceftriaxone ……..…1gm (USP Specifications)	Vial	Rs.321/-

However, the firm has clarified that they didn't submit renewal application within due date, therefore, they applied for fresh registration.

Accordingly, the instant case has been placed before the Registration Board for cancellation of previously granted registrations before issuance of registration letter of products approved in 307th meeting of Registration Board.

Decision: **Registration Board cancelled the registrations of below-mentioned products of M/s Shazal's Pharmaceuticals Plot No.41/1-A, Phase-I, Industrial Estate, Hattar due to non-submission of renewal application within due date.**

S. No.	Reg. No.	Name of Drug(s) & Composition
1.	**045452**	**Sonacef 250mg IV Injection** **Each vial contains:** **Ceftriaxone Sodium eq. to Ceftriaxone…….….250mg** **(USP Specifications)**
2.	**045453**	**Sonacef 500mg IV Injection** **Each vial contains:** **Ceftriaxone Sodium eq. to Ceftriaxone …….500mg** **(USP Specifications)**
3.	**045454**	**Sonacef 1g IV Injection** **Each vial contains:** **Ceftriaxone Sodium eq. to Ceftriaxone ……..…1gm** **(USP Specifications)**

Case. No.6. Surrendering of Already Approved/ Licensed Sections of M/s Zephyr Pharmatec (Pvt) Ltd., Karachi under Drug Manufacturing License No. 000403 (Formulation).

The Central Licensing Board in its 282nd meeting held on 31st August, 2021, considered and acceded to the request of M/s Zephyr Pharmatec (Pvt) Ltd., Plot No. A-39, S.I.T.E II, Super Highway Karachi for surrendering their following sections, licensed under DML No.000403(Formulation):

S. No.	Sections
1.	Capsule (Penicillin)
2.	Dry Powder Suspension (Penicillin)
3.	Ware House (Penicillin)

Accordingly, the firm was issued a show-cause notice regarding cancellation of registration of drugs issued under capsule (penicillin) and dry powder suspension (penicillin) sections vide letter dated 26-10-2021.

In response, the firm has now requested for cancellation of registration of following products registered against the sections withdrawn:

S. No.	Reg. No.	Product Name & Composition	Date of Reg. & Renewal Status
1.	037438	Zekatac Capsule 250mg Each capsule contains: Amoxicillin trihydrate 287.5 eq. to Amoxicillin…….250mg	**Reg. Date** 28-02-2005 **Last Renewal** 21-01-2020
2.	037439	Zekatac Syrup 250mg Each 5ml contains: Amoxicillin trihydrate 287.5 eq. to Amoxicillin……..250mg	**Reg. Date** 28-02-2005 **Last Renewal** 21-01-2020
3.	018784	Zekatac Capsule 500mg Each capsule contains: Amoxicillin trihydrate eq. to Amoxicillin base……..500mg	**Reg. Date** 04-04-1996 **Last Renewal** 22-05-2021
4.	018785	Zekatac Suspension Each 5ml contains: Amoxicillin trihydrate eq. to Amoxicillin base ……..125mg	**Reg. Date** 04-04-1996 **Last Renewal** 22-05-2021

Decision: **Keeping in view the decision taken by the Central Licensing Board in its 282nd Meeting held on 31st August, 2021, Registration Board decided to cancel registration of all the products registered under Capsule (Penicillin) Section and Dry Powder Suspension (Penicillin) Section of M/s Zephyr Pharmatec (Pvt) Ltd., Plot No. A-39, S.I.T.E II, Super Highway Karachi w.e.f date of surrendering/ cancellation of aforementioned sections i.e., 28-09-2021.**

Case No.7. Cancellation of Drug Manufacturing Licenses by Central Licensing Board

The Central Licensing Board has cancelled drug manufacturing licenses of following firms. Details are as under:

Sr. No.	Name of Firm	DML No.	Meeting No. of CLB	Date of Cancellation of DML
1.	M/s Medicure Laboratories, F-109, Hub River Road, S.I.T.E Karachi.	DML#000034 (Formulation).	282nd meeting held on 31-08-2021	18-10-2021
2.	M/s. Gaba Pharmaceuticals Laboratories, S-76, S.I.T.E Maripur Road Karachi. (DML #000168) formulation.	DML#000168 (Formulation).		11-10-2021

Accordingly, above-mentioned firms have been issued show-cause and personal hearing notices under sections 7(11) and 42 of the Drugs Act, 1976 & advised to appear before the Registration Board on 18th November, 2021 at 3:00 P.M.

Proceedings and Decision of 313th meeting of Registration Board:

Sr. No.	Name of Firms	Proceedings of 313th meeting of Registration Board	Decision of 313h meeting of Registration Board
1.	M/s Medicure Laboratories, F-109, Hub River Road, S.I.T.E Karachi. (DML #000034) formulation.	The Board was apprised that M/s Medicure Laboratories, Karachi (in response to the show-cause notice issued vide letter dated 03-11-2021) has informed regarding an appeal filed by them (on 28-10-2021) before the Appellate Board against cancellation of DML by CLB. Furthermore, the firm has informed that they have received personal hearing notice dated 16-11-2021 through Area FID, Mr. Abdul Rasool Sheikh and requested to defer the hearing owing to the illness of their CEO who is hospitalized and cannot attend the meeting.	**Keeping in view the decision taken by the Central Licensing Board in its 282nd meeting (held on 31-08-2021) regarding cancellation of DML, Registration Board cancelled the registration of all products registered in the name of Medicure Laboratories, F-109, Hub River Road, S.I.T.E Karachi w.e.f date of cancellation of their DML i.e., 18-10-2021.**
2.	M/s. Gaba Pharmaceuticals Laboratories, S-76, S.I.T.E Maripur Road Karachi. (DML #000168) formulation.	The Board was apprised that M/s. Gaba Pharmaceuticals Laboratories, Karachi was issued show-cause notice vide letter dated 03-11-2021 & personal hearing notice vide letter dated 16-11-2021. The same was also communicated through Area FID, Mr. Abdul Rasool Sheikh. However, the firm has not responded yet.	**Keeping in view the decision taken by the Central Licensing Board in its 282nd meeting (held on 31-08-2021) regarding cancellation of DML, Registration Board cancelled the registration of all products registered in the name of M/s. Gaba Pharmaceuticals Laboratories, S-76, S.I.T.E Maripur Road Karachi w.e.f date of cancellation of their DML i.e., 11-10-2021.**

Case No.8. Cancellation of Registration of Perval Syrup 250mg/5ml (R#092478) of M/s Perk Pharma, Plot No. 197/1-B, Industrial Estate, Gadoon

M/s Perk Pharma, Plot No. 197/1-B, Industrial Estate, Gadoon has inadvertently been issued following 02 registrations of same product i.e., Perval 250mg/5ml Syrup:

S/N	Reg. No.	Name of Drug(s) & Composition	Packing	MRP	RB Meeting No. & Date of Reg.
1.	095171	Perval 250mg/5ml Syrup Each 5ml contains: Sodium Valproate eq to Valproic Acid ……..……250mg (USP specification)	60ml	Rs.50/-	M-284 29-04-2019
2.	092478	Perval 250mg/5ml Syrup Each 5 ml contains: Sodium Valproate Eq to Valproic Acid ……....250mg (As per *Innovator's Specifications)	60ml	Rs.50.00	M-282 05-10-2018

Although, the registration at S.No.2 was approved & issued earlier, however, keeping in view that the registration at S.No.1 has been issued with pharmacopeial specifications, therefore, the case has been placed before the Registration Board for cancellation of registration of product at S.No.2 i.e., issued vide Reg No. 092478.

Decision: **Registration Board cancelled the registrations of Perval 250mg/5ml Syrup; Reg. No. 092478 of M/s Perk Pharma, Plot No. 197/1-B, Industrial Estate, Gadoon as the firm holds registration of same formulation issued vide Reg. No.095171.**

Case No.9. Request for Change in Registration Status of Products from M/s OBS Pakistan (Pvt.) Ltd., Karachi to M/s Aspin Pharma (Pvt.) Ltd., Karachi

Registration Board in its 307th meeting held on 8th – 10th June, 2021 deferred the request of M/s. Aspin Pharma (Pvt.) Ltd; Plot No. 10 & 25, Sector 20, Korangi Industrial Area Karachi-74900 for change of registration status of following products from M/s. OBS Pakistan (Pvt.) Ltd; Karachi to their name. Detail is as under:

Administrative Documents in the light of SOP approved by the Registration Board in its 283rd meeting
i. Copy of last GMP inspection report dated 01-06-2020 (**Good** Level of Compliance).
ii. Panel Inspection report for renewal of DML dated 26-01-2021.
iii. Section approval of M/s Aspin verified from Licensing Division's letter for renewal of DML (dated 09th June, 2016) confirming following sections; ➢ Tablet (General) ➢ Capsule (General) ➢ Liquid Syrup ➢ Ointment/ Cream.
iv. NOC from M/s. OBS Pakistan (Pvt.) Ltd; Karachi dated 07-01-2021 & 16-03-2021.
v. Relevant undertakings & commitments.

1. Nexprazole 20mg Capsule:

I	II	III	IV	V
S/N	**Reg. No.**	**Name of drug(s) & Composition**	**Registration Trail**	**Remarks**
1.	039680	Nexprazole 20mg Capsule Each capsule contains **:** (Enteric coated pellets) of Esomeprazole Magnesium Trihydrate eq. to Esomeprazole……20mg	Initial Reg. Date: 28-11-2005 Transfer of Reg. 25-07-2009 Remarks of RRR Section Renewal application of year 2019 received on 26-03-2019 i.e within time, under the Rule 27 of Drug Licensing,	Dy.No.325/DDC(Reg-I) 16-04-2019 Rs.20,000/- Dy.No.421/DDC(Reg-I) 03-05.2019 Rs.100,000/-

			Registering & Advertising Rules, 1976.	
	Name, address of Applicant / Marketing Authorization Holder		M/s Aspin Pharma (Pvt) Ltd, Karachi. Plot No. 10&25 Korangi Industrial Area, Karachi-Pakistan	
	Name, address of Manufacturing site.		M/s Aspin Pharma (Pvt) Ltd, Karachi. Plot No. 10&25 Korangi Industrial Area, Karachi-Pakistan. (DML 000045) (Transfer of Registration from M/s OBS Pakistan Pvt. Ltd Karachi, [NOC attached dated 07-01-2021]	
	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 Aspin Pharma (Pvt) Ltd. Plot No. 10&25 Korangi Industrial Area, Karachi dated 18.06.2020.	
	Evidence of approval of manufacturing facility		Applicant has provided copies of renewal of DML letter, and GMP certificates of manufacturing site mentioning Capsule (General) 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. 325/DDC/Reg-I), 16-04-2019 & Dy.No 2586 (21-1-2021)	
	Details of fee submitted		For transfer of registration: PKR 20,000/-: 11-04-2019	
	proposed proprietary name / brand name		Nexprazole 20 mg Capsule	
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit		Each Capsule contains: Esomeprazole Magnesium Trihydrate (enteric coated pellets) equivalent to 20 mg of Esomeprazole	
	Pharmaceutical form of applied drug		Hard Gelatin Capsule #3, Green Opaque Cap and Green Opaque Body containing white spherical pellets.	
	Pharmacotherapeutic Group of (API)		Proton Pump Inhibitor	
	Reference to Finished product specifications		USP Specification	
	Proposed Pack size		2 x 7's	
	Proposed unit price		-	
	status in reference regulatory authorities		Nexium 20mg Capsule, AstraZeneca	
	For generic drugs (me-too status)		Esomax 20mg Capsule, Martin Dow, Karachi (Reg# 043349)	
	Name and address of API manufacturer.		M/s Surge Laboratories (Pvt) Ltd, 10th Km Faisalabad Road, Bikhi, District Sheikhupura (DML 000649)	
	1.5.11-Proposed Label		Not submitted	
	Module-II (Quality Overall Summary)		Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to general properties, solubilities, physical form, specification, impurities, specifications, analytical procedures, batch analysis, pharmacopeial specifications, working standard, container closure system and stability studies of drug substance and drug product. Following	

		points require clarification from firm: Firm has used secondary reference standard provided by Drug Substance manufacturer. Firm has not summarized development of formulation and manufacturing process under 2.3.P.2.2.1 and 2.3.P.2.3.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, physical form, DS and raw material specifications, manufacturing process and its devolopement, process validation report, excipients specifications, analytical methods and certificate of analysis, Control of critical steps of manufacturing and intermediates, impurities, specifications based on USP-42, analytical procedures, batch analysis and justification of specification, reference standard and its standrdization, 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 6 batches (03 pilot 20kg ,and 03 commercial 200kg) 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 and the real time stability data is conducted at 30oC ± 2oC / 65% ± 5% RH for 36 months. The Esomeprazole Pellets were filles in blue HDPE container lined with double polythene bag. Stability concluded that Esomeprazole pellets 22.5% is stable.
	Module-III Drug Product:	Firm has submitted data of drug product including its 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. The Specifications and control tests are in compliance to USP. However, following comments are submitted for consideration: Firm has provided formulation development under 3.2.P.2.2.1 and validation of manufacturing process but not manufacturing process and process controls of drug product under 3.2.P.3. Significant difference for the manufacturing process used for primary stability batch and process for commercial batches were not identified. Instead of pharmacopeial reference standards, firm used working standards provided by DS manufacturer. Firm has not conducted Container Closure System suitability studies, however, commitment is given to perform upon commercialization.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not performed in this strength, however firm attached data of CDP of higher strength i.e. Nexprazole 40mg.
	Analytical method validation/verification of product	Firm has claimed USP specifications for which report of verification of analytical method for the drug product has been provided.

STABILITY STUDY DATA	
Manufacturer of API	M/s Surge Laboratories (Pvt) Ltd, 10th Km Faisalabad Road, Bikhi, District, Sheikhupura (DML 000649)
API Lot No.	EPC-22EC-014

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 Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9,12 (Months)		
Batch No.	197DS04	197DS05	197DS06
Batch Size	2500 Capsules	2500 Capsules	2500 Capsules
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	16-03-2020	16-03-2020	16-03-2020
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 Additional Director DRAP, Lahore dated 04-07-2019. The GMP certificate was granted based on inspection dated 03-07-2019.
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 03 Kg Esomeprazole pellets dated 15-01-2020.
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 are 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:

Shortcomings communicated	**Response by the firm**
Stability studies conducted at new manufacturing site i.e M/s Aspin Pharma (Pvt) Ltd, Karachi.	Firm provided data of stability studies both accelerated and long term, at new manucaturing site. However, 12 months data for long term studies have been provided yet and studies are continued for 24months.
Comparative Dissolution Profile	Not performed in this strength, however firm attached data of CDP of higher strength i.e. Nexprazole 40mg.
Process validation protocols and Analytical method validation/ verification	Firm provided manufacturing process validation protocol, and also provided analytical method verification report for USP analytical method. However, they need to improve with regards to good documentation practices as certain standard documents are without effective date.

Decision of M-307:	***Deferred for submission of CDP.***

Current Submission by the Applicant:

The firm has submitted Pharmaceutical Equivalence & Comparative Dissolution Studies of the product against the respective reference product. Summary of CDP report is as under:-

<table>
<tr><td colspan="2">Comparative Dissolution Profile</td></tr>
<tr><td>Dy. No and date of submission</td><td>29364 / DRAP (R&I) 27-Oct-2021</td></tr>
<tr><td>proposed proprietary name/brand name</td><td>Nexprazole 20 mg Capsule</td></tr>
<tr><td>Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit</td><td>Each Capsule contains:
Esomeprazole Magnesium Trihydrate (enteric coated pellets) equivalent to 20 mg of Esomeprazole</td></tr>
<tr><td>Pharmaceutical form of applied drug</td><td>Hard Gelatin Capsule #3, Green Opaque Cap and Green Opaque Body containing white spherical pellets.</td></tr>
<tr><td>Container Closure System</td><td>Alu/PVC blister in unit carton</td></tr>
<tr><td>Pharmaceutical Equivalence and Comparative Dissolution Profile</td><td>The comparative dissolution profile was performed for Nexpazole 20mg Capsule (Batch # 197DS06) against the Nexum 20mg Capsule (Getz Pharma, Batch # 358C12). Comparison was performed in phosphate buffer (pH 6.8) only, using 12 samples at 10, 15,20, 30, 45 and 60 minutes intervals using USP type II (paddle) apparatus at 37.0 ± 0.5 ºC.
<table>
<tr><th>Sr</th><th>Mediums</th><th>Time interval</th><th>Nexprazole 20mg Cap</th><th>Nexum 20mg Cap</th></tr>
<tr><td rowspan="8">i.</td><td rowspan="8">phosphate buffer (pH 6.8)</td><td>10 min</td><td>36.162 %</td><td>36.173 %</td></tr>
<tr><td>15 min</td><td>63.004 %</td><td>66.920 %</td></tr>
<tr><td>20 min</td><td>80.9999 %</td><td>91.860 %</td></tr>
<tr><td>30 min</td><td>102.337 %</td><td>99.758 %</td></tr>
<tr><td>45 min</td><td>101.627 %</td><td>97.269 %</td></tr>
<tr><td>60 min</td><td>99.969 %</td><td>94.881 %</td></tr>
<tr><td colspan="3">f1 = 5.538
f2= 62.439</td></tr>
<tr><td>ii</td><td>Acid stage medium (0.1 N HCl)</td><td>02 hours</td><td colspan="2">No peak observed</td></tr>
</table>
Calculation of value revealed that both dissimilarity factor f1 and similarity factor f2 fall under acceptable criteria at the pH 6.8, while no active release was observed in acidic medium.</td></tr>
</table>

2. Pepcidine 40mg Tablets:

I	II	III	IV	V
S/N	**Reg. No.**	**Name of drug(s) & Composition**	**Registration Trail**	**Remarks**
2.	009729	Pepcidine 40mg Tablet Each tablet contains: Famotidine ……40mg	As per provisional list of renewal applications received within due date (retrieved from www.dra.gov.pk accessed on: 03-06-2021) Initial Reg. Date: 21-04-1998 Renewal Due Date: 08-07-2014 Renewal Application Date (R&I): 17-06-2014 Last renewal application Date (R&I): 26-03-2019 with fee of Rs.10000/-	Dy.No. 9844-R & I dated 31-03-2021

	Name, address of Applicant / Marketing Authorization Holder	M/s Aspin Pharma (Pvt) Ltd, Karachi. Plot No. 10&25 Korangi Industrial Area, Karachi-Pakistan
	Name, address of Manufacturing site.	M/s Aspin Pharma (Pvt) Ltd, Karachi. Plot No. 10&25 Korangi Industrial Area, Karachi-Pakistan. (DML 000045) (Transfer of Registration from M/s OBS Pakistan Pvt. Ltd Karachi, [NOC attached dated 07-01-2021]
	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 Aspin Pharma (Pvt) Ltd. Plot No. 10&25 Korangi Industrial Area, Karachi dated 18.06.2020.
	Evidence of approval of manufacturing facility	Applicant has provided copies of DML and renewal application, and GMP certificates of manufacturing site mentioning Tablet (General) 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. 9844 : 28-03-2021
	Details of fee submitted	For transfer of registration: PKR 20,000/-: 02-05-2019
	proposed proprietary name / brand name	**Pepcidine 40 mg Tablet (Reg.009729)**
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Famotidine 40mg
	Pharmaceutical form of applied drug	Pink to red color oval shaped, film coated tablets, having score line on both sides.
	Pharmacotherapeutic Group of (API)	H2 receptor blocker
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	1x10x4's
	Proposed unit price	-

	status in reference regulatory authorities	Pepcid 40mg Tablet, Merck Sharp &Dohme (Australia) Pty Ltd.
	For generic drugs (me-too status)	Pepton 40mg Tablets, Paramount Pharmaceuticals, Pakistan. (Reg# 023077)
	Name and address of API manufacturer.	M/s SMS Pharmaceuticals Limited Unit-I, Sy.No. u180/2, Kazipalli (V), Jinnaram (M), Medak District, Telagana, India GMP certificate issued on 07-08-2019 by Drug Control Administration, Government of Telangana, India
	1.5.11-Proposed Label	Not submitted
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to general properties including physical form, solubility profiles and polymorphic form (A & B). Claimed that DS and finish product comply to USP specification. Brief information related to analytical procedures, specification, working standard, container closure system and stability studies of drug substance and drug product has been provided. Following points require clarification from firm: Firm has used secondary reference standard provided by Drug Substance manufacturer. Firm has not conducted compatibility studies of DS with excipients under 2.3.P.2.1, neither discussed choice of excipients Firm has not summarized development of formulation and manufacturing process under 2.3.P.2.2 and 2.3.P.2.3.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, manufacturing process, Characterization, impurities formation, specifications based on USP, analytical procedures and its verification, batch analysis, reference standard, container closure system, residual solvents determination with method validation and stability studies. However, following points need consideration: -
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 6 batches (50 Kg each) of drug substance at both accelerated as well as real time conditions. The accelerated stability data was conducted at 40oC ± 2oC / 75% ± 5% RH for 6 months and the long term stability data is conducted at 30oC ± 2oC / 65% ± 5% RH for 36 months. The famotidine powder were placed in double poly bags and krpt in HDPE drum. Also conducted degradation stress study. Firm also conducted forced degradation studies in different conditions which revealed maximum degradation in acidic conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its composition, pharmaceutical development, manufacture, manufacturing process, 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. The Specifications and control tests are in compliance to USP. However, following comments are submitted for consideration: Firm claimed for using selecting same excipients as in innovator and not conducted DS & excipients compatibility studies. Neither provided specification of excipients 3.2.P.4. Significant difference for the manufacturing process used for primary stability batch and process for commercial batches were

		not identified. Instead of pharmacopeial reference standards, firm used working standards provided by DS manufacturer. Specifications and analytical methods used for testing of excipients were not described. Firm has not conducted Container Closure System suitability studies; however, commitment is given to perform upon commercialization. Suitability of container closure system is not discussed.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has not submitted Pharmaceutical Equivalence and Comparative Dissolution Profile stating the instant product as "Originator/Innovator" which was transferred from Merck Sharp & Dome of Pakistan, Karachi to M/s OBS Pakistan Pvt. Ltd. Karachi vide letter dated 09-07-2009.
	Analytical method validation/verification of product	Firm has claimed USP specifications for which report of verification of analytical method for the drug product has been provided.

STABILITY STUDY DATA

Manufacturer of API	M/s SMS Pharmaceuticals Limited Unit-I, Sy.No. u180/2, Kazipalli (V), Jinnaram (M), Medak District, Telagana, India		
API Lot No.	FMT 263 02 17		
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	Accelerated: 6 months Real time: 12 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9,12 (Months)		
Batch No.	202DS06	202DS05	202DS04
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	01-2020	01-2020	12-2019
Date of Initiation	14-01-2020	14-01-2020	14-01-2020
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)	-
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 Drug Control Administration, Government of Telangana, India dated 07-08-2019. GMP certificate was granted based on inspection dated 02nd to 3rd July, 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 50Kg of Famotidine USP Batch FMT 263 02 17 dated 18-03-2017 by M/s OBS Pakistan 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 their HPLC system is 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:

Shortcomings communicated	Response by the firm
Stability studies conducted at new manufacturing site i.e M/s Aspin Pharma (Pvt) Ltd, Karachi.	Firm provided data of stability studies of 03 batches, both accelerated and long term, at new manufacturing site. However, 12 months data for long term studies have been provided yet and studies are continued for 24months.
Comparative Dissolution Profile	Firm claimed that CDP is not applicable
Process validation protocols and Analytical method validation/ verification	Firm provided manufacturing process validation protocol, and also provided analytical method verification report for USP analytical method. However, they need to improve with regards to good documentation practices as certain standard documents are without effective date.

Decision of M-307:	***Deferred for submission of CDP.***

Current Submission by the Applicant:

The firm has submitted Pharmaceutical Equivalence & Comparative Dissolution Studies of the product against the respective reference product. Summary of CDP report is as under:-

Comparative Dissolution Profile	
Dy. No and date of submission	26861 / DRAP (R&I) 21-Oct-2021
proposed proprietary name / brand name	Pepcidine 40 mg Tablet
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Famotidine 40mg
Pharmaceutical form of applied drug	Pink to red color oval shaped, film coated tablets, having score line on both sides
Container Closure System	Alu/PVC blister in unit carton
Pharmaceutical Equivalence and Comparative Dissolution Profile	The comparative dissolution profile was performed for Pepcidine 40mg Tablet (Batch # 202DS04) against the NOCID 40mg Tablet (Sandoz, Batch # WB3T). Comparison was performed in acidic buffer (pH 1.2), acetate buffer (pH 4.5) and phosphate buffer (pH 6.8) at 10, 15,20, 30, and 45 intervals using USP type II (paddle) apparatus at 37.0 ± 0.5 ºC. Famotidine belongs to Class IV in Biopharmaceutics Classification System (BCS) which has low solubility and membrane permeability.

Sr	Mediums	Time interval	Pepcidine 40mg Tab	NOCID 40mg Tab
i	Acidic buffer (pH 1.2)	10 min	41.215 %	45.358%
		15 min	38.188%	43.980%
		20 min	35.495%	40.815%
		30 min	32.431%	36.534%
		45 min	28.800%	27.752%
		f1 = 10.495 f2= 67.265 **Both sample and reference products degraded in pH 1.2 dissolution medium.**		
ii	Acetate buffer (pH 4.5)	10 min	96.698%	87.930%
		15 min	95.997%	92.023%
		20 min	94.561%	92.133%
		30 min	94.657%	91.423%
		45 min	92.981%	91.307%

<table>
<tr><td></td><td>
<table>
<tr><td></td><td></td><td colspan="3">f1 = 4.414
f2= 65.786</td></tr>
<tr><td rowspan="6">iii</td><td rowspan="6">Phosphate Buffer (pH 6.8)</td><td>10 min</td><td>99.723 %</td><td>89.006%</td></tr>
<tr><td>15 min</td><td>99.436%</td><td>97.479%</td></tr>
<tr><td>20 min</td><td>99.156%</td><td>96.502%</td></tr>
<tr><td>30 min</td><td>97.414%</td><td>98.068%</td></tr>
<tr><td>45 min</td><td>95.844%</td><td>97.212%</td></tr>
<tr><td colspan="3">f1 = 3.628
f2= 64.374</td></tr>
</table>
Calculation of value revealed that both dissimilarity factor f1 and similarity factor f2 fall under acceptable criteria at the pH 1.2, pH 4.5 and pH 6.8.
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Decision **Registration Board decided as under:**

i. Cancelled registration of following products from the name of M/s OBS Pakistan (Pvt.) Ltd., C-14, Manghopir Road, S.I.T.E. Karachi:

S. No.	Reg. No.	Product Name & Composition
i.	039680	Nexprazole 20mg Capsule Each capsule contains **:** (Enteric coated pellets) of Esomeprazole Magnesium Trihydrate eq. to Esomeprazole……20mg
ii.	009729	Pepcidine 40mg Tablet Each tablet contains: Famotidine ……40mg

ii. Approved registration of following products in the name of M/s Aspin Pharma (Pvt.) Ltd; Plot No. 10 & 25, Sector 20, Korangi Industrial Area Karachi:

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
i.	**Each Capsule contains:** **Esomeprazole Magnesium Trihydrate (Enteric Coated Pellets)** **Equivalent to Esomeprazole…….. 20mg** **(USP Specifications)** **<u>Source of Pellets:</u>** **M/s Surge Laboratories (Pvt) Ltd, 10th Km Faisalabad Road, Bikhi, District Sheikhupura**
ii.	**Pepcidine 40mg Tablet** **Each film coated tablet contains:** **Famotidine……...40mg** **(USP Specifications)**

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.1: Cancellation of Drug Manufacturing Licenses by Central Licensing Board

a. Central Licensing Board in its 273rd meeting cancelled the DML of M/s. Rehmat Pharma. Details is as under;

Sr. No.	Name of Firm	Decision of CLB
1.	M/s Rehmat Pharma, 10-Km, Sheikhupura Road, Lahore	The Central Licensing Board cancelled the Drug Manufacturing License **No.000476** by way of formulation in the name of M/s Rehmat Pharma, 10-Km, Sheikhupura Road, Lahore with immediate effect under the Drugs Act, 1976 and rules framed there under.

Decision of M-307: *Keeping in view the decisions taken by the Central Licensing Board for cancellation of Drug Manufacturing Licenses, the Registration Board deliberated and decided to issue show cause notices to above mentioned firms under section 7 (11) of the Drugs Act, 1976 as to why the registrations issued under these DMLs may not be cancelled w.e.f date of cancellation of their DMLs.*

Accordingly, above-mentioned firm was issued show cause and personal hearing notice to appear before the Registration Board in its 309th meeting.

Proceedings of M-309:

The firm was issued show cause and personal hearing notices vide letter dated 8th July, 2021 to appear before the Registration Board. However, No one appeared before 309th meeting of Registration Board.

Registration Board in its 309th meeting deferred the case of M/s Rehmat Pharma, 10-Km, Sheikhupura Road, Lahore till the decision of Appellate Board as firm had filed an appeal before the Appellate Board against the decision of Central Licensing Board.

Decision of 156th meeting of Appellate Board:

The Board, after hearing arguments and perusing the record of the case, decided to upheld the decision of Central Licensing Board. The appeal is dismissed, accordingly.

Registration Board in its 312th meeting decide to issue show cause and personal hearing notice to M/s. Rehmat Pharma for cancellation of registration of their products.

Accordingly, M/s. Rehmat Pharma has been issued show cause and personal hearing notice to appear before the Registration Board.

b. Central Licensing Board in its 282nd meeting held on 31-08-2021 cancelled Drug manufacturing licenses of following firms. Detail is as under;

Sr. No.	Name of Firm	Decision of CLB
1.	M/s. Caylex Pharmaceuticals (Pvt) Ltd. 27-Km Mian Raiwind Road Lahore.	The considering the facts on the record and after thread deliberation decided that Drug Manufacturing License **No. 000415** by way of formulation in the name of M/s. Caylex Pharmaceuticals (Pvt) Ltd. 27-Km Mian Raiwind Road Lahore stands cancelled vide letter dated 05-10-2021 under Section 41 of the Drugs Act, 1976 read with Rule 12 of the Drugs (Licensing, Registering and Advertising) Rules, 1976 as an application for renewal of the Drug Manufacturing License is not submitted as prescribed under the Rules.
2.	M/s. Helicon Pharmacutek Pakistan (Pvt) Ltd. Model Town Road Faisalabad.	The considering the facts on the record and after thread deliberation decided that Drug Manufacturing License **No. 000117** by way of formulation in the name of M/s. Helicon Pharmacutek Pakistan (Pvt) Ltd. Model Town Road Faisalabad stands cancelled vide letter dated 05-10-2021 under Section 41 of the Drugs Act, 1976 read with Rule 12 of the Drugs (Licensing, Registering and Advertising) Rules, 1976 as an application for renewal of the Drug Manufacturing License is not submitted as prescribed under the Rules.
3.	M/s. Syntex Pharmaceuticals Opp. People's Colony Kamra Road Attock City.	The considering the facts on the record and after thread deliberation decided that Drug Manufacturing License **No. 000290** by way of formulation in the name of M/s. Syntex Pharmaceuticals Opp. People's Colony Kamra Road Attock City stands cancelled vide letter dated 05-10-2021 under Section 41 of the Drugs Act, 1976 read with Rule 12 of the Drugs (Licensing, Registering and Advertising) Rules, 1976 as an application for renewal of the Drug Manufacturing License is not submitted as prescribed under the Rules.

Registration Board in its 307th meeting has authorized its Chairman for issuance of show cause notice for cancellation of registration after cancellation of DML. Accordingly, above mentioned firms were issued show cause notices and now all firms are called for personal hearing before the Registration Board.

Proceedings and Decision of 313th meeting of Registration Board:

Sr. No.	Name of Firms	Proceedings of 313th meeting of Registration Board	Decision of 313th meeting of Registration Board
3.	M/s Rehmat Pharma, 10-Km, Sheikhupura Road, Lahore	The firm was issued showcause and personal hearing notices vide letter dated 10th November, 2021 to appear before the Registration Board. However, No one appeared before 313th meeting of Registration Board.	**Keeping in view the decision taken by the Central Licensing Board in its 273rd meeting regarding cancellation of DML, Registration Board cancelled the registration of all products registered in the name of M/s Rehmat Pharma, 10-Km, Sheikhupura Road, Lahore w.e.f cancellation of their DML.**
4.	M/s. Caylex Pharmaceuticals (Pvt) Ltd. 27-Km Mian Raiwind Road Lahore.	Secretary CLB has communicated decision of 283rd meeting of CLB vide letter No. 1-10/96-Lic Pt (Vol-I) dated 29th October, 2021 in wich it was decided to revoke previous decision of cancellation of Drug Manufacturing License No. 000451 by way of formulation in the name of M/s. Caylex Pharmaceuticals (Pvt) Ltd., 27-Km, Main Raiwing Road, Lahore	**Keeping in view the decision of 283rd meeting of Central Licensing Boad, Registration Board decised to withdraw the show cause notice issued to M/s. Caylex Pharmaceuticals (Pvt) Ltd., 27-Km, Main Raiwing Road, Lahore**
5.	M/s. Helicon Pharmacutek Pakistan (Pvt) Ltd. Model Town Road Faisalabad.	Mr. Tariq Mahmood on behalf of M/s. Helicon, Faisalabad appeared before the Board and informed that they have filed an appeal in the Appellate Board and their case is pending for decision of Appellate Board.	**Keeping in view the decision taken by the Central Licensing Board in its 283rd meeting regarding cancellation of DML, Registration Board cancelled the registration of all products registered in the name of M/s. Helicon Pharmacutek Pakistan (Pvt) Ltd. Model Town Road Faisalabad w.e.f cancellation of their DML.**
6.	M/s. Syntex Pharmaceuticals Opp. People's Colony Kamra Road Attock City.	The firm was issued showcause vide letter dated 21st October, 2021 and personal hearing notices vide letter dated 10th November, 2021 to appear before the Registration Board. However, No one appeared before 313th meeting of Registration Board.	**Keeping in view the decision taken by the Central Licensing Board in its 283rd meeting regarding cancellation of DML, Registration Board cancelled the registration of all products registered in the name of M/s. Syntex Pharmaceuticals Opp. People's Colony Kamra Road Attock City w.e.f cancellation of their DML.**

Case No.2: Registration of Products of M/s Mediceena Pharma (Pvt) Ltd. Lahore.

Registration Board in its 234th meeting held on 16-07-2012 approved the following Products of M/s. Mediceena Pharma, Lahore and decided as under:-

S. No.	Name of Drugs & Composition	Demanded MRP & Pack Size	Decision of 234th meeting	Remarks
1.	Klaridox Injection Each vial contains:- Clarithromycin Lactobionate eq.to Clarithromycin.....500mg (antibiotics)	1's As per SRO	Approved subject to verification of dry powder injection General from Licensing Section.	Approved in MHRA Product is available in BP
2.	Lyphocin Infusion Each vial contains:- Vancomycin hydrochloride eq. to vancomycin….1gm (antibiotics)	1's As per SRO	Approved subject to verification of dry powder injection General from Licensing Section.	Approved in MHRA Product is available in USP
3.	Rabizol Injection Each vial contains:- Rabeprazole.....20mg	1's As per SRO	Approved subject to verification of dry powder injection General from Licensing Section.	International availability not confirmed
4.	Fosfomin Injection Each vial contains:- Fosfomycin Sodium eq.to fosfomycin….....1gm	1's As per SRO	Approved subject to verification of dry powder injection General from Licensing Section.	Approved in Spain Product is available in JP
5.	Azimycin Injection Each vial contains:- Azithromycin dihydrate eq. to Azithromycin…....250mg (Macrolides (Antibiotics)	10ml As per SRO	Approved subject to verification of dry powder injection General from Licensing Section.	Approved in MHRA Product is available in USP

Firm has submitted following documents and requested for issuance of registration letters for above mentioned.

i. Differential fee of Rs. 12000/- for each product (Yellow copies)
ii. GMP inspection reports conducted on dated 28-05-2013 and 14-07-2014 which are reflecting that firm has Dry Powder Injection (General) as dedicated area for manufacturing of dry powder injections.

Registration Board in 288th meeting referred the case to QA&LT Division for updated GMP status of firm. Now firm has submitted GMP certificate issued based upon evaluation conducted on 24-09-2019

Decision: Registration Baord deferred the case for confirmation of section approval from Licensing Division and updated status of GMP from QA & LT Division.

Case No.3 Correction in Minutes of Registration Board Meetings.

i. M/s Standpharm Pakistan Pvt. Ltd. 20-km, Ferozepur Road, Lahore

Registration Board in its 297th meeting approved following product of M/s. StandPharm. Registration letter was not issued as there is some typo error while drafting minutes regarding strength of formulation. Details are as under;

Sr. No.	Name of Approved Drug(s) & Composition	Corrected Name of Drug(s) & Composition	Remarks
1.	C-Pime 500 mg Injection Each Vial Contains: **Cefepime (as hydrochloride) …… 250mg** **(With L-arginine)** USP Specifications	C-Pime 500 mg Injection Each Vial Contains: **Cefepime (as hydrochloride) …… 500mg** **(With L-arginine)** USP Specifications	Registration letter not yet issued

Firm has submitted receiving of registration application along with yellow copy of fee challan which reveals that applied strength is 500mg instead of 250mg.

Decision: Registration Board approved the correction with following details.

C-Pime 500 mg Injection

Each Vial Contains:
Cefepime (as hydrochloride) … 500mg
(With L-arginine)

Case No.4 Registration of Drug M/s. PharmaWise Labs (Pvt) Ltd., Lahore

Registration Board in its various meeting approved the following products of M/s. PharmaWise Labs, Lahore and the firm has informed that they have not yet got registration letter:-

Sr. No.	Name of Drug(s)	Demanded Pack Size/Price	Decision	Remarks
1.	Zinco wise Syrup Each 5ml contains:- Zinc sulphate Monohydrate elemental zinc…….20mg	60ml Rs.20.00	**M-223** Approved. The Board decided to send reference to Licensing section for no requirement of HVAC in Liquid syrup section.	WHO Approved formulation Product is available in International Pharmacopoeia
2.	Ciprus Tablets Each tablet contains:- Ciprofloxacin……500mg	10 Tablets As per SRO	**M-229** Deferred till installation of HVAC.	Film coated tablet is approved in MHRA and firm has submitted fee of Rs.5000/- for such correction Product is available in USP
3.	Ciprus Tablets Each tablet contains:- Ciprofloxacin……250mg	10 Tablets As per SRO	-do-	Film coated tablet is approved in MHRA and firm has submitted fee of Rs.5000/- for such correction Product is available in USP
4.	Ciprus Dry Syrup Each 5ml contains:- Ciprofloxacin……125mg/5ml	60ml As per SRO	-do-	USFDA Approved Product is available in USP Firm has submitted source of granules as "M/s. Vision, Islamabad."
5.	Alerwise Syrup Each 1ml contains:- Cetirizine dihydrochloride…….1mg	60ml As per SRO	**M-236** Approved subject to Installation of HVAC system in section.	MHRA Approved. Product is available in USP
6.	Promin Suspension Each 5ml contains:- Ibuprofen …100mg/5ml	60ml As per SRO	-do-	MHRA Approved Product is available in USP

Firm has submitted following documents;

i. Form 5
ii. Photocopy of fee challan of Rs.8000/- and fresh submission of Rs.12000/- for each product
iii. GMP certificate issued based upon evaluation conducted on 16-10-2019
iv. Last inspection report dated 29-10-2018 confirming that firm has installed HVAC system in their manufacturing facility.

Registration Board in its 297th meeting deferred the case due to GMP non-compliance.

Now area FID has forwarded an inspection report dated 25-10-2021 in which it was concluded as under;

> In view of above inspection proceedings, it was observed that the firm had rectified most of the deficiencies pointed out during last GMP inspection, hence the firm had displayed positive approach towards compliance.

Decision: Registration Baord deferred the case for confirmation of updated status of GMP from QA & LT Division.

Case No.4 Registration of Drug(s) of M/s. Life Pharmaceutical Company 24-III Industrial Estate, Multan.

Registration Board in its 234th meeting approved following product of M/s. Life Pharmaceutical Company, Multan and the firm has requested that they have not yet received the registrations of these product. They have requested to issue the registration of below mentioned product:-

Sr. No.	Name of Drug(s)	Demanded Pack size	Demanded MRP	Decision of Registration Board M-234	Remarks
1.	Mupirocin Topical Ointment 2% Each gram contains:- Mupirocin……2% w/w (USP Specifications)	15gm	Rs.280.00	Approved subject to verification of dosage form in reference books.	MHRA approved product.

Firm has submitted following documents;

1. Copy of Form-5
2. Photocopies of fee challans of Rs.8000/- and Rs.12000/-
3. Section approval of Tablet (General) Section, Capsule (General) Section and cream / Ointment (General, Steroidal).
4. GMP Certificate issued based upon evaluation conducted on 16-06-2021.

Decision: Registration Baord approved above product in the name of M/s. Life Pharmaceutical Company 24-III Industrial Estate, Multan. Fee shall be verified as per the decision taken by the Registration Board in its 285th meeting.

Case No.5 Request for Contract Testing by M/s. Dew-Max Pharmaceuticals (Pvt) Ltd., Islamabad.

Registration Boars in its 312th meeting approved following products of M/s. Dew-Max Pharmaceuticals (Pvt) Ltd., Islamabad. Detail is as under;

Sr. No.	Product Name and Composition	Decision of 312th meeting Registration Board
1.	DEWNEM Injection 500mg Each vial contains: Meropenem trihydrate eq to meropenem…….500mg In-house specs USP	*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.* • *The firm shall purchase atomic absorption spectrophotometer for testing of sodium contents as per USP monograph and submit evidence of purchase and Installation Qualification (IQ) and Operational Qualification (OQ) alongwith performance data for sodium content test on stability batches before issuance of registration letter.*
2.	DEWNEM Injection 1g Each vial contains: Meropenem trihydrate eq to meropenem……...1g USP	*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.* • *The firm shall purchase atomic absorption spectrophotometer*

		for testing of sodium contents as per USP monograph and submit evidence of purchase and Installation Qualification (IQ) and Operational Qualification (OQ) alongwith performance data for sodium content test on stability batches before issuance of registration letter.

Firm has submitted a request stating that they started manufacturing from last two years and they are not in position to purchase new atomic absorption spectrophotometer but they will perform the sodium content test from M/s. Rotex Pharma, Islamabad.

Firm has also submitted contact agreement between M/s. Dew-Max, Islamabad and M/s. Rotex Pharma (Pvt) Ltd. Islamabad regarding testing of raw materials on atomic absorption spectrophotometer.

Decision: Registration Baord deferred the case for further deliberation as per Rule 20A of Drugs (L,R&A) Rules, 1976.

Case No.01: Referred Cases of 68-Meeting of Post Registration Variation Committee:

i. Rationale for Claim of GSK Specification & Rectification in Label Claim.

Dy.No.686; 826 & 1278 (PR-I) dated: 2nd; 22nd Jun & 29th Sep-21.

M/s GlaxoSmithKline Consumer Healthcare Pakistan Limited, Karachi has requested for rational claim of GSKCHC Specification & rectification in label claim of QalSium-D Chewable Tablet.

Sr.#	Reg.No.	Name of Drug with Composition & Specification	Date of Reg.	Documents Submitted
1.	083220	QalSium-D Chewable Tablet Each chewable tablet contains: Calcium Carbonate……1250mg eq.to Elemental Calcium…….500mg Vitamin D3……125IU (USP Specification)	17-May-17	Fee Rs.10,000/- **(28-Sep-21)**. Copy of initial registration letter. Analytical reports/Stability Data Comparison table as mentioned below.

In this regard, the firm has also submitted comparison of GSK, USP & BP parameters as under;

Test	GSK Specifications	USP Specification (*Dietary Supplements Compendium)*	BP Specification	Remarks
Appearance	Rectangular flat tablets with one side with break line & other side plain	Not given	Not given	Additional test in GSK specifications
Color	Milky orange tablets	Not given	Not given	Additional test in GSK specifications
Odour	Fruity odour	Not given	Not given	Additional test in GSK specifications
Average weight Individual weight	Not less than 2090 mg and not more than 2310 mg	Not given	Not given	Additional test in GSK specifications
Weight variation	Min 18/20 ±5% of Avg weight 02/20 ±10% of Avg weight	Min 18/20 ±5% of Avg weight 02/20 ±10% of Avg weight	Min 18/20±5% of Avg weight 02/20 ±10% of Avg weight	Equivalent to BP/ USP
Crushing strength/Hardness	Not less than 140 N	Not given	Not given	Additional test in GSK specifications
Friability and Resistance to Roll wear and tear	Friability → Not more than 5.0percent Breakage → Not more than 2 tablets	Not given for chewable tablets	Not given for chewable tablets	Additional test in GSK specifications
Loss on drying	Not more than 1.5%	Not given	Not given	Additional test in GSK specifications
Identification of Vitamin D	Complies	Complies	Complies	Equivalent to BP/ USP
Identification of Calcium	Complies	Complies	Complies	Equivalent to BP/ USP
Assay of Calcium	90.0 –110 % of the declared content	90 to 125% of the stated amount.	85 to 115% of the stated amount.	More stringent than BP/ USP
Assay of Vitamin D	90% - 165% of the declared content	90% - 165% of the declared content	90 to 120% of the stated amount	Equivalent to USP. Lower limit equivalent to BP, Higher limit is broader due to formulation contains 50% excess quantity of Vit D.
Microbial Enumeration test Total aerobic microbial count	Not more than 10^3 cfu/g	Not more than $3x10^3$ cfu/g	Not given	More stringent than USP

Total yeast & moulds count Specified Microorganism	Not more than 10^2 cfu/g Not detectable/g	Not more than $3x10^2$ cfu/g Not detectable/g	Not given Not given	More stringent than USP More stringent than USP
Disintegration and Dissolution Test	Not applicable	NLT 75% of the labeled amount of calcium (Ca) is dissolved	Not applicable	Since QalSium D tablet is a chewable formulation, the tests for disintegration and dissolution are not applicable.

Remarks:

The already granted specification "USP" is required to be changed because formulation available in USP is not chewable while approved formulation is in chewable form. As far as comparison with BP is concerned, all parameters are equivalent or stringent to BP except assay limit of Vitamin-D. The assay limit in **BP is 90 to 120%** of the stated amount while assay limit adopted by firm is **90% - 165%** of the declared content. Justification provided by the firm is that *"Upper limit is broader due to formulation contains 50% excess quantity of Vitamin-D"*

Decision of 68-PRVC:

The Committee referred the case to Registration Board Since Assay limit for Vitamin-D is more stringent in BP (90 to 120%) than that of Manufacturer specification (90% - 165%).

Decision: Registration Board deliberated the matter and decided to grant BP specification. Since Assay limit for Vitamin-D is more stringent in BP (90 to 120%) than that of Manufacturer specification (90% - 165%).

Case No.ii: Change of Primary Packaging Material of Drug(s) of M/s. ICI Pakistan Ltd., S-33, Hawkes Bay Road, S.I.T.E., Karachi (Page No. 1567 – 1615 /C).

Dy.Nos.1149 (PR-I) dt: 1-Sep-21; 1167 (PR-I) dt: 8-Sep-21 & 1258-A (PR-I) dt: 24-Sep-21

M/s. ICI Pakistan Ltd, has requested for change in primary packaging material of their following registered product details are as under:

Sr.#	Reg. No.	Name of Product with composition	Existing Packaging	Proposed Packaging	Remarks
1.	000086	Mucaine Suspension Each 5ml contains Oxethazaine……..…10mg Aluminium Hydroxide…….…...291mg Magnesium hydroxide……..…..98mg	Amber glass bottle with Aluminum cap	Amber PET bottle with HDPE cap	Applied formulation is not found in any reference country. Similar formulation (containing Aluminum hydroxide, Magnesium hydroxide and Simeticone) of Maalox Plus (MHRA approved) found in PET bottle

Firm has submitted the following documents as per SOP (approved in 283rd meeting).

Sr.#	Documents Required (as per SOP M-283)	Information Provided
1.	Application with required fee as per relevant SRO.	Fee of Rs.10,000/- **(30-August-2021)** Dy.No.24001 (R&I) dated: 31-08-2021
2.	Copy of registration letter and last renewal status	Reg. No. 000086 (dated 22-Mar-1976) Last renewal (dated 18-Sep-2020)
3.	Justification of proposed change including data on the suitability of the container-closure system (e.g. extractable/ leachable testing (where applicable), permeation testing, light transmission) demonstrating equivalent or superior protection compared to the current packaging system. For changes to functional packaging related to container closure (e.g. MDIs etc.), data to demonstrate the functioning of the new	The applicant (MAH) has elected to introduce PET bottle due to satisfactory results of stability studies. The proposed container closure system is unbreakable, easy to transport, inert, light in weight etc. Data regarding suitability of proposed packaging material is provided by the firm**.** Test performed for PET bottles in compliance of container closure

	packaging	system USP 31/NF 26 <661> Plastic packaging system and their material of construction are: 1. Multiple Internal reflectance using Infrared spectroscopy. 2. Thermal analysis using Differential scanning calorimetry 3. Testing of heavy metals and nonvolatile residues
4.	If the container closure system of applied formulation is different from that of the reference product, manufacturer will place first three lab scale batches or developmental scale batches as set by Registration Board in 276th meeting, at 3 months of accelerated and 3months of real time studies for compatibility of applied formulation with container closure system as directed by Pharmacopeia of Reference Regulatory Authorities. Registration Board shall be informed immediately and along with market withdrawal in case of any significant change about result of stability studies	Firm has submitted stability data as follows: **Accelerated studies** (Temp 40◦C±2◦C/ RH 75%±5%) Interval: 0,3,6 months **Long term studies** (Temp 30◦C±2◦C /RH 65%±5%) **Interval**: 0,3,6 months **Testing parameters**: Physical inspection, pH, Ant acid test, acid neutralizing capacity, Assay, Total aerobic count, Total mold and yeast count, Test for E.Coli. **Reference Test Method:** In house method **Batch No:** T-01, T-02, T-03 **Batch size**: 350 L
5.	Shelf life of the drug product supported with justification.	Provided
6.	Existing and proposed container closure system with differences (e.g. description, materials of construction of primary packaging components, specifications, if appropriate) highlighted in tabular form.	Provided
7.	If proposed change requires change in manufacturing section/ facility, then a new registration application with prescribed fee shall be submitted.	Not applicable
8.	An Undertaking that: • To perform stress studies. • 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 information is true & correct.	Provided

In addition to above mentioned documents (required as per SOP) following supporting documents have been submitted by the firm:

1) Stability study protocol
2) Analytical method validation studies (accuracy, precision, linearity etc.)
3) Summary data sheets, certificate of analysis, raw data sheets, digital data logger.
4) Following suitability tests were performed by firm as per USP 39 <661.1> Plastic packaging system and their material of construction:

S.No.	Tests	Sample	Difference	Result
1.	IR spectroscopy	PET	The IR spectrum of sample is identical and exhibit the major absorption band at same wavelength of a PET sample IR spectrum as present in data base of instrument.	Pass
2.	Differential scanning calorimetry	PET	The difference between Melting Temperature obtained from DSC thermograms of sample and the reference standard was 3℃ (do not exceed 9℃). The difference between Crystallization Temperature obtained from DSC thermograms of sample and the reference standard was 3℃ (do not exceed 4℃).	Pass

3.	Heavy metals	PET	Color produced after 10 minutes in the tube containing extracting media of the test bottles (PET Bottles) is not exceeded that in the tube containing the standard lead solution which is less than 1 ppm (NMT 1ppm)	Pass
4.	Moisture vapor transmission	PET	The average rate of moisture vapor transmission is obtained as 1.40% (NMT 2.5% per year)	Pass
5.	Colorant extraction	PET	Max. Absorbance observed as 0.001 at 443nm (NMT 0.01)	Pass
6.	Spectral transmission	PET	The maximum spectral transmittance observed for the test sample is 7.100% at a wavelength of 370nm (NMT 10% at any wavelength in the range of 290 – 450nm)	Pass

Above mentioned tests at Sr. No, 1-2 were submitted by packaging material (PET raisins) manufacturer i.e. M/s Novatex limited, Karachi Pakistan, performed by Biochem Srl Via G.Benini 13 - 40069 Zola Predosa BO – Italy while tests at Sr. No.3-6 were performed at M/s. ICI Pakistan Ltd., S-33, Hawkes Bay Road, S.I.T.E., Karachi (PET bottle manufacturer M/s Sunrise Pharmaceutical Pvt Ltd)

Mucaine Gel (by Pfizer Limited, India) is available in India in Amber PET bottle packaging. Similarly, Mucaine oral suspension (by Wyeth NZ, Ltd) was approved by MEDSAFE (New Zealand Medicines and Medical Devices Safety Authority) in plastic bottle however product withdrawn by manufacturer due to commercial reason.

Decision of 68-PRVC:

The Committee referred the case to Registration Board since there no evidence available for approval of similar formulation (with same drug substances) in RRA country with proposed container closure system i.e. PET bottle.

Decision: Registration Board considered the case and decided as follows:

- **acceded to request of the firm for change of primary packaging material of product Mucaine Suspension (Reg.No.000086) from Amber glass bottle to Amber PET bottle after consideration of provided stability data and suitability testing as per USP.**
- **Firm shall place first three batches on concurrent stability studies along-with suitability testing of newly approved packaging material (PET Bottle). 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.**

EXPORT FACILITATION DESK

Export of Tramadol Containing Products.

Matter regarding export of Tramadol containing products was discussed in various Authority meetings (74th meeting and 104th meeting), after thorough discussions and deliberations, Authority in 115th meeting held on 27th July, 2021 advised QA&LT Division to assure that following additional pre-requisites are also verified before issuance of NOC for export of Tramadol containing products:

i. Registration of Tramadol containing product(s) of exporter in importing country.

ii. Legal status of Tramadol in importing country whether controlled under INCB convention or otherwise.

iii. In case of any already exported consignment, clearance document of Customs and regulatory authority of the importing country.

QA&LT Division was also advised:

a. to request Ministry of Narcotics Control and Anti-Narcotics Force to take up the matter with their relevant counterpart in Nigeria regarding recent trends for, for information and liaison to check illegality, if any.

b. to verify the legitimate import of raw material i.e. Tramadol imported by the manufacturers intending to export their Tramadol containing products. Complete facts and figures along with

decision of the Authority be incorporated in the parawise comments of Constitutional Petition No. D-4425 of 2021 before Honorable Sindh High Court.

Decision 312th meeting:

Registration Board deliberated that decision of Authority is applicable at time of export before granting NOC and has no impact on grant of export registration as after grant of export registration, manufacturer will start process of registration in importing country

Hence Registration Board approved Tramadol containing products for export registration.

Decision: **Registration Board deliberated the matter regarding export of tramadol containing formulations and apprised that after grant of export registration, manufacturer will start process of registration in importing country however decision of Authority will be implemented at time of export before granting NOC.**

Furthermore, Registration Board apprised that to avoid illegitimate utilization and export of Tramadol containing formulation proposal will be moved by Authority to Ministry of Narcotic Control for inclusion of Tramadol in list of controlled drugs.

Case No.01: Registration of Drug (s) of M/s Cure Laboratories (Pvt.) Ltd, Plot No. 11&12, Street No. NS-2, National Industrial Zone, Rawat Rawalpindi, 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.	Form5D;
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 1-13/2017-Lic dated 08-10-2020
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based on inspection dated 12-08-2020
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.	Cure Kit Each tablet contains: Levofloxacin (as hemihydrate).....500mg Each tablet contains: Metronidazole.....400mg Each capsule contains: Dexlansoprazole (enteric coated pellets) eq to Dexlansoprazole.....30mg **Source of Pellets:** M/s Vision Pharmaceuticals (Pvt.) Ltd Plot No. 22-23, Industrial Triangle Kahuta Road Islamabad.	Not available Purchase order from Afghanistan	Dy. No. 6743/21 (13.9.2021) Rs.30,000/- (23.08.2020) Rs.45,000/- (08.09.2021)

Decision: **Registration Board approved above mentioned product of M/s Cure Laboratories (Pvt.) Ltd, Plot No. 11&12, Street No. NS-2, National Industrial Zone, Rawat Rawalpindi. Since applied formulation is neither registered for local use nor approved by any RRA (as decided by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues**

Case No.02: Registration of Drug (s) of M/s Ophth Pharma (Pvt.) Ltd, Plot No. 241, Sector 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.	Form5D;
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 28-06/2016
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 27-09-2019 .
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.	Ophth-Atropine 0.5% (Sterile Ophthalmic Solution) Each ml contains: Atropine sulphate.....5 mg	Not available Purchase order from Tajkistan	Dy. No. 6811/21 (28.9.2021) Rs.75,000/- (17.09-2021)

Decision: Registration Board approved above mentioned product of M/s Ophth Pharma (Pvt.) Ltd, Plot No. 241, Sector 24, Korangi Industrial Area, Karachi. Since applied formulation is neither registered for local use nor approved by any RRA (as decided by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues

Case No.03: Registration of Drug (s) of M/s Genetics Pharmaceuticals (Pvt.) Ltd, Plot No. 539-A, Sunder Industrial Estate 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.	Form5D;
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 1-9/2008-Lic dated 01-09/2016
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 29-03-2019 .
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.	Favigen 800mg tablet Each film coated tablet contains: Favipiravir.....800mg	Not available Purchase order from Vietnam	Dy. No. 6836/21 (05.10.2021) Rs.30,000/- (13.09-2021) Rs.45,000/- (30.09-2021)

Decision: Registration Board approved above mentioned product of M/s Genetics Pharmaceuticals (Pvt.) Ltd, Plot No. 539-A, Sunder Industrial Estate Lahore, Since applied formulation is neither registered for local use nor approved by any RRA (as decided by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues.

Case No.04: Registration of Drug (s) of M/s Medisure Laboratories (Pvt.) Ltd, A115, 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.	Form5D;
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 2-2/2001-Lic dated 16-07/2012
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 19-07-2019 .
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.	Medi-Vit K3 Injection Each ml contains: Menadione Sodium Bisulphite 10mg	Not available Purchase order from Mynamar	Dy. No. 6838/21 (06.10.2021) Rs.75,000/- (10.09-2021)
2.	Argicarn I.V Infusion 100ml Each ml contains: L-Arginine.....42mg L-Carnitine.....20mg	Not available Purchase order from U.A.E	Dy. No. 6880/21 (21.10.2021) Rs.20,000/- (17.10-2019) Rs.55,000/- (12.10-2021)

Decision: Registration Board approved above mentioned products of M/s Medisure Laboratories (Pvt.) Ltd, A115, S.I.T.E. Super Highway, Karachi. Since applied formulation is neither registered for local use nor approved by any RRA (as decided by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues.

Case No.05: Registration of Drug (s) of M/s Maxitech Pharma (Pvt.) Ltd, Plot No. E-178, S.I.T.E. Phase-II, 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.	Form5D;
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 2-12/2012-Lic dated 25-11/2016
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.	Molpiravir 400mg Capsule Each capsule contains: Molnupiravir.....400mg	Not available Purchase order from Myanmar	Dy. No. 6938/21 (06.10.2021) Rs.75,000/- (27.10-2021)

Decision: Registration Board approved above mentioned product of M/s Maxitech Pharma (Pvt.) Ltd, Plot No. E-178, S.I.T.E. Phase-II, Super Highway, Karachi. Since applied formulation is neither registered for local use nor approved by any RRA (as decided

by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues.

Case No.06: Registration of Drug (s) of M/s MTI Medical (Pvt.) Ltd, Plot No. 586-587, Sunder Industrial Estate Raiwind 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 letter No. F 1-39/2005-Lic dated 23-09-2014
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificate based / on inspection dated 23-11-2020 .
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.	Molaver 800mg Capsule Each capsule contains: Molnupiravir.....800mg	Not available Purchase order from Kazakhstan	Dy. No. 6951/21 (12.11.2021) Rs.75,000/- (11.10-2021)
2.	Molaver 400mg Capsule Each capsule contains: Molnupiravir.....400mg		Dy. No. 6952/21 (12.11.2021) Rs.75,000/- (09.11-2021)

Decision: Registration Board approved above mentioned products of M/s MTI Medical (Pvt.) Ltd, Plot No. 586-587, Sunder Industrial Estate Raiwind Road Lahore. Since applied formulation is neither registered for local use nor approved by any RRA (as decided by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues.

DEFERRED CASE OF 297th RB

Case No.07: Registration of Drug(s) of M/s PharmaWise Labs. Pvt Ltd., 25-M, Q.A. Industrial Estate, KotLakhpat, Lahore for Export Purpose 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.	Form5D submitted
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 panel inspection for renewal of DML dated 09-04-2014.
GMP Status. Copy of Inspection report/GMP certificate.	GMP status verified from GMP certificated based on inspection dated 16.10.2019
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.	Nystwise Vaginal Cream Each 5gm Contains: - Nystatin……. 100,000 IU	Not available	Dy.No.2815/20 (31.12.2020) Rs. 20,000/- (26.11.2020) Rs. 30,000/- (07-01-2021)

2.	Hexirub Plus Solution Each ml contains: - Chlorhexidine Gluconate……5% w/v	Purchase order from Afghanistan	Dy.No.2816/20 (31.12.2020) Rs. 20,000/- (26.11.2020) Rs. 30,000/- (07-01-2021)
3.	Febrinol Tablet Each Tablet Contains: Paracetamol…… …100mg		Dy.No.2816/20 (31.12.2020) Rs. 20,000/- (26.11.2020) Rs. 30,000/- (07-01-2021)
4.	FerroWise Plus Tablet Each film coated tablet contains: Ferrous sulphate (Anhydrous).....200mg) eq. to elemental Iron 65mg Folic Acid.....0.40mg		Dy. No.2816/20 (31.12.2020) Rs. 20,000/- (26.11.2020) Rs. 30,000/- (07-01-2021)

Decision of 297th meeting:

Registration Board deferred due to GMP non-compliance.

UPDATED STATUS

Last inspection conducted on 01.12-2020 and 03.12.2020 wherein GMP issues were observed later on firm submitted compliance report. Accordingly AD (QA-1) has written letter to Additional Director DRAP , Lahore (dated 14th June 2021) for conducting inspection

Decision: **Registration Board approved above mentioned products of M/s PharmaWise Labs. Pvt Ltd., 25-M, Q.A. Industrial Estate, KotLakhpat, Lahore. Since applied formulation is neither registered for local use nor approved by any RRA (as decided by Registration Board 275th meeting) hence manufacturer shall be responsible for any safety/efficacy related issues**

Case No 01: Change of registration status from previous manufacturing site i.e M/s Gray's Pharmaceuticals Plot No 442, Street No. 7, Sector I-9/2, Industrial Area Islamabad to new manufacturing site i.e M/s Gray's Pharmaceuticals Plot No. 02 Street No 03 National Industrial Zone, Rawat (DML No. 517).

M/s Gray's Pharmaceuticals, Islamabad has requested for grant of registration of following products in to new manufacturing site i.e **M/s Gray's Pharmaceuticals Plot No. 02 Street No 03 National Industrial Zone, Rawat.**

Panel inspection for renewal of DML and grant of additional section (sachet general) was conducted on 11th October 2021 wherein following sections were renewed/ regularized:

1) **Capsule (General)**
2) **Cream/ointment (General)**
3) **Tablet (General)**
4) **Dry powder suspension (Ceph)**
5) **Capsule (Ceph)**
6) **Dry powder injection (Ceph)**
7) **Tablet (psychotropic)**
8) **Ampoule (General)**

Panel unanimously recommended grant of additional section i.e. Sachet (General).

Below mentioned products were considered by Registration Board in 233rd meeting, held on 15-06-2012 and decided as follows:

Decision:

The Registration Board decided to accede to the request of firm subject to fulfillment of latest fee requirement and confirmation of sections, required for each category of drugs.

Afterward following products were granted approval into new manufacturing site vide letter No. F.8-6/2015-Reg-III(M-252) dated 19 October 2015.

S.No.	Reg.No.	Brand Name / Label Claim
1.	056023	Z-Nest 0.5mg Tablets Each tablet contains: Alprazolam……0.5mg (USP Specification)
2.	056027	Pazam 3mg Tablets Each tablet contains: Bromazepam…..3mg (USP Specification)
3.	033321	Fungigray Cream 1% Each gram contains: Clotrimazole……10mg
4.	033326	Fungigray V Cream Each gram contains: Clotrimazole…..100mg
5.	033333	Panarodin 550mg Tablets Each tablet contains: Naproxen Sodium……550mg
6.	056936	Grazeth 250mg Tablets Each tablet contains: Azithromycin (as dihydrate)……..250mg (USP Specification)
7.	038248	Topirat 50mg Tablets Each tablet contains: Topiramate……50mg
8.	038243	Loxaspar 100mg Tablets Each tablet contains: Sparfloxacin…….100mg

The firm has requested for grant of approval for rest of the products as well. List of these products along with their status is placed below:

Products submitted within time:

Sr. No	Reg. No.	Brand Name & Composition	Initial date of Reg. PRV (If any)	Date of application (R&I) Fee submitted	RRA status	Remarks of RRR	Remarks of PR-II
	I	II	III	IV	V	VI	VII
M/s Gray's Pharmaceuticals Plot No. 02 Street No 03 National Industrial Zone, Rawat (DML No. 517)							
1.	065240	Cloplate 75mg Tablet Each tablet contains: Clopidogrel as Hydrogen Sulphate… 75mg (Grays Specs)	28-7-2010	2099 - (R&I) dated 26.05.2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	Film coated tablet is available in RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The formulation shall be corrected as "Film coated tablet" and firm shall also submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
2.	065242	Deprosulp 50mg Tablet Each tablet contains: Levosulpride… 50mg (Grays Specs)	28-7-2010	1804 - (R&I) dated 07.05.2012 Rs. 8000/- 190-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-	ok	**The renewal application for year 2020 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
3.	065243	Secodic B Cream Each gm contains:- Fusidic Acid… 20mg Betamethasone as Valerate… 1mg (BP Specs)	28-7-2010	1849 - (R&I) dated 07.05.2012 Rs. 8000/- 242-(R&I) dated 13-1-2016 Rs. 12000/- **16.6.2020** Rs. 10000/-	ok	**The renewal application for year 2020 is within time.**	
4.	056933	Rimp Tablets Each film coated tablet contains:- Levocetirizine	29-7-2009	1820 - (R&I) dated	ok	**The renewal application for year 2019 is**	The firm shall submit the reference of

		dihydrochloride ..... 5mg (Grays Specs)		07.05.2012 Rs. 8000/- 215-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-		**within time.**	finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
5.	056934	Olanz 5mg Tablets Each film coated tablet contains:- Olanzapine…5mg (Grays Specs)	29-7-2009	1821 - (R&I) dated 07.05.2012 Rs. 8000/- 214-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
6.	056935	Olanz 10mg Tablets Each film coated tablet contains:- Olanzapine…10mg (Grays Specs)	29-7-2009	1822 - (R&I) dated 07.05.2012 Rs. 8000/- 213-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
7.	056939	Deprosulp 25mg Tablets Each tablet contains:- Levosulpiride 25mg (Grays Specs)	29-7-2009	1803 - (R&I) dated 07.05.2012 Rs. 8000/- 194-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
8.	056940	Deprosulp 100mg Tablets Each tablet contains:- Levosulpiride 100mg (Grays Specs)	29-7-2009	1805 - (R&I) dated 07.05.2012 Rs. 8000/- 192-(R&I) dated 13-01-2016	ok	**The renewal application for year 2019 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration

				Rs. 12000/- **15.07.2019** Rs. 10000/-			Board with prescribed fee.
9.	056941	Infladex Tablets Each tablet contains:- Piroxicam (as Beta-cyclodextrin) 20mg (Grays Specs)	29-7-2009	1842 -(R&I) dated 07.05.2012 Rs. 8000/- 224-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
10.	056942	Boneheel 0.5mcg Tablets Each tablet contains:- Alfacalcidol…0.5mcg (Grays Specs)	29-7-2009	1861 -(R&I) dated 07.05.2012 Rs. 8000/- 201-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
11.	068659	Cinocid 100mg Tablet Each film coated tablet contains:- Minocycline (as HCl)… 100mg (USP Specs)	31-1-2011	2094 -(R&I) dated 26.05.2016 Rs. 20000/- **28.01.2021** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in year 2016. **The renewal application for year 2021 is within time.**	
12.	068660	Divalp 250mg Tablet Each tablet contains: Divalproex Sodium … 250mg (Grays Specs)	31-1-2011	50 -(R&I) dated 11.01.2016 Rs. 20000/- **28.01.2021** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in year 2016. **The renewal application for**	The firm shall also submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.

						year 2021 is within time.	
13.	068661	Divalp 500mg Tablet Each tablet contains: Divalproex Sodium … 500mg (Grays Specs)	31-01-2011	49 -(R&I) dated 11.01.2016 Rs. 20000/- **28.01.2021** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in year 2016. **The renewal application for year 2021 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
14.	068662	Grafazole 200mg Capsule Each hard gelatin capsule contains: Fluconazole…. 200mg (USP Specs)	31-01-2011	54 -(R&I) dated 11.01.2016 Rs. 20000/- **28.01.2021** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in year 2016. **The renewal application for year 2021 is within time.**	
15.	068756	Epra 40mg Capsule Each hard gelatin capsule contains: Omeprazole (as enteric coated pellets)… 40mg (BP Specs)	29-1-2011	1817 -(R&I) dated 07.05.2012 Rs. 8000/- 1462-(R&I) dated 03-05-2016 Rs. 12000/- **28.01.2021** Rs. 10000/-	ok	**The renewal application for year 2021 is within time.** Approval of source of pellets.	The firm shall submit the approval of source of pellets and in case the source pf pellets is not approved, submit application with requisite fee for approval.
16.	041875	Esomep 20mg Capsule Each capsule contains: Esomeprazole (as magnesium trihydrate) enteric coated pellets…20mg	17-12-2005	1073 -(R&I) dated 07.05.2012 Rs. 8000/- 1463-(R&I) dated 03-05-2016 Rs. 12000/- **07.12.2020** Rs. 10000/-	ok	**The renewal application for year 2020 is within time.** Approval of source of pellets.	The firm shall submit the following: a. Approval of source of pellets and incase the source is not approved, submit application with requisite fee for approval. b. Firm shall also submit the reference of finish product

							specifications as per decision of 295th meeting of Registration Board with prescribed fee.
17.	041876	Esomep 40mg Capsule Each capsule contains: Esomeprazole (as magnesium trihydrate) enteric coated pellets…40mg	17-12-2005	1569 - (R&I) dated 07.05.2012 Rs. 15000/- 1465- (R&I) dated 03-05-2016 Rs. 5000/- **07.12.2020** Rs. 10000/-	ok	**The renewal application for year 2020 is within time.** Approval of source of pellets.	The firm shall submit the following: a. Approval of source of pellets and incase the source is not approved, submit application with requisite fee for approval. b. The firm shall also submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
18.	063381	Ferrifort Tablet Each tablet contains: Iron Protein Succinylate 400mg eq. to Elemental Iron.. 20mg Folic Acid… 2.5mg (Grays Specs)	28-6-2010	2091 - (R&I) dated 26.05.2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	Iron preparation	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
19.	041701	Cephagray 250mg Capsule Each capsule contains: Cephradine…. 250mg	26-11-2005	2067- (R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
20.	041700	Cephagray 500mg Capsule Each capsule contains: Cephradine… 500mg	26-11-2005	2066- (R&I) dated	Ok	Transfer of registration to new site was	The firm shall submit the reference of

				26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-		approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
21.	041704	Grafadrox 500mg Capsule Each capsule contains: Cefadroxil (as monohydrate)…. 500mg	26-11-2005	36-(R&I) dated 11.01.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
22.	041706	Grafadrox 125mg Suspension Each 5ml contains: Cefadroxil (as Monohydrate)… 125mg	26-11-2005	35-(R&I) dated 11.01.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	Deferred for confirmation of approval of formulation in RRA.
23.	041705	Grafadrox 250mg Suspension Each 5ml contains: Cefadroxil (as Monohydrate)… 250mg	26-11-2005	34-(R&I) dated 11.01.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
24.	041707	Ceforal 125mg Capsule Each capsule contains: Cefuroxime (as Axetil)…. 125mg	26-11-2005	2073-(R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs.	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted	Deferred for confirmation of approval of formulation in RRA.

				10000/-		fee in 2016. **The renewal application for year 2020 is within time.**	
25.	041708	Ceforal 250mg Capsule Each capsule contains:- Cefuroxime (as Axetil)…. 250mg	26-11-2005	2072-(R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	Deferred for confirmation of approval of formulation in RRA.
26.	041710	Celexin 250mg Capsule Each capsule contains: Cephalexin… 250mg	26-11-2005	2069-(R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The salt form shall be corrected as Cephalexin as monohydrate and the firm shall also submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
27.	041711	Celexin 500mg Caspule Each capsule contains: Cephalexin… 500mg	26-11-2005	2068-(R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The salt form shall be corrected as Cephalexin as monohydrate and the firm shall also submit the reference of finish product specifications as per decision of 295th meeting of Registration Board with prescribed fee.
28.	041709	Ceforal 125mg Suspension Each 5ml contains:- Cefuroxime (as Axetil)… 125mg	26-11-2005	2071-(R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.

						year 2020 is within time.	
29.	041712	Celexin 125mg Suspension Each 5ml contains: Cephalexin… 125mg	26-11-2005	2070-(R&I) dated 26.05.2016 Rs. 20000/- **23.11.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The salt form shall be corrected as Cephalexin as monohydrate and the firm shall also submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
30.	041714	Breath 10mg Tablet Each tablet contains: Montelukast as Sodium….10mg	26-11-2005	1858 -(R&I) dated 07.05.2012 Rs. 8000/- 202-(R&I) dated 13-01-2016 Rs. 12000/- **23.11.2020** Rs. 10000/-	Approved in film coated	**The renewal application for year 2020 is within time.**	The formulation shall be corrected as "Film coated tablet" and the firm shall also submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
31.	040867	Topirat 25mg Each tablet contains: Topiramate… 25mg	19-07-2005	2074-(R&I) dated 26-05-2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	Approved in film coated	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The formulation shall be corrected as "Film coated tablet" and the firm shall also submit reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
32.	069824	Hazid 500mg Capsule Each capsule contains: Azithromycin (as Dihydrate) … 500mg	04-4-2011	591-(R&I) dated 30-03-2016 Rs. 20000/- **29.03.2021** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2021 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
33.	069825	Gemibee 320mg Tablet	04-04-	46 -(R&I)	Approved	Transfer of	The formulation

		Each tablet contains: Gemifloxacin (as Mesylate)… 320mg	2011	dated 11.01.2016 Rs. 20000/- 590-(R&I) dated 30-03-2016 Rs. 20000/- **29.03.2021** Rs. 10000/-	in film coated	registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2021 is within time.**	shall be corrected as "Film coated tablet" and the firm shall also submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
34.	069826	Dispartes Super Tablet Each dispersible tablet contains: Artemether… 80mg Lumefantrine… 480mg	04-04-2011	1809 - (R&I) dated 07.05.2012 Rs. 8000/- 196-(R&I) dated 13-01-2016 Rs. 12000/- 589-(R&I) dated 30-03-2016 Rs. 20000/- **29.03.2021** Rs. 10000/-	Ok	**The renewal application for year 2021 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
35.	037009	Lincogray 500 Capsule Each capsule contains: Lincomycin (as HCl)… 500mg	31-01-2005	1224-(R&I) dated 14-02-2017 Rs. 20000/- **10.01.2020** Rs. 10000/-	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-6-2012 but firm submitted fee in 2017. **The renewal application for year 2020 is within time.**	Deferred for confirmation of approval of formulation in RRA.
36.	037010	Silvagray Cream 1% Contains: Silver Sulphadiazine…1%	31-01-2005	749-(R&I) dated 02.09.2016 Rs. 20000/- **10.01.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is within time.**	The firm shall submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.

37.	035430	Diclogray 50mg Tablet Each tablet contains: Diclofenac Sodium…50mg	22-12-2004	2093-(R&I) dated 26.05.2016 Rs. 20000/- **19.12.2009** Rs. 10000/-	Approved in gastro resistant form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2019 is within time.**	The formulation shall be corrected as "Enteric coated tablet" and the firm shall also submit the reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
38.	035431	Metrostat Plus Tablet Each tablet contains: Metronidazole…250mg Di-Iodohydroxyquinolone…325mg	22-12-2004	2082-(R&I) dated 26.05.2016 Rs. 20000/- **19.12.2009** Rs. 10000/-	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2019 is within time.**	Deferred for confirmation of approval of formulation in RRA.
39.	035433	Graymaf Forte Tablet Each tablet contains: Mefenamic Acid…500mg	22-12-2004	2090-(R&I) dated 26.05.2016 Rs. 20000/- **19.12.2009** Rs. 10000/-	Approved in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2019 is within time.**	The formulation shall be corrected as "Film coated tablet" and the firm shall also submit reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
40.	035435	Paragray Extra Tablet Each tablet contains: Paracetamol…500mg Caffeine Anhydrous…65mg	22-12-2004	32-(R&I) dated 11.01.2016 Rs. 20000/- **19.12.2009** Rs. 10000/-	Approved in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2019 is within time.**	The formulation shall be corrected as "Film coated tablet" and the firm shall also submit reference of finish product specifications as per decision of 295th Meeting of Registration Board with prescribed fee.
41.	030679	Abrotin 10mg Tablets/ Anti-Sneeze 10mg Tablet Each Tablet Contains: Loratadine…….10 mg	26-07-2003 Change of	1840 - (R&I) dated 07.05.2012 Rs. 8000/-	ok	**The renewal application for year 2020 is within time.**	The firm shall also submit the reference of finish product

			BN 30-05-2005 & **07-6-2005**	208-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-			specifications as per decision of 295th Meeting of Registration Board with prescribed fee.

Products which require differential fee:

Sr. No	Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	RRA status	Remarks of RRR	Decision
	1	II	III	IV	V	VI	VII
M/s Gray's Pharmaceuticals Plot No. 02 Street No 03 National Industrial Zone, Rawat (DML No.000517)							
42.	030656	Grexcin 200 mg Tablets Each Tablet contains: Ofloxacin…200 mg	26-07-2003	1837-(R&I) dated 07.05.2012 Rs. 8000/- 225-(R&I) dated 13-01-2016 Rs. 12000/- 15.07.2019 Rs. 10000/-	Teravid Tablets (MHRA) Film coated	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year.	Deferred for submission of differential fee (Rs. 165000/-) under SRO 1005(I)/2017.
43.	030657	Levotril 250 mg Tablets Each Tablet contains: Levofloxacin (as Levofloxacin hemihydrate) …250 mg	26-07-2003 Change of BN: **23.06.2004**	1814 -(R&I) dated 07.05.2012 Rs. 8000/- 221-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in RRA	Firm has to submit fee as renewal application is submitted after due date but within 60 days. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 15000/-).
44.	030658	Levotril 500 mg Tablets Each Tablet contains: Levofloxacin (as Levofloxacin hemihydrate)…500 mg	26-07-2003 Change of BN: **23.06.2004**	1815 -(R&I) dated 07.05.2012 Rs. 8000/- 222-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in RRA	Firm has to submit fee as renewal application is submitted after due date but within 60 days. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 15000/-).
45.	030659	Fagastril 40 mg Tablets Each Tablets Contains: Famotidine….. 40 mg	26-07-2003	1830 -(R&I) dated 07.05.2012 Rs. 8000/-	Film coated tablet is approved in RRA	Firm has to submit fee under SRO 1005/2019 as	Deferred for submission of differential fee (Rs. 165000/-)

				232-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-		renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	under SRO 1005(I)/2017.
46.	030660	Fagastril 20 mg Tablets Each Tablets Contains: Famotidine…. 20 mg	26-07-2003	1829 -(R&I) dated 07.05.2012 Rs. 8000/- 231-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in RRA	Firm has to submit fee under SRO 1005/2019 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 165000/-) under SRO 1005(I)/2017.
47.	030661	Clo-Tassium 50 mg Tablets Each Tablet Contains: Diclofenac Potassium…….50 mg	26-07-2003	47-(R&I) dated 11-01-2016 Rs. 20000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee which was submitted on 2016. **Firm has to submit fee under SRO 1005/2019 as renewal application is submitted after due date but within one year.** The case was also deferred by Renewal Sub-Committee in	Deferred for submission of differential fee (Rs. 165000/-) under SRO 1005(I)/2017.

						its 3rd Meeting for completion of renewal application.	
48.	030662	Epra Capsules Each Capsule Contains: Omeprazole…20 mg	26-07-2003	1871 -(R&I) dated 07.05.2012 Rs. 8000/- 1464-(R&I) dated 03-05-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	To be standardized as enteric coated pellets of omeprazole eq. to omeprazole	Firm has to submit fee under SRO 1005/2019 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application. Source of pellets is required.	Deferred for submission of differential fee (Rs. 165000/-) under SRO 1005(I)/2017 along with approval of source of pellets.
49.	030663	Ecomin Tablets Each Tablet Contains: Mecobalamin….500 mcg	26-07-2003	1808 -(R&I) dated 07.05.2012 Rs. 8000/- 189-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Sugar coated tablet is approved in PMDA	Firm has to submit fee under SRO 1005/2019 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 165000/-) under SRO 1005(I)/2017.
50.	030664	Elient Tablets Each Tablet Contains: Flurbiprofen…100 mg	26-07-2003	1826 -(R&I) dated 07.05.2012 Rs. 8000/- 188-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in FDA Sugar coated tablet is approved in MHRA Coating to be clarified	Firm has to submit fee under SRO 1005/2019 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion	Deferred for submission of differential fee (Rs. 165000/-) under SRO 1005(I)/2017.

						of renewal application.	
51.	030665	Healcin 250 mg Tablets Each Tablet contains: Clarithromycin…250 mg	26-07-2003 Change of BN **08-01-2004**	8199 -(R&I) dated 18.12.2013 Rs. 20000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee for renewal (Rs. 90000/-) under SRO 1005(I)/2017.
52.	030666	Healcin 500 mg Tablets Each Tablet contains: Clarithromycin…500 mg	26-07-2003 Change of BN **08-01-2004**	8200 -(R&I) dated 18.12.2013 Rs. 20000/- **15.07.2019** Rs. 10000/-	Film coated tablet is approved in RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012. Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee for renewal (Rs. 90000/-) under SRO 1005(I)/2017.
53.	030668	Intrafer Tablets Each Tablet Contains: Elemental Iron…..100 mg (Iron III hydroxide Polymaltose complex)	26-07-2003	1838 -(R&I) dated 07.05.2012 Rs. 8000/- 240-(R&I) dated 13-01-2016 Rs. 12000/-	To be clarified whether chewable formulation or intended to be swallowed	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one	Deferred for submission of differential fee for renewal (Rs. 165000/-) under SRO 1005(I)/2017.

				15.07.2019 Rs. 10000/-		year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	
54.	030670	Ecoloxib 200 mg Tablets Each Tablet Contains: Celecoxib 200 mg	26-07-2003	1807 -(R&I) dated 07.05.2012 Rs. 8000/- 190-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	RRA status not confirmed	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee for renewal (Rs. 90000/-) under SRO 1005(I)/2017 and evidence of approval of formulation in RRA.
55.	030671	Hazid 250 mg Capsules Each Capsule Contains: Azithromycin(as dehydrate)..250mg	26-07-2003	1869 -(R&I) dated 07.05.2012 Rs. 8000/- 237-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	ok	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee for renewal (Rs. 90000/-) under SRO 1005(I)/2017.
56.	030672	Roxicute 150mg Tablet Each tablet contains: Roxithromycin… 150mg	26-07-2003 Change of BN **30-03-2005**	**16.06.2020** Rs. 10000/-	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee which is yet to be submitted. **The renewal application is submitted after the due date but within one year under**	Deferred for submission of differential fee (Rs.45000/-) under SRO 1005(I)/2017 along with evidence of approval of formulation in RRA.

						SRO 1005/2017. Hence, differential fee is required. Case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	
57.	030673	Jorr 7.5mg Tablet Each tablet contains: Meloxicam…. 7.5mg	26-07-2003 Change of BN **08-01-2004**	1812 -(R&I) dated 07.05.2012 Rs. 8000/- 223-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	ok	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.150,000/-) under SRO 1005(I)/2017.
58.	030674	Jorr 15 mg Tablets Each Tablet Contains: Meloxicam……15 mg	26-07-2003 Change of BN **08-01-2004**	1813 -(R&I) dated 07.05.2012 Rs. 8000/- 222-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	ok	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.150,000/-) under SRO 1005(I)/2017.
59.	030675	Exilide 100mg Tablets Each Tablet Contains: Nimesulide 100 mg	26-07-2003	1828 -(R&I) dated 07.05.2012 Rs. 8000/- 186-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Uncoated tablet approved in EMA	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. The case was also deferred	Deferred for submission of differential fee (Rs.165,000/-) under SRO 1005(I)/2017.

						by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	
60.	030677	Secodic Cream Contains: Fusidic Acid…….2 %	26-07-2003 Approval of change of formulation **28-01-2004**	1851 -(R&I) dated 07.05.2012 Rs. 8000/- 210-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Ok	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.90,000/-) under SRO 1005(I)/2017.
61.	030678	Secodic H-Cream Fusidic Acid…….2% Hydrocortisone acetate……1%	26-07-2003 Approval of change of formulation **28-01-2004**	1850 -(R&I) dated 07.05.2012 Rs. 8000/- 209-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Ok	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.90,000/-) under SRO 1005(I)/2017.
62.	030681	Tekostine 10mg Tablets Contains: Ebastine…….10 mg	26-07-2003	8201-(R&I) dated 18.12.2013 Rs. 20000/- **15.07.2019** Rs. 10000/-	Film coated tablet is available RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 *The renewal application is submitted after the due date but within one year under SRO 1005/2017. Hence, differential fee is required.* Case was also deferred by	Deferred for submission of differential fee (Rs.165,000/-) under SRO 1005(I)/2017.

						Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	
63.	030682	Initial 2mg Tablets Each Tablet Contains: Glimepride…….2 mg	26-07-2003 Change of BN **08-01-2004**	53-(R&I) dated 11-01-2016 Rs. 20000/- **15.07.2019** Rs. 10000/-	OK	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee which was submitted in 2016. **The renewal application is submitted after the due date but within one year under SRO 1005/2017. Hence, differential fee is required.** Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.90,000/-) under SRO 1005(I)/2017.
64.	030683	Initial 4mg Tablets Each Tablet Contains: Glimepride…….4 mg	26-07-2003 Change of BN **08-01-2004**	51-(R&I) dated 11-01-2016 Rs. 20000/- **15.07.2019** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee which was submitted in 2016. **The renewal application is submitted after the due date but within one year under SRO 1005/2017. Hence, differential fee is**	Deferred for submission of differential fee (Rs.90,000/-) under SRO 1005(I)/2017.

						required. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	
65.	030685	Axodine 120mg Tablets Each Tablet Contains: Fexofenadine HCl…….120 mg	26-07-2003 Approval of change of formulation **28-01-2004**	1843 -(R&I) dated 07.05.2012 Rs. 8000/- 205-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Film coated tablet is available in RRA	Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.90,000/-) under SRO 1005(I)/2017.
66.	030688	Cicloxal 400mg Capsules Each Capsule Contains: Cefixime 400 mg Toll manufactured by M/s Global Pharmaceuticals, Islamabad	26-07-2003	1849 -(R&I) dated 07.05.2012 Rs. 8000/- 238-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Drug substance to be standardized as cefixime (as trihydrate)	Approval of subsequent PRVs are required. Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.165,000/-) under SRO 1005(I)/2017.
67.	030689	Cicloxal Dry Suspension Each 5ml contains Cefixime 100mg Toll manufactured by M/s Global Pharmaceuticals, Islamabad	26-07-2003	1856 -(R&I) dated 07.05.2012 Rs. 8000/- 236-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	Drug substance to be standardized as cefixime (as trihydrate	Approval of subsequent PRVs are required. Firm has to submit fee under SRO 1005/2017 as renewal application is submitted after due date but	Deferred for submission of differential fee (Rs.165,000/-) under SRO 1005(I)/2017.

						within one year. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	
68.	030686	Zita 2mg Tablet Each table contains:- Tizanidine (as HCl)… 2mg	24-08-2004	1823 -(R&I) dated 07.05.2012 Rs. 8000/- 212-(R&I) dated 13-01-2016 Rs. 12000/- **27.09.2019** Rs. 10000/-	ok	Firm has to submit differential fee as renewal application is submitted after due date but within 60 days. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.15000/-) as renewal application is submitted after due date but within 60 days.
69.	030676	Graygesic Tablet Each tablet contains:- Paracetamol… 450mg Orphenadrine Citrate… 35mg	24-03-2004 Change of BN **30-03-2005**	1835 -(R&I) dated 07.05.2012 Rs. 8000/- 227-(R&I) dated 13-01-2016 Rs. 12000/- **10.04.2020** Rs. 10000/-	RRA status not confirmed	Firm has to submit differential fee as renewal application is submitted after due date but within 60 days. Case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs.15000/-) as renewal application is submitted after due date but within 60 days.
70.	036868	Polygray Ointment Each gram contains: Polymycin B Sulphate… 10000IU Bacitracin Zinc…. 500Unit	28-02-2005 Change of BN **07-06-2005**	**10.01.2020** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 **but firm did not submit fee. The renewal application for year 2020 is within time.**	Deferred for submission of fee (Rs. 30000/-) as required under initial application.
71.	034972	Bascistat Plus Ointment Each gm contains: Polymyxin B Sulphate…10000units Bacitracin Zinc…500units	01-12-2004	**19.12.2019** Rs. 10000/-	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-	Deferred for submission of following: i) Initial application fee Rs. 30,000/-

		Lignocaine…40mg				2012 but firm did not submit fee. **The renewal application was submitted after due date but within 60 days. Differential fee is required.** Case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	ii) Differential fee as renewal application was submitted after due date but within 60 days. iii) Evidence of approval of formulation in RRA.
72.	056937	Co-Artesinate DS Tablets Each tablet contains:- Artemether 40mg Lumefantrine 240mg (Grays Specs)	29-07-2009	**15.07.2019** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **The renewal application for year 2019 is within time.**	Deferred for submission of Initial application fee Rs. 30,000/-
73.	068663	Duloxet 20mg Capsule Each capsule contains:- Coated Pelllets of Duloxetine eq. to Duloxetine… 20mg (Grays Specs) **Source of Pellets**: M/s. R.A Chempharma, Ltd., 6-3-1239/2 Amar House, 4th Floor Raj Bhawan Road, Somajiguda, Hyderabad 500082-India	29-01-2011	1466 -(R&I) dated 03.05.2016 Rs. 20000/- **28.01.2021** Rs. 10000/-	To be standardized as "Enteric coated pellets of duloxetine eq to duloxetine	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in year 2016. **The renewal application for year 2021 is within time but the differential fee for the year 2016 & 2021 is required being imported source of pellets.**	Deferred for submission of differential fee for the year 2016 & 2021 being imported source of pellets.
74.	068664	Duloxet 40mg Capsule Each capsule contains:- Coated Pelllets of Duloxetine eq. to Duloxetine… 40mg	29-01-2011	33 -(R&I) dated 11.01.2016 Rs. 20000/-	To be standardized as "Enteric coated pellets of duloxetine	Transfer of registration to new site was approved in 233rd Meeting	Deferred for submission of differential fee for the year 2016 & 2021 being

		(Grays Specs) **Source of Pellets**: M/s. R.A Chempharma, Ltd., 6-3-1239/2 Amar House, 4th Floor Raj Bhawan Road, Somajiguda, Hyderabad 500082-India		**28.01.2021** Rs. 10000/-	eq to duloxetine"	held on 15-06-2012 but firm submitted fee in year 2016. **The renewal application for year 2021 is within time but the differential fee for year 2016 & 2021 is required being imported source of pellets.**	imported source of pellets.
75.	060218	Duloxet 60mg Capsule Each capsule contains:- Duloxetine HCl 67.3mg eq. to enteric coated pellets of Duloxetine… 60mg	02-09-2009	1870 -(R&I) dated 07.05.2012 Rs. 8000/- 1461-(R&I) dated 03-05-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	To be standardized as "Enteric coated pellets of duloxetine eq to duloxetine	**The renewal application for year 2019 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017**	Deferred for submission of differential fee (Rs. 45,000/-) under SRO 1005/2017
76.	033337	Ladazole 30mg Capsule Each capsule contains:- Lansoprazole (as enteric coated pellets)…. 30mg	05-08-2004	**27.09.2019** Rs. 10000/-	ok	Proof of PRVs (if any). Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. The case was also deferred by Renewal Sub-Committee in its 3rd Meeting for completion of renewal application. **The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.** Approval of source of pellets.	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential fee (Rs. 15,000/-) as renewal application was submitted after due date but within 60 days. iii) Proof of PRV (if any)
77.	034479	Baccidal 400mg Tablet	22-11-2004	2100 -(R&I)	Approved in	**The renewal**	Deferred for

		Each tablet contains:- Norfloxacin… 400mg		dated 26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-	film coated form in RRA	**application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	submission of differential fee (Rs. 15,000/-) as renewal application for year 2019 is submitted after due date but within 60 days.
78.	034480	Metform 500mg Tablet Each tablet contains:- Metformin HCl… 500mg	22-11-2004	2085 -(R&I) dated 26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-	Approved in film coated form in RRA	**The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for submission of differential fee (Rs. 15,000/-) as renewal application for year 2019 is submitted after due date but within 60 days.
79.	034481	Metform 1gm Tablet Each tablet contains:- Metformin HCl… 1000mg	22-11-2004	2083 -(R&I) dated 26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-	Approved in film coated form in RRA	**The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for submission of differential fee (Rs. 15,000/-) as renewal application for year 2019 is submitted after due date but within 60 days.
80.	034482	Cling 300mg Capsule Each capsule contains:- Clindamycin (as HCl) … 300mg	22-11-2004	2064 -(R&I) dated 26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-	Ok	**The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for submission of differential fee (Rs. 15,000/-) as renewal application for year 2019 is submitted after due date but within 60 days.
81.	034483	Nidase 1000mg Tablet Each tablet contains:- Secnidazole… 1000mg	22-11-2004	2080 -(R&I) dated 26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-	RRA status not confirmed	**The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for submission of differential fee (Rs. 15,000/-) as renewal application for year 2019 is submitted after due date but within 60 days.
82.	034484	Coniuren 5mg Tablet Each tablet contains:- Enalapril Maleate… 5mg	22-11-2004	2096 -(R&I) dated 26.05.2016 Rs. 20000/- **17.12.2019** Rs. 10000/-	Ok	**The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for submission of differential fee (Rs. 15,000/-) as renewal application for year 2019 is submitted after due date but within 60 days.
83.	034485	Gratifen 1mg Tablet Each tablet contains:- Ketotifen (as	22-11-2004	**17.12.2019** Rs. 10000/-	OK	Transfer of registration to new site was	Deferred for submission of following:

		Fumarate)… 1mg				approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application. **The renewal application for year 2019 is submitted after due date but within 60 days.** **Differential fee is required.**	i) Initial application fee Rs. 30,000/- ii) Differential fee Rs. 15,000/- as renewal application for year 2019 is submitted after due date but within 60 days.
84.	034486	Protifen 100mg EC Tablet Each tablet contains:- Ketoprofen… 100mg	22-11-2004	**17.12.2019** Rs. 10000/-	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application. **The renewal application for year 2019 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential fee Rs. 15,000/- as renewal application for year 2019 is submitted after due date but within 60 days. iii) Evidence of approval of formulation in RRA.
85.	034487	Intrafer FA Tablet Each tablet contains:- Iron (III) Hydroxide Polymaltose Complex eq. to Elemental Iron… 100mg Folic acid… 0.35mg	22-11-2004	1847 -(R&I) dated 07.05.2012 Rs. 8000/- 239-(R&I) dated 13-01-2016 Rs. 12000/-	Ok	Proof of PRVs (if any). The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal	Deferred for following: i) Proof of PRV approval (if any). ii) Differential fee for year 2019 is submitted

				17.12.2019 Rs. 10000/-		application. **The renewal application for year 2019 is submitted after due date but within 60 days. Differential fee is required.**	after due date but within 60 days.
86.	033324	Gastrocure 10mg Tablet Each tablet contains:- Domperidone… 10mg	**26-07-2004** Corrigendum dated 08-09-2004	1833 -(R&I) dated 07.05.2012 Rs. 8000/- 229-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.** The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 60,000/-) under SRO 1005/2017.
87.	033325	Gastrocure V Tablet Each tablet contains:- Domperidone Maleate 12.72mg eq. to Domperidone… 10mg	**26-07-2004** Corrigendum dated 08-09-2004	1834 -(R&I) dated 07.05.2012 Rs. 8000/- 228-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	ok	**The renewal application for year 2019 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.** The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 60,000/-) under SRO 1005/2017.
88.	033327	Ratidin 150mg Tablet Each tablet contains: Ranitidine (as HCl)…150mg	**26-07-2004** Corrigendum dated 08-09-2004	2076-(R&I) dated 26-05-2016 Rs. 20000/- **07.11.2019** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2019**	Suspension of registration for ranitidine containing formulations is recommended by RB due to safety reason as per decision in its 294th meeting.

						is submitted after due date but within one year. Differential fee is required under SRO 1005/2017. The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	
89.	033334	Panazole 40mg Tablet Each tablet contains:- Pantoprazole (as Sodium Sesquihydrate)… 40mg	**26-07-2004** Corrigendum dated 08-09-2004	1816 -(R&I) dated 07.05.2012 Rs. 8000/- 219-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	Approved in RRA in gastro resistant form	**The renewal application for year 2019 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.** Case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.	Deferred for submission of differential fee (Rs. 60,000/-) under SRO 1005/2017.
90.	037677	Axodine-D Tablets Each Tablet Contains: Fexofenadine HCl…….60mg Pseudoephedrine HCl…120mg	19-03-2005	**16.06.2020** Rs. 10000/-	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential fee Rs. 45,000/- under SRO 1005/2017.
91.	037678	Healcin XL Modified Release Tablets Each tablet contains: Clarithromycin…500mg	19-03-2005	**16.06.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential

						firm did not submit fee. **The renewal application for year 2020 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	fee Rs. 45,000/- under SRO 1005/2017.
92.	037679	Protifen 200mg SR Tablet Each tablet contains:- Ketoprofen… 200mg	19-03-2005	**16.06.2020** Rs. 10000/-	RRA status not confirmed	*Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee.* *The renewal application for year 2020 is submitted after due date but within one year.* *Differential fee is required under SRO 1005/2017.* *Another registration letter bearing same brand name and composition and price has issued to the firm vide letter No.3-7/2004-Reg-II(M-188) dated 12-02-2005.*	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential fee Rs. 45,000/- under SRO 1005/2017. iii) Evidence of approval of formulation in RRA.
93.	038397	Nycopren 250mg Tablet Each tablet contains:- Naproxen… 250mg	26-05-2005	2078 -(R&I) dated 26.05.2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is submitted after due date but within 60 days. Differential**	Deferred for submission of differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days.

						fee is required.	
94.	038398	Nycopren 500mg Tablet Each tablet contains:- Naproxen… 500mg	26-05-2005	2079 -(R&I) dated 26.05.2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **The renewal application for year 2020 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for submission of differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days.
95.	042557	Progra Tablet Each tablet contains:- Paroxetine as HCl… 20mg	**13-02-2006** Change of BN 09-08-2007	1817 -(R&I) dated 07.05.2012 Rs. 8000/- 219-(R&I) dated 13-01-2016 Rs. 12000/- **29.03.2021** Rs. 10000/-	Approved in film coated form	**The renewal application for year 2021 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for submission of differential fee Rs. 15,000/- as renewal application for year 2021 is submitted after due date but within 60 days.
96.	041721	Rispinol 1mg Tablet Each tablet contains: Risperidone…1mg	08-12-2005	**07.12.2020** Rs. 10000/-	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for submission of Initial application fee Rs. 30,000/-
97.	041722	Rispinol 2mg Tablet Each tablet contains: Risperidone…2mg	08-12-2005	**07.12.2020** Rs. 10000/-	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Evidence of approval of formulation in RRA.
98.	041723	Rispinol 3mg Tablet Each tablet contains: Risperidone…3mg	08-12-2005	**07.12.2020** Rs. 10000/-	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting	Deferred for submission of Initial application fee Rs. 30,000/-

						held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	
99.	041724	Rispinol 4mg Tablet Each tablet contains: Risperidone…4mg	08-12-2005	**07.12.2020** Rs. 10000/-	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for submission of Initial application fee Rs. 30,000/-
100	036237	Metrostat 400mg Tablet Each tablet contains:- Metronidazole … 400mg	10-01-2005	2084-(R&I) dated 26.05.2016 Rs. 20000/- **10.01.2020** Rs. 10000/-	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in 2016. *The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.*	Deferred for submission of differential fee as renewal application for year 2020 is submitted after due date but within 60 days.
101	036240	Hydrogray Cream 1% Each gm contains: Hydrocortisone Acetate… 10g	10-01-2005	**10.01.2020** Rs. 10000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential fee Rs.15000/- as renewal application for year 2020 is submitted after due date but within 60 days.
102	036241	Gametanil Tablet Each tablet contains: Pyrimethamine… 25mg Sulphadoxine… 500mg	10-01-2005	**10.01.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-	Deferred for following: i) Initial application fee Rs. 30,000/

						2012 but firm did not submit fee. *The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.*	ii) Differential fee Rs.15000/- as renewal application for year 2020 is submitted after due date but within 60 days.
103	036242	Givitol Tablet Each tablet contains:- Ferrous Fumerate… 150mg Folic Acid…0.5mg	10-01-2005	**10.01.2020** Rs. 10000/-	Iron formulation	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for following: i. Initial application fee Rs. 30,000/-. ii. Differential fee Rs.15000/- as renewal application for year 2020 is submitted after due date but within 60 days.
104	036248	Neogray Cream Contains: Neomycin Sulphate… 0.5%	10-01-2005	**10.01.2020** Rs. 10000/-	RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for following: i. Initial application fee Rs. 30,000/-. ii. Differential fee Rs.15000/- as renewal application for year 2020 is submitted after due date but within 60 days. iii. Deferred for confirmation of formulation in RRA.
105	052614	Basimox Tablets 400mg. Each film coated Tablet contains: Moxifloxacin as HCl…400mg. (Grays Specs)	07-10-2008	887 -(R&I) dated 07.05.2012 Rs. 8000/- 203-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	To be confirmed	**The renewal application for year 2018 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i. Differential fee Rs.135000/- under SRO 1005/2017. ii. Deferred for confirmation of formulation in RRA.

106	052615	Cicloxal DS Suspension. Each 5ml contains: Cefixime as Trihydrate …….200mg (USP Specs)	07-10-2008	**15.07.2019** Rs. 10000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2018 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i. Differential fee Rs.135000/- under SRO 1005/2017. ii. Initial application fee Rs.30000/- iii. Deferred for confirmation of formulation in RRA.
107	037013	Inflacid Gel Each gram contains:- Piroxicam 5mg	31-01-2004	1865 -(R&I) dated 07.05.2012 Rs. 8000/- 234-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	To be confirmed	**The renewal application for year 2018 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i. Differential fee Rs.90,000/- under SRO 1005/2017. ii. Deferred for confirmation of formulation in RRA.
108	060220	Zita 4mg Tablet Each tablet contains:- Tizanidine (as HCl)… 4mg (USP Specs)	02-09-2009	1829 -(R&I) dated 07.05.2012 Rs. 8000/- 211-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	To be confirmed	**The renewal application for year 2018 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i. Differential fee Rs.45,000/- under SRO 1005/2017. ii. Deferred for confirmation of formulation in RRA.
109	060221	Diclogray SR 100mg Tablet Each sustained release tablet contains:- Diclofenac Sodium… 100mg	02-09-2009	1825 -(R&I) dated 07.05.2012 Rs. 8000/- 195-(R&I) dated 13-01-2016 Rs. 12000/- **07.11.2019** Rs. 10000/-	Ok	**The renewal application for year 2018 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i. Differential fee Rs.45,000/- under SRO 1005/2017.
110	041713	Celexin 250mg Suspension Each 5ml contains:- Cephalexin… 250mg	26-11-2005	**23.11.2020** Rs. 10000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm	Deferred for following: i) Initial application fee Rs. 30,000/-

						did not submit fee. **The renewal application for year 2020 is within time.**	
111	041715	Breath 4mg Tablet Each tablet contains:- Montelukast as Sodium…. 4mg	26-11-2005	**23.11.2020** Rs. 10000/-	Approved in chewable form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for following: i) Initial application fee Rs. 30,000/-
112	041716	Breath 5mg Tablet Each tablet contains:- Montelukast as Sodium…. 5mg	26-11-2005	**23.11.2020** Rs. 10000/-	Approved in chewable form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Deferred for confirmation of formulation in RRA.
113	041717	Mycorid Tablet Each tablet contains:- Ethambutol… 275mg Rifampicin… 150mg Isoniazid… 75mg	**26-11-2005** Approval of formulation 24-08-2011	**23.11.2020** Rs. 10000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Deferred for confirmation of approval of formulation in RRA / WHO.
114	041718	Mycorid P Tablet Each tablet contains:- Ethambutol… 275mg Rifampicin… 75mg Isoniazid… 150mg Pyrazinamide… 400mg	**26-11-2005** Approval of formulation 24-08-2011	**23.11.2020** Rs. 10000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Deferred for confirmation of approval of formulation in RRA / WHO.
115	041719	Intrivin 200mg Capsule Each capsule contains:-	26-11-2005	**23.11.2020** Rs. 10000/-	Ok	Transfer of registration to	Deferred for following:

		Ribavirin…. 200mg				new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time**	i) Initial application fee Rs. 30,000/-
116	041720	Intrivin 400mg Capsule Each capsule contains: Ribavirin…. 400mg	26-11-2005	**23.11.2020** Rs. 10000/-	Not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Deferred for confirmation of approval of formulation in RRA.
117	063317	Escit Dispersible Tablet 10mg Each dispersible tablet contains: Escitalopram (as Oxalate) … 10mg (Gray's Specs)	02-06-2010	1806 -(R&I) dated 07.05.2012 Rs. 8000/- 191-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-	Not confirmed	**The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. **ii)** Deferred for confirmation of approval of formulation in RRA.
118	063318	Chew Artes Tablet Each tablet contains:- Artemether… 20mg Lumefantrine… 120mg	02-06-2010	2095-(R&I) dated 26-05-2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	Not found in chewable form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in 2016. **The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. ii) Deferred for confirmation of approval of formulation in RRA.
119	063319	Disp Artes Tablet Each tablet contains:-	02-06-2010	1811 -(R&I) dated	Ok	**The renewal application**	Deferred for following:

		Artemether… 20mg Lumefantrine… 120mg		07.05.2012 Rs. 8000/- 198-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-	Label claim to be clarified whether dispersible or otherwise	**for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. **ii)** Deferred for clarification whether dispersible or otherwise.
120	063320	Disp Artes Plus Tablet Each tablet contains:- Artemether… 40mg Lumefantrine… 240mg	02-06-2010 Corrigendum dated 07-07-2010	1810 -(R&I) dated 07.05.2012 Rs. 8000/- 197-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-	Ok	**The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: **i)** Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days.
121	038013	Graypyrine Tablet Each tablet contains:- Paracetamol… 250mg Mepyramine Maleate… 6.5mg Pheniramine Maleate… 6.5mg Pseudoephedrine (as HCl)… 15mg	10-05-2005	2089-(R&I) dated 26-05-2016 Rs. 20000/- **16.06.2020** Rs. 10000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in 2016. **The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. ii) Deferred for confirmation of approval of formulation in RRA.
122	038243	Loxaspar 100mg Tablet Each tablet contains:- Sparfloxacin… 100mg	10-05-2005	**07.11.2019** Rs. 10000/-	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is within time**	Deferred for following: i) Initial application fee Rs. 30,000/-. ii) Deferred for confirmation of approval of formulation in RRA.
123	038244	Fungigray V Tablet 100mg Each tablet contains:- Clotrimazole… 100mg	10-05-2005	1832 -(R&I) dated 07.05.2012 Rs. 8000/-	To be confirmed	**The renewal application for year 2020 is submitted**	Deferred for following: i) Differential fee Rs.

				231-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-		**after due date but within 60 days. Differential fee is required.**	15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. ii) Deferred for confirmation of approval of formulation in RRA.
124	038245	Fungigray V Tablet 500mg Each tablet contains:- Clotrimazole… 500mg	10-05-2005	1832 -(R&I) dated 07.05.2012 Rs. 8000/- 230-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-	To be confirmed	**The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. ii) Deferred for confirmation of approval of formulation in RRA.
125	038246	Ibugray Gel 10% Each 100gm contains:- Ibuprofen… 100mg	10-05-2005	**16.06.2020** Rs. 10000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days. ii) Deferred for confirmation of approval of formulation in RRA.
126	038249	Diclogray Gel Each 100gm contains:- Diclofenac Diethylammonium Salt 1.16gm eq. to Diclofenac Soidum… 1gm	10-05-2005	1859 -(R&I) dated 07.05.2012 Rs. 8000/- 235-(R&I) dated 13-01-2016 Rs. 12000/- **16.06.2020** Rs. 10000/-	To be confirmed	**The renewal application for year 2020 is submitted after due date but within 60 days. Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2020 is submitted after due date but within 60 days.

							ii) Deferred for confirmation of approval of formulation in RRA.
127	033322	Initial 1mg Tablet Each tablet contains:- Glimepiride.. 1mg	26-08-2004	2088-(R&I) dated 26-05-2016 Rs. 20000/- **27.09.2019** Rs. 10000/-	OK	Transfer of registration to new site was approved in 233rd Meeting held on 15-6-2012 but firm submitted fee in 2016 **The renewal application for year 2019 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2019 is submitted after due date but within 60 days.
128	033339	Limirid 3mg Tablets Each Tablet Contains: Glimepride…….3 mg	26-08-2004	52-(R&I) dated 11-01-2016 Rs. 20000/- **27.09.2019** Rs. 10000/-	OK	Transfer of registration to new site was approved in 233rd Meeting held on 15-6-2012 but firm submitted fee in 2016. **The renewal application for year 2019 is submitted after due date but within 60 days.** **Differential fee is required.**	Deferred for following: i) Differential fee Rs. 15,000/- as renewal application for year 2019 is submitted after due date but within 60 days.
129	035427	Grafazole Capsule 150mg Each capsule contains: Fluconazole…150mg	22-12-2004	**19.12.2009** Rs. 10000/-	OK	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2019 is within time**	Deferred for following: i) Initial application fee Rs. 30,000/-
130	035428	Ibugray Tablet 400mg Each tablet contains: Ibuprofen…400mg	22-12-2004	**19.12.2009** Rs. 10000/-	OK	Transfer of registration to new site was approved in 233rd Meeting held on 15-6-	Deferred for following: i) Initial application fee Rs. 30,000/-

						2012 but firm did not submit fee. **The renewal application for year 2019 is within time**	
131	035429	Grenocin Jelly 2% Each gm contains: Lignocaine HCl Anhydrous…20mg	22-12-2004	**19.12.2009** Rs. 10000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2019 is within time**	Deferred for following: i) Initial application fee Rs. 30,000/-
132	035434	Peflogray Tablet Each tablet contains: Pefloxacin (as mesylate)…400mg	22-12-2004	**19.12.2009** Rs. 10000/-	Not found	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2019 is within time**	Deferred for following: i) Initial application fee Rs. 30,000/-
133	052617	Co – Artesinate Tablet Each tablet contains:- Artemether…20mg Lumefantrine…120mg	07-10-2008	**15.07.2019** Rs. 10000/-	OK	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm did not submit fee. **The renewal application for year 2019 is submitted after due date but within one year. Differential fee is required under SRO 1005/2017.**	Deferred for following: i) Initial application fee Rs. 30,000/- ii) Differential fee Rs.135000/- under SRO 1005/2017.

Invalid Registrations:

Sr. No	Reg. No.	Brand Name & Composition	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	RRA status	Remarks of RRR
	I	II	III	IV	V	VII
M/s Gray's Pharmaceuticals Plot No. 02 Street No 03 National Industrial Zone, Rawat (DML No. 517)						
134.	030669	Ecoloxib 100mg Tablet Each tablet contains:- Celecoxib…. 100mg	26-07-2003	2092 - (R&I) dated 26.05.2016 Rs. 20000/- **07.11.2019** Rs. 10000/-	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee which was submitted on 2016. **The renewal application is submitted after the prescribed time period under SRO 1005/2017. Hence, registration is invalid.** The case was also deferred by Renewal Sub-Committee in its 4th Meeting for completion of renewal application.
135.	030684	Axodine 60mg Capsule Each capsule contains: Fexofenadine…60mg	26-07-2003	Nil	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application is not submitted in year 2018. Hence, registration is invalid.**
136.	030687	Itopram 20mg Tablet Each tablet contains:- Citalopram (as Hydrobromide)… 20gm	26-07-2003	**16.06.2020** Rs. 10000/-	Film coated tablet is available in RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application is not submitted in year 2018 but submitted in year 2020 after prescribed time period. Hence, registration is invalid.**
137.	048037	Lumovid 100mg Tablet Each tablet contains: Lamivudine…100mg (Grays Specs)	08-01-2008	2087 - (R&I) dated 20.05.2016 Rs. 20000/-	Film coated tablet is approved in RRA	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in year 2016. **Firm has not submitted the renewal for year 2018. Hence, registration is invalid.**
138.	048038	Heptogray Tablet Each tablet contains:-	08-01-2008	**16.06.2020** Rs. 10000/-	RRA status not	Transfer of registration to new site was approved in

		Silymarin… 200mg			confirmed	233rd Meeting held on 15-06-2012 but the firm did not submit fee. **The firm has not submitted the renewal for year 2018. Hence, registration is invalid.**
139.	037779	Graycip 500mg Capsule Each capsule contains: Ciprofloxacin as HCl…500mg	21-03-2005 Change of BN 13-09-2005	Nil	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **The renewal application is not submitted in year 2020. Hence, registration is invalid.**
140.	037780	Gephoxin 250mg Capsule Each capsule contains: Levofloxacin (Hemihydrate)…250mg	21-03-2005	Nil	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application is not submitted in year 2020. Hence, registration is invalid.**
141.	037781	Gephoxin 500mg Capsule Each capsule contains: Levofloxacin (Hemihydrate)…250mg	21-03-2005	Nil	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application is not submitted in year 2020. Hence, registration is invalid.**
142.	033331	Aviant 5mg Tablet Each tablet contains: Amlodipine (as Amlodipine Besylate)…5mg	05-08-2004	1841 -(R&I) dated 07.05.2012 Rs. 8000/- 207-(R&I) dated 3-5-2016 Rs. 12000/-	ok	**The renewal application for year 2019 is not submitted hence, registration is invalid.**
143.	033332	Aviant 10mg Tablet Each tablet contains: Amlodipine (as Amlodipine Besylate)…10mg	05-08-2004	1842 -(R&I) dated 07.05.2012 Rs. 8000/- 206-(R&I) dated 03-05-2016 Rs. 12000/-	ok	**The renewal application for year 2019 is not submitted hence, registration is invalid.**
144.	032328	Grayzine Tablet Each tablet contains: Cetrizine 2HCl…10mg	06-08-2009	1836 -(R&I) dated 07.05.2012 Rs. 8000/- 226-(R&I) dated 03-	Approved in RRA as cetirizine hydrochloride (HCl)	**The renewal application for year 2019 is not submitted hence, registration is invalid.**

				01-2016 Rs. 12000/-		
145.	065265	Graycip 250mg Capsule Each capsule contains: Ciprofloxacin (as HCl)…250mg (Grays Specs)	30-07-2010	Nil	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
146.	033323	Inflacid 20mg Capsule Each capsule contains: Piroxicam…20mg	**26-07-2004** Corrigendum dated 08-09-2004	2098-(R&I) dated 26-05-2016 Rs. 20000/-	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **Renewal application for year 2019 is not submitted hence, registration is invalid.**
147.	033329	Fluctine 20mg Capsule Each capsule contains: Fluoxetine (as HCl)…20mg	26-07-2004 Corrigendum dated 08-09-2004	Nil	ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application for year 2019 is not submitted hence, registration is invalid.**
148.	033330	Axodine 180mg Tablets Each Tablet Contains: Fexofenadine HCl…….180 mg	**26-07-2004** Corrigendum dated 08-09-2004	1840 -(R&I) dated 07.05.2012 Rs. 8000/- 204-(R&I) dated 13-01-2016 Rs. 12000/-	Approved in RRA in film coated form	**The renewal application for year 2019 is not submitted hence, registration is invalid.**
149.	033335	Tenif 50mg Tablet Each tablet contains: Atenolol…50mg	**26-07-2004** Corrigendum dated 08-09-2004	2075 -(R&I) dated 26.05.2016 Rs. 20000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but firm submitted fee in 2016. **Renewal application for year 2019 is not submitted hence, registration is invalid.**
150.	033336	Tenif 100mg Tablet Each tablet contains: Atenolol…100mg	**26-07-2004** Corrigendum dated 08-09-2004	2077 -(R&I) dated 26.05.2016 Rs. 20000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **Renewal application for year 2019 is not submitted hence, registration is invalid.**

151.	033343	Nidase 500mg Tablet Each tablet contains: Secnidazole… 500mg	31-08-2004	2081 - (R&I) dated 26.05.2016 Rs. 20000/-	RRA status not confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **Renewal application for year 2019 is not submitted hence, registration is invalid.**
152.	033344	Ostacs Tablet Each tablet contains: Tenoxicam…20mg	31-08-2004	Nil	Approved in RRA in film coated form	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application for year 2019 is not submitted hence, registration is invalid.**
153.	033345	Cling 150mg Capsule Each capsule contains: Clindamycin (as HCl) … 150mg	31-08-2005	2063- (R&I) dated 26.05.2016 Rs. 20000/-	Ok	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
154.	036246	Graynis Tablet Each tablet contains: Nystatin…500,000units	10-01-2005	Nil	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
155.	036247	Benzyl Benzoate Lotion Each 60ml contains: Benzyl Benzoate…25%	10-01-2005	Nil	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
156.	041702	Cephagray 125mg Suspension Each 5ml contains: Cephradine…125mg	26-11-2005	753-(R&I) dated 02.09.2016 Rs. 20000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
157.	041703	Cephagray 250mg Suspension Each 5ml contains:	26-11-2005	752-(R&I) dated 02.09.2016	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-

		Cephradine…250mg		Rs. 20000/-		06-2012 but the firm submitted fee in 2016. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
158.	038242	Lome 200mg Tablet Each tablet contains: Lomefloxacin (as HCl)…200mg	10-05-2005	Nil	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm did not submit fee. **Renewal application for year 2020 is not submitted hence, registration is invalid.**
159.	033342	Coniuren 10mg Tablet Each tablet contains:- Enalapril Maleate… 10mg	27-08-2009	2097-(R&I) dated 26-05-2016 Rs. 20000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. Renewal application for year 2019 is not submitted hence, registration is invalid.
160.	048040	Es-Itopram Tablets 10mg. Each tablet contains:- Escitalopram (as Oxalate)… 10mg.	08-01-2008 Change of BN **13-06-2008**	1827 -(R&I) dated 07.05.2012 Rs. 8000/- 187-(R&I) dated 13-01-2016 Rs. 12000/- **15.07.2019** Rs. 10000/-	To be confirmed	The renewal application for year 2018 is submitted after prescribed time period hence, registration is invalid.
161.	052616	Lyclean Cream Each 100gm contains: Permethrin…5gm (Grays Specs)	07-10-2008	759-(R&I) dated 02.09.2016 Rs. 20000/-	To be confirmed	Transfer of registration to new site was approved in 233rd Meeting held on 15-06-2012 but the firm submitted fee in 2016. *Renewal application for year 2018 is not submitted hence, registration is invalid.*

Decision: **Decision: Registration Board considered the case and decided as follows:**

a) **Cancelled the registration of products at Sr. No. 1-21, 23, 26-34, 36-37 and 39-41 in name of M/s Gray's Pharmaceuticals Plot No 442, Street No. 7, Sector I-9/2, Industrial Area Islamabad and grant to new manufacturing site i.e. M/s Gray's Pharmaceuticals Plot No. 02 Street No 03 National Industrial Zone, Rawat (DML No. 517). However, before issuance of approval letter requirements shall be fulfilled as mentioned in Column VII**
b) **For product at Sr. No. 3, approval letter shall be issued after confirmation of separate dispensing booth for steroidal material**
c) **Products at Sr No. 22,24,25,35 and 38 are deferred for approval status in RRA.**
d) **Products at Sr. No. 42 to 133 are deferred for submission of differential fee as recorded in Column VII**

e) Products at Sr. No 134-161 are deferred for clarification from firm for submission of last renewals and PRV approvals (if any) in order to confirm the validity of registration.

Reference will be sent to Costing and Pricing Division for confirmation of Maximum Retail Price (MRP).

Case No.02: Change in Specifications

Sr.#	Required Documents as per approved SOP
a.	Copy of registration letter and last renewal status
b.	Document in support of proposed change
c.	Analytical reports as per monograph of FPP
d.	Undertaking that: i. The change is made exclusively to comply with the pharmacopeia of Reference Regulatory ii. No case is pending at any forum / court of law regarding this product. iii. 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. iv. The provided information/ documents are true/ correct.

The following firms have requested for change in specifications Pharmaceutical Form/ registration letter of their registered products as per following details:

Sr. #	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
i.	**M/s. Medipak Limited, Kot Lakhpat Lahore (Pages 846-1043/C)**				
1.	008239	Medisol S Sodium Chloride 0.9% and Dextrose 5% IV Infusion B.P Each 1000ml contains Dextrose Monohydrate……55gm (eq. to Dextrose anhydrous 50gm) Sodium Chloride……..…9gm	Medisol S Sodium Chloride 0.9% and Dextrose 5% IV Infusion B.P Each 100ml contains **Dextrose Anhydrous……5.0gm** Sodium Chloride……..0.9gm Water for injection……Q.S. **(BP Specifications)**	25-07-1985 Change of brand name dated 03-01-2013 02-01-2018 08-05-2017 Renewal is ok	Fee Rs. 5000/- deposited for each product dated 20-04-2021 Dy. No. 12724 R&I dated 29-04-2021 Dy. No. 602 PR-II dated 30-04-2021
2.	009692	Medisol Hartmann's Compound Sodium Lactate IV Inf. B.P (Ringer Lactate) Each 1000ml contains Potassium Chloride……0.400gm Calcium Chloride.$2H_2O$ 0.270gm Sodium Chloride……6.000gm Sodium Lactate 50%…….6.100gm Hydrochloric Acid 25% 0.200ml Water for Injection ..1000ml	Medisol Hartmann's Compound Sodium Lactate IV Inf. B.P Each 100ml contains Potassium Chloride……0.040gm Calcium Chloride.$2H_2O$….0.027gm Sodium Chloride……0.600gm **Sodium Lactate……..0.320gm** Water for injection…….Q.S. **(BP Specifications)**	11-06-1987 Change of brand name 04-12-2012 03-12-2017 19-10-2016 Renewal is ok	
3.	009695	Medisol Paed's Sodium Chloride 0.18% and Dextrose 4.3% IV Infusion B.P	Medisol Paed's Sodium Chloride 0.18% and Dextrose 4.3% IV Infusion B.P Each 100ml contains	01-06-1987 Change of brand name 04-12-2012	

		Each 100ml contains Dextrose Monohydrate…….4.73gm Sodium Chloride……0.18gm Water for Injection……QS	**Dextrose Anhydrous…..4.3gm** Sodium Chloride……0.18gm Water for injection…….Q.S. **(BP Specifications)**	03-12-2017 19-10-2016 Renewal is ok	
4.	010005	Medigyl Injection 0.5% Each 100ml contains Metronidazole .. 500mg **Sodium chloride…....**740mg	Medigyl Injection 0.5% Each 100ml contains Metronidazole…….. 500mg. **Water for injection**…. Q.S. **(BP Specifications)**	30-10-1988 29-10-2018 16-07-2018 Renewal is ok sodium chloride is mentioned as excipient in RRA (USFDA) approved formulation (alongwith citric acid, dibasic sodium phosphate)	
5.	011183	Medisol 25% Dextrose 25% Intravenous Infusion B.P Each 1000ml contains Dextrose Monohydrate for parenteral use……..…275gm Water for Injection to…….. 1000ml	Medisol 25% Dextrose 25% Intravenous Infusion B.P Each 100ml contains **Dextrose anhydrous……25.0gm** Water for injection…. Q.S. **(BP Specifications)**	06-06-1990 05-06-2020 24-03-2020 Renewal is ok	
6.	014262	Medilact-D Solution for Injection Each 1000ml contains Potassium Chloride……0.300gm Calcium Chloride.$2H_2O$ 0.270gm Sodium Chloride……6.000gm Sodium Lactate 50%……3.100gm Dextrose Monohydrate…55gm for parenteral use equivalent to Dextrose anhydrous 50gm Water for Injection……. 1000ml	Medilact-D Solution for Injection Each 100ml contains Potassium Chloride…..….0.030gm Calcium Chloride.$2H_2O$…...0.020gm Sodium Chloride……0.600gm **Sodium Lactate……..0.310gm** **Dextrose anhydrous……....5.000gm** Water for injection……Q.S. **(USP Specifications)**	05-08-1993 04-08-2018 Registration Board granted the renewal w.e.f 05-08-2018 to 04-08-2023 Renewal is ok	
7.	022538	Medisol Mannitol 20% Infusion Each 1000ml contains Mannitol……200gm Water for injection q.s 1000ml	Medisol Mannitol 20% Infusion Each 100ml contains Mannitol…..…20gm. Water for injection…. Q.S. **(BP Specifications)**	26-11-1998 25-11-2018 Registration Board granted the renewal w.e.f 26-11-	

				2018 to 25-11-2023 Renewal is ok	
8.	024012	Medisol AC Concentrate for Bicarbonate Dialysis Each 1000ml contains Sodium Chloride……210.69gm Potassium Chloride……5.220gm Glacial Acetic Acid…….6.310gm Calcium Chloride $2H_2O$…….6.430gm Magnesium Chloride.$6H_2O$ 3.560g Dextrose Monohydrate 38.500gm	Medisol AC Concentrate for Bicarbonate Dialysis Each 1000ml contains Sodium Chloride……210.69gm Potassium Chloride……5.22gm Glacial Acetic Acid…….6.31gm Calcium Chloride.$2H_2O$...6.43gm Magnesium Chloride.$6H_2O$ 3.56g **Dextrose Anhydrous…35.00gm** **(BP Specifications)**	06-03-2002 25-03-2017 10-01-2017 Renewal is ok	
9.	024013	Dextrose 2.5% & Sodium Chloride 0.45% Intravenous Infusion Each 1000ml contains Dextrose……..…25.0gm Sodium Chloride……4.5gm	Dextrose 2.5% & Sodium Chloride 0.45% Intravenous Infusion Each 100ml contains **Dextrose Anhydrous…..2.50gm** Sodium Chloride…..…..0.45gm Water for injection…….Q.S. **(BP Specifications)**		
10.	024300	Medisol 3.3% Dextrose with 0.3% NaCl Intravenous Infusion Each 100ml contains Dextrose Monohydrate.…3.30gm Sodium Chloride……..0.30gm	Medisol 3.3% Dextrose with 0.3% NaCl Intravenous Infusion Each 100ml contains **Dextrose Anhydrous...3gm** Sodium Chloride…….0.30gm Water for injection….. Q.S. **(BP Specifications)**	12-03-2002 11-03-2017 10-01-2017 Renewal is ok	
11.	032220	Medisol Medilyte-M IV Infusion Each 1000ml contains Calcium Chloride.$2H_2O$..0.22gm Potassium Chloride……1.50gm Sodium Chloride…….2.16gm Sodium Acetate $3H_2O$…3.13gm Dextrose anhydrous……50.00gm	Medisol Medilyte-M IV Infusion Each 100ml contains Calcium Chloride.$2H_2O$….0.022gm Potassium Chloride…….0.150gm Sodium Chloride…..…0.216gm Sodium Acetate.$3H_2O$….0.313gm **Dextrose anhydrous…5.000gm** Water for injection…. Q.S. **(Innovator's Specification)**	10-03-2004 Change of brand name dated 12-12-2013 11-12-2018 11-02-2019 Renewal is ok	
12.	086437	Medisol ACD Solution Anticoagulant Citrate Dextrose Solution USP	Medisol ACD Solution Anticoagulant Citrate Dextrose Solution USP	06-07-2018 05-07-2023 Renewal is not	

		Formula A Each liter contains Citric Acid (Anhydrous)….7.30gm Sodium Citrate (Dihydrate)….22.00gm Dextrose (Monohydrate) 24.50gm Water for Injection QS 1000ml (USP Specs)	Formula A Each 100ml contains Citric Acid (Anhydrous) … 0.73gm Sodium Citrate (Dihydrate)…2.20gm **Dextrose anhydrous….2.22gm** Water for injection…. Q.S. **(USP Specifications)**	required	
13.	094647	Medisol ½ + 5% Infusion Each 1000ml contains Dextrose Monohydrate…… 55gm Sodium Chloride……..4.5gm (BP Specifications)	Medisol ½ + 5% Infusion Each 100ml contains **Dextrose anhydrous…5.0gm** Sodium Chloride……..0.45gm Water for injection…. Q.S. **(BP Specifications)**	13-05-2019 12-05-2024 Renewal is not required	
Decision of 70th PRVC		**The Committee considered the case and decided to refer the case to Registration Board**			

Decision: The Registration Board acceded to request of firm for grant of pharmacopoeial specifications for above mentioned products alongwith change/standardization of formulations as mentioned in Column -IV

Case No.03 Change of brand name of M/s. Rotex Pharma (Pvt.) Limited, Islamabad due to similarity/resemblance of brand name

M/s. Rotex Pharma (Pvt.) Limited, Islamabad was advised to change brand name vide DRAP's letter no. 3-1/2021 (PR-II) dated 15-09-2021 wherein it was mentioned that brand name **Prograf 0.5mg, 1mg and 5mg capsule (Reg. Mo. 102321, 102322 & 102323)** has resemblance with research product / international brand Prograf 1mg Capsule of M/s. Astellas Pharma Limited. This similarity of your brand name, with an already registered brand is against the condition of registration and may be misleading.

Now the firm has submitted following points in support of case:

- ***Our products were registered with DRAP on 29th April, 2020 after pharmaceutical evaluation, similarity, safety, efficacy under the DRAP Act, thereby creating rights, obligations, marketing of and right over the product with this name, the DRAP approved our product namely "Prograf" after proper scrutiny, availability, similarity and resemblance.***
- ***M/s. Astellas Pharma Limited as no locus-standi under the DRAP Act as their product namely Prograf 1mg is not registered, doing any business in Pakistan and therefore, is not an aggrieved party, therefore, they cannot claim any right which is prejudicial to the right of our product. It has no legal entity, therefore, not entitled for any relief.***
- ***Our product is well established is the market all over Pakistan and has not infringed any rights of other party which are not visually and structurally deceptive or confusingly similar to other product.***

We have explained our defense in the above paras and there is not violation of any law regarding the matter in dispute. Further, the registered brand name of our products cannot be challenged or question after fulfilling's all the legal requirements under DRAP Act.

It is therefore, letter dated 15-09-2021 may kindly be withdrawn in the interest of justice

Decision: Registration Board deliberated the matter that Prograf is brand name of innovator product (tacrolimus) by M/s. Astellas Pharma US, Inc. Deerfield, US which has been approved in RRA since long (1994 in USFDA). M/s. Rotex Pharma (Pvt.) Limited, Islamabad got registration of same formulation (Tacrolimus) with same brand name i.e Prograf 0.5mg, 1mg and 5mg capsule (Reg. Mo. 102321, 102322 & 102323) recently. In order to avoid confusion for prescriber regarding innovator product and generic product Registration Board decided to again advise M/s Rotex Pharma (Pvt.) Limited, Islamabad **to apply for change of brand name. In case of non-**

compliance, the Board authorized its Chairman for approval for issuance of issue show cause notice to the firm for suspension/cancellation of registered drug product.

Case No:04 Change of formulation of registered product of M/s Werrick Pharmaceuticals, Plot # 216-217, Sector I-10/3 Industrial Area ,Islamabad

1.	Name, address of Applicant / Marketing Authorization Holder	M/s Werrick Pharmaceuticals, Plot # 216-217, Sector I-10/3 Industrial Area ,Islamabad
	Name, address of Manufacturing site.	M/s Werrick Pharmaceuticals, Plot # 216-217, Sector I-10/3 Industrial Area, 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 26523 dated: 24/09/2021
	Details of fee submitted	PKR 30,000/-: dated: 17/09/2021
	The proposed proprietary name / brand name	Peptiban Dry Suspension 40mg/5ml **Reg No. 025037** Renewal submitted on 04.07.2019 (**within due date)**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 ml (After reconstitution) Contains: Famotidine…….. 40mg
	Pharmaceutical form of applied drug	Dry Suspension
	Pharmacotherapeutic Group of (API)	Histamine -2 (H_2) Receptor antagonist
	Reference to Finished product specifications	USP
	Proposed Pack size	60 ml suspension after reconstitution
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pepcid for Oral dry suspension USFDA Approved.
	For generic drugs (me-too status)	Sofem dry suspension 40mg by M/s Roryan Pharmaceuticals Reg. No. 082573
	GMP status of the Finished product manufacturer	Last GMP conducted on on 09/11/2018
	Name and address of API manufacturer.	M/s Vaasavaa Pharmaceuticals(Pvt) Ltd. India Plot # C-216 & 217 Maharashtra- 413 255, 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 Famotidine 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 compound D,C, F, B, E and Famotidine cyanomide & Famotidine amidine related compound, 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: (FM-IV/05/001, FM-IV/05/002, FM-IV/05/003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (Pharmaceutical equivalence for assay and pH) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence	Pharmaceutical Equivalence have been established against the competitor Product Sofem dry suspension 40mg per 5ml by Roryan Pharma by performing quality tests (Identification, Assay, pH).
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Vaasavaa Pharmaceuticals(Pvt) Ltd. India Plot# C-216 & 217 Maharashtra- 413 255, India.		
API Lot No.	FAM-0120013		
Description of Pack (Container closure system)	Amber colored Bottle with white pilfer proof cap (60ml suspension after reconstitution in 90ml 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, 9,12, 18, 24 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	200 Bottles	200 Bottles	200 Bottles
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	25-02-2021	26-02-2021	01-03-2021
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 submitted the 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. 6100728 issued by FDA (Maharashtra State) valid till 19/07/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of invoice No. EP-20-21/089 Dated 13-06-2020 wherein the permission to import Famotidine USP for the purpose of test/ analysis / stability studies and manufacturing is granted. Copy of letter No. 2110/2020-/AD (I&E) dated 17-08-2020. Batch No. FAM-0120013
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:

- Firm applied for change of already registered formulation i.e Peptiban Suspension (Famotidine 10mg/5ml) Reg No. 025037 into Peptiban Dry Suspension (Famotidine 40mg/5ml) in line with USFDA approved formulation i.e Pepcid oral dry suspension (40mg/5ml)
- **Dry powder section (General) has not been approved by CLB.**
- **Last GMP conducted on 09/11/2018**
- **Volume of diluent for reconstitution is not been provided by firm along with justification (weight/ml calculation) with reference to innovator/reference product.**
- **Stability data of reconstituted suspension up to proposed shelf life is not provided by the firm**

Decision: Registration Board deferred the request of firm for following requirements:

a) Confirmation of updated GMP status
b) Submission of evidence for section approval i.e Dry powder section (General) by CLB
c) Submission of Volume of diluent for reconstitution along with justification (weight/ml calculation) with reference to innovator/reference product.
d) Submission of Stability data of reconstituted suspension up to proposed shelf life

Case No:5 Change of formulation of registered product of M/s Wilson's Pharmaceutical, Islamabad. Plot:387-388,Sector I-9,Industrial area, Islamabad.

	Name, address of Applicant / Marketing Authorization Holder	M/s Wilson's Pharmaceutical,Islamabad.
	Name, address of Manufacturing site.	M/s Wilson's Pharmaceutical, Islamabad. Plot:387-388,Sector I-9,Industrial area,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. 15144 dated:01/06/2021
	Details of fee submitted	PKR 20,000/-:dated 09/04/2021 & PKR 10,000/-(differential fee):dated 26/05/2021
	The proposed proprietary name / brand name	Polypep Suspension (Dry Powder) Reg No. 023355 Last renewal dated 02.01.2014 **(within due date)**
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Famotidine……40mg
	Pharmaceutical form of applied drug	Dry powder suspension
	Pharmacotherapeutic Group of (API)	Anti-Histamine(H_2-receptor antagonist)
	Reference to Finished product specifications	USP

	Proposed Pack size	60ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pepcid For Oral Suspension, (USFDA approved)
	For generic drugs (me-too status)	Sofem Dry Suspension(40mg/5ml) by M/s Roryan Pharmaceuticals Pvt. Ltd, Reg. No.082573
	GMP status of the Finished product manufacturer	The firm was inspected on 24.01.2018 and conclusion was cGMP Compliance at the time of inspection. Oral Dry suspension (General) granted on 27.07.2015
	Name and address of API manufacturer.	Vaasavaa Pharmaceuticals (P) Ltd. 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, 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 data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process & controls, impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system & 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 i-e; Batches: (FM-IV/05/001, FM-IV/05/002, FM-IV/05/003) 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):	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, verification of analytical procedures, batch analysis, justification of specifications, reference standard , container closure system and stability study data.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the local product that is Sofem Dry suspension by Roryan Pharmaceutical (Pvt.) Ltd. by performing quality tests (Identification, Assay). CDP is not available in official pharmacopoeia.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, system suitability.

STABILITY STUDY DATA	
Manufacturer of API	M/s Vaasavaa Pharmaceuticals (P) Ltd, India.
API Lot No.	FAM-1219177 FAM-0919122
Description of Pack (Container closure system)	White color flavored powder filled in PET bottles.

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	Trial 03
Batch Size	200 BOTTLES	200 BOTTLES	200 BOTTLES
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	04-02-2020	04-02-2020	04-02-2020
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 stability study data because onsite inspection for verification of authenticity of submitted data, panel shall be constituted for verification.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 6094634 issued by Food &Drugs Administration (Maharashtra state), India valid till 15/07/2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the copy of clearance certificate/DRAP-AD-(I&E) dated 7/1/2020 along with the copy of commercial Invoice No EP/19-20/358 dated:23-12-2019. Batch no. FAM-1219177 and FAM-0919122
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	Firm has submitted the 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 real time and accelerated stability chambers.

Remarks OF Evaluator:

- Firm applied for change of already registered formulation i.e Polypep Suspension (Famotidine 10mg/5ml) Reg No. 023355 into Polypep Dry Suspension (Famotidine 40mg/5ml) in line with USFDA approved formulation i.e Pepcid oral dry suspension (40mg/5ml)
- The GMP inspection was conducted more than 3 years ago i.e 24.01.2018
- Volume of diluent for reconstitution is not been provided by firm along with justification (weight/ml calculation) with reference to innovator/reference product.
- Stability data of reconstituted suspension up to proposed shelf life is not provided by the firm.

Decision: Registration Board deferred the request of firm for following requirements:

a. **Confirmation of updated GMP status**
b. **Submission of Volume of diluent for reconstitution along with justification (weight/ml calculation) with reference to innovator/reference product.**
c. **Submission of Stability data of reconstituted suspension up to proposed shelf life**

VETERINARY

Case No. 01:- Request of M/s. Onesto Enterprises (Private) Limited, Islamabad for Transfer of Registration of Already Registered Imported Veterinary Drugs.

M/s. Onesto Enterprises (Pvt) Ltd, Flat No.304, Third Floor, Civic Centre, Phase-4, Bahria Town, Islamabad request for transfer of registration of their already registered imported veterinary drugs from the name of previous importer M/s. Eli Lilly Pakistan (Private) Limited, Karachi to their name. The details are as under:-

S. No.	Regn. No.	Name of Drug (s)/ Composition as per initial registration letters.	Manufacturer as per initial registration letter	Manufacturer/ Product License Holder as per CoPP	Approved pack size as per initial registration letter/ shelf life as initial registration letter	Initial date of registration/ renewal status
1.	002097	Tylan Soluble Each gm contains:- Tylosin Tartrate…100gm As per CoPP Tylan Soluble Powder for oral Solution Each bottle contains:- Tylosin (asTartrate)…100gm	Manufactured by M/s. Eli Lilly S.A. Geneva, Switzerland.	**Manufacturer by: -** M/s. Elanco UK AH Limited, Elanco Speke Operations, Fleming Road, Speke, Liverpool, L24 9LN, United Kingdom.	100gm powder in bottle as per Form-5A 3 years as per Form-5A	25-02-2003 for transfer of registration 19-02-2018
2.	013730	Tylan 250gm Premix Each Kg contains:- Tylosin Phosphate as 250gm Tylosin activity	Manufactured by M/s. Eli-Lilly France S.A. Fegersheim.	**Manufacturer by: -** M/s. Elanco UK AH, Elanco Speke Operations, Fleming Road, Speke, Liverpool, L24 9LN, United Kingdom.	1Kg 5Kg 25Kg 2 years as per Form-5A	01-08-1993 25-02-2003 for transfer of registration 19-02-2018
Stability data is not as per VICH guidelines.						

M/s. Onesto Enterprises (Pvt) Ltd, Flat No.304, Third Floor, Civic Centre, Phase-4, Bahria Town, Islamabad has deposited required fee of Rs.100,000/- and submitted the following documents:-

i) No Objection Certificates from M/s. Eli Lilly Pakistan (Pvt) Ltd. Karachi issued on 22-06-2020 (**Validity of NOC expired).**
ii) Original legalized certificate issued by USFDA.
iii) Letter of Authorization.
iv) Termination of Authorization.
v) Original Legalized Certificate issued by Veterinary Medicines Directorate.
vi) Copy of valid Drug Sale License.
vii) Undertaking.
viii) Site Master File along with Form-5A of above-mentioned drugs.

Decision of 307th meeting of Registration Board:

Deferred the product for Stability data is not as per VICH guidelines and Fresh NOC as more than 6 months' time has been passed.

Firm has submitted NOC dated 13th July 2021 from M/s. Eli Lilly Pakistan (Private) Limited, Karachi to their name along with real time stability data **25^0C/60%RH.**

Decision:- Registration Board considered and deferred the products for submission of stability data as per VICH Guidelines.

Case No. 02:- Request of M/s. Onesto Enterprises (Private) Limited, Islamabad for Transfer of Registration of Already Registered Imported Veterinary Drugs.

M/s. Onesto Enterprises (Pvt) Ltd, Flat No.304, Third Floor, Civic Centre, Phase-4, Bahria Town, Islamabad request for transfer of registration of their already registered imported veterinary drugs from the name of previous importer M/s. Eli Lilly Pakistan (Private) Limited, Karachi to their name. The details are as under:-

Reg. No.	Name of Drug (s)/ Composition as per initial registration letters.	Current Manufacturer/ Marketing Authorization Holder	Manufacturer as per GMP certificate	Address as per letter of Authorization & Certificate for registration of product	Termination of Authorization in the name of existing registration holder by	Initial date of registration/ renewal status
083242	Clinacox 0.5% Oral Premix Each gram contains:- Diclazuril.5mg	**Manufacturing site:** M/s. Laboratoria Smeets nv, Neerlandweg 24 & Fotografielaan 42-46, 2610 Wilrijk-Belgium. **Market Authorization Holder:** M/s. Eli Lilly and Company Elanco Animal Health, Lilly House, Priestley Road, Basingstoke, Hampshire RG24 9NL-United Kingdom.	M/s Laboratoria Smeets NV Site Address: Fotografielaan **44**-46, 2610 Belgium	**Manufactured by:** M/s Laboratoria Smeets NV, Neerlandweg 24 & Fotografielaan **42**-46, 2610 Wilrijk, Belgium **Product License Holder:** -M/s. Elanco GmbH Heinz-Lohmann-stranbe 4, 27472 Cuxhaven Germany	Elanco Animal Health Incorporated (Elanco) 2500 Innovation Way, Greenfield, Indiana 46140 United States (USA)	27th February, 2017

(i) Copy of registration Letter/variation letter.
(ii) No Objection Certificates from M/s. Eli Lilly Pakistan (Pvt) Ltd. Karachi issued on 13th July, 2021.
(iii) Letter of Authorization.
(iv) Termination of Authorization.
(v) Original Legalized Certificate for registration of product issued by Federal Agency for the safety of the food chain which shows product type is feed additive and freely availavle in Belgium.
(vi) Legalized copy of GMP issued by Federal Agency for Medicines and Health Products.
(vii) Copy of valid Drug Sale License.
(viii) Undertaking.
(ix) Site Master File along with Form-5A of above-mentioned drugs.

Remarks:

Termination letter issued to previous importer by Elanco USA but approved Marketing authorization holder is M/s Eli Lilly UK, need Clarification.

Decision:- Registration Board considered and deferred the case for submission of termination letter to previous importer by M/s. Eli Lilly and Company Elanco Animal Health, Lilly House, Priestley Road, Basingstoke, Hampshire RG24 9NL-United Kingdom and authorization letter to applicant.

Case No. 03:- **CANCELLATION OF REGISTRATION OF VETERINARY DRUGS REGISTERED IN YOUR NAME FROM PRODUCT LICENSE HOLDER M/S. BOEHRINGER INGELHEIM VETMEDICA GMBH, GERMANY.**

Registration Board in its **288th** meeting held on 14th – 15th February, 2019, while considering the termination of your distribution agreement by the product license holder *M/s. Boehringer Ingelheim Vetmedica GmbH, Germany* for product "Ubrolexin Inflammatory suspension" (Reg.No.080765), decided to issue show cause notice to M/s. Marush (Pvt) Ltd, K-123, Model Town, Lahore. **M/s. Boehringer** Ingelheim Vetmedica GmbH, Germany has **requested** to terminate their distribution agreement and withdraw / cancel the registration of below products registered / submitted with M/s. **Marush** (Pvt) Ltd, Lahore with effect from 31-12-2017.

S.No.	Reg. No.	Product Name & Composition	Category
1.	080765	Ubrolexin Inflammatory Suspension Each 1 injector with 10g (12ml) contains:- Cefalexin Monohydrate...200mg Kanamycin Monosulfate..133mg (Corresponds to 100,000 I.U).	Cattle-Pharmaceutical

Accordingly show **cause notice issued on** 26-08-2019 which is undelivered again dated 12th September, 2019 issued show cause notice reminder dated 11-02-2020.

M/s. Marush (Pvt) Ltd, Lahore requested dated **12-09-2019** that reply will be submitted in your good office within 20 days. But **reply is still awaited**.

M/s. Marush (Pvt) Ltd, Lahore CEO Dr. Muzammil Hussain Shah submitted a letter dated **01-10-2019** to Federal Minister for Ministry of National Health Services, Regulation and Coordination on subject "Product Registrations in the name of M/s. Marush (Pvt) Ltd, for products Manufactured by Boehringer Ingelheim Vetmedica Inc. which is reproduced as under:

"M/s. Boehringer Ingelheim Vetmedica GmbH, Germany owes an approximate sum of USD 250,000.00 in shape of compensation/claim to M/s. Marush (Pvt) Ltd, Lahore on account of the following heads.

- Losses incurred in shape of mortalities, due to outbreaks of diseases in farms, as the vaccines were shipped to Pakistan in substandard packaging (domestic grade) instead of proper international grade packaging which led to exposure of vaccines in transit. Boehringer officials cleared these vaccines for sales. Upon use, farmers faced mortalities and Marush had to settle their accounts, facing financial loss as well as loss of reputation in the industry.
- Expenses incurred in shape of product development (Product launching events), marketing (seminars) and product training of staff which included international visits.
- Boehringer management at the UAE office Cheated Marush Pvt Ltd, as they used us for product promotion, development and awareness but on the other hand sold vaccines directly to Pakistani farmers through their UAE distributor.

In order to avoid making the due payment, the foreign company (Boehringer Ingelheim Vetmedica Inc) is trying to manipulate the situation by getting the registration letters, already issued in the name of Marush Pvt. Ltd, cancelled by DRAP and hence trying to evade making the due compensation.

It is requested to your high offices that this matter of cancellation of registration be put to rest, until the accounts are settled. If this act of manipulation is allowed, all foreign manufacturers will adopt this practice of using Pakistani companies to their advantage and then discarding them once their desired objectives have been fulfilled.**"**

The case related to biological drugs including above reply presented by Biological Division in 293rd meeting of Registration Board held on 6 – 8th January, 2020 and Board upheld its decision of 288th meeting for issuance of Show Cause notice. Show cause issued by Biological Division dated 09th December 2020.

M/s. Marush Pvt Ltd CEO Dr. Muzammil Hussain Shah submit a letter dated 29th December 2020 in the name of Director Biological on reply of show cause issued by Biological Division dated 09th December 2020 which is as under:

"Our reply was accepted and made a part of the agenda of 293rd meeting of Registration Board".

The case was discussed in its 307th meeting of Registration Board. Registration Board decided to issue final show cause reminder to M/s Marush (Pvt) Ltd, Lahore to submit reply within 15 days. Accordingly reminder issued to M/s. Marush (Pvt) Ltd, Lahore to submit reply within 15 days. **No reply received as yet.**

Proceeding:

As Product license holder *M/s. Boehringer Ingelheim Vetmedica GmbH, Germany* for product "Ubrolexin Inflammatory suspension" (Reg.No.080765), terminate their distribution agreement and withdraw / cancel the registration of said product with M/s. **Marush** (Pvt) Ltd, Lahore with effect from 31-12-2017 Registration Board issue multiple show cause notices to importer M/s. **Marush** (Pvt) Ltd, Lahore including the option of personal hearing Board decided to cancel the registration of said drug.

Decision: - **Keeping in view the above facts and discussion; Registration Board considered and cancelled the product "Ubrolexin Inflammatory Suspension" (Regn.No. 080765) from the name of M/s Marush (Pvt) Limited, K-123, Model Town, Lahore.**

Case No.04:- Request of M/s. International Pharma Labs., Lahore for Standardization of Formulation with the Innovator's Product/Reference Regulatory Authorities and Pharmacopeia.

M/s. International Pharma Labs., Lahore has requested for standardization of formulation with the innovator's product/reference regulatory authorities and pharmacopeia of their following registered drug as per detail mentioned against each:-

S. No.	Regn. No.	Product Granted Composition	Demanded Composition	Remarks/ Diary No. R&I
I	II	III	IV	V
1.	080950	Amoxi-Clav Injection **Each ml contains:-** Amoxicillin Trihydrate…..140mg **Clavulanic Acid…….….35mg**	Amoxi-Clav Injection **Each vial contains:-** Amoxicillin Trihydrate……..140mg **Clavulanic Acid as Potassium Clavulanate…….35mg**	Dy. No. 9019-R&I DRAP dated 19-03-2021.

M/s. International Pharma Labs., Lahore has deposited required fee of Rs.5,000/- and submitted following supporting documents: -

(i) Copy of registration letter.
(ii) Copy of approved sections.
(iii) Copy of inspection report conducted by area FID on 19th December, 2018 & 2nd March, 2018.
(iv) Undertaking.

Letter issued to the firm to clarify that your approved dosage form is liquid but submitted monograph shows powder. In response the firm reply that we have both liquid penicillin injectable section and powder. Injectable section both approvals and they want to standardize our product so yes it is powder in monograph please change our product specification as per pharmacopeia and makes us to that you for better GMP practice as per
guidance from DRAP.
Remarks:
Currently firm was manufacturing liquid dosage form but now they want to manufacture as per official monograph i.e. powder dosage form.

The case was discussed in its 66th Post Registration Variation Committee and the Committee evaluated the case and Chairman Registration Board, on the recommendations of the committee, decided to refer the case to Registration Board.

Decision:- Registration Board considered and approved the standardization of composition of already registered drug as per British Pharmacopeia. Firm will deposit differential requisite fee of Rs. 25000/- before issuance of letter. The details are as under: -

S. No.	Regn. No.	Existing Name of Drug & Composition	New Approved Name of Drug & Composition
1.	080950	Amoxi-Clav Injection Each ml contains:- Amoxicillin Trihydrate…140mg Clavulanic Acid…….35mg	Amoxi-Clav Injection Each vial contains:- Amoxicillin Trihydrate……140mg Clavulanic Acid as Potassium Clavulanate…….....35mg

Case No. 05:- Request of M/s. Mylab (Pvt) Ltd., Bahawalpur for Change of Composition.

Registration Board in its 290th meeting approved drug of M/s. Mylab (Pvt) Ltd., Bahawalpur registration letter withheld that generic has different composition/strength. Now the firm has requested for change of composition of their following approved drug as per detail mentioned against each:-

S. No.	Product Granted Composition	Demanded Composition	Approved Packs Size	Decision & Remarks
1.	Vita Mineral Gold Powder Each Kg contains:- **Vitamin A……..…..0.08gm** Vitamin D3……..0.16gm Vitamin E……0.38gm Thiamine (Vitamin B1…..…1gm Riboflavin (Vitamin B2).1.25gm Niacin (Vitamin B3…….6.25gm Pyridoxine (Vitamin B6)….4gm Cyanocobalamin (Vitamin B12).....0.001gm Copper Sulphate……..0.25gm Magnesium Sulphate……..25gm Calcium Chloride……..0.023gm Zinc Sulphate.....2.17gm Maganese Sulphate……10gm Potassium Iodide…….0.50gm Sodium Selenite.....0.01gm Dibasic Calcium Phosphate.....150gm Sodium Chloride……..120gm	Vita Mineral Gold Powder Each Kg contains:- **Vitamin A……..…...…...0.8gm** Vitamin D3……..0.16gm Vitamin E……....0.38gm Thiamine (Vitamin B1…....1gm Riboflavin (Vitamin B2).1.25gm Niacin (Vitamin B3….....6.25gm Pyridoxine (Vitamin B6)…..4gm Cyanocobalamin (Vitamin B12).....0.001gm Copper Sulphate…….….0.25gm Magnesium Sulphate…….25gm Calcium Chloride……..0.023gm Zinc Sulphate.....2.17gm Maganese Sulphate…….....10gm Potassium Iodide…..…...0.50gm Sodium Selenite.....0.01gm Dibasic Calcium Phosphate……..…150gm Sodium Chloride…...…....120gm	1Kg 2.5Kg 5Kg 10Kg 20Kg 25Kg	Approved with change of brand name & with Innovators specifications .

Furthermore, the firm has inform that due to clerical mistake/small typing mistake in a quantity of ***"Vitamin A……0.08gm"*** instead of ***"Vitamin A……0.8gm"*** and request to issuance of registration letter. The firms submit clarification about D.C.P. (Phosphorous) as Dibasic Calcium Phosphate.

M/s. Mylab (Pvt) Ltd., Bahawalpur has deposited the required fee Rs.30,000/- and submitted following supporting documents:-

(i) Generic me-too.
(ii) Copy of Form-5

The case was discussed in its 312th meeting of Registration Board defer for further deliberation. As per available record the demanded composition is already registered various firms *"Maximal Powder"* vide Regn.No.106674 of M/s. S.J & G. Fazul Ellahie (Pvt) Ltd., Karachi & *"Min Rold Water Soluble Powder"* vide Regn.No.109284 of M/s. Haarolds Pharmaceuticals (Pvt) Ltd., Bhimber, AJK.

Decision:- keeping in view the already registered generic drugs, Registration Board considered and approved the standardization of formulation as under:-

S. No.	Product Granted Composition	New Approved Composition	Approved Packs Size
1.	Vita Mineral Gold Powder Each Kg contains:- **Vitamin A……..…..0.08gm** Vitamin D3……..0.16gm Vitamin E……0.38gm Thiamine (Vitamin B1…..…1gm Riboflavin (Vitamin B2).1.25gm Niacin (Vitamin B3…….6.25gm Pyridoxine (Vitamin B6)….4gm Cyanocobalamin (Vitamin B12).....0.001gm Copper Sulphate……..0.25gm Magnesium Sulphate……..25gm	Vita Mineral Gold Powder Each Kg contains:- **Vitamin A……..…...…...0.8gm** Vitamin D3……..0.16gm Vitamin E……....0.38gm Thiamine (Vitamin B1…....1gm Riboflavin (Vitamin B2).1.25gm Niacin (Vitamin B3….....6.25gm Pyridoxine (Vitamin B6)…..4gm Cyanocobalamin (Vitamin B12).....0.001gm Copper Sulphate…….….0.25gm Magnesium Sulphate…….25gm	1Kg 2.5Kg 5Kg 10Kg 20Kg 25Kg

	Calcium Chloride……..0.023gm Zinc Sulphate.....2.17gm Maganese Sulphate……10gm Potassium Iodide…….0.50gm Sodium Selenite.....0.01gm Dibasic Calcium Phosphate.....150gm Sodium Chloride……..120gm	Calcium Chloride……..0.023gm Zinc Sulphate.....2.17gm Maganese Sulphate……...10gm Potassium Iodide…..…...0.50gm Sodium Selenite.....0.01gm Dibasic Calcium Phosphate……..…150gm Sodium Chloride…...…...120gm	

Case No.06:- Registration of Drugs under the Drugs Act, 1976-Inspection Report of Manufacturer Abroad.

The Registration Board in its various meetings approved following products of M/s. Ghazi Brothers, Karachi, manufactured & product license holder M/s. Hebei Yuanzheng Pharmaceutical Co. Ltd., No.16, Liuyuan Road, Road, Chang'an District, Shijiazhuang City, Hebei Province, China subject to inspection of manufacturer abroad as per import policy and verification of storage facility (where applicable) as per detailed mentioned against each:-

S. No.	Name of Importer/ Manufacturer	Name of Drugs/ Composition & Meeting	Packs Size	Shelf Life	Decision/ Remarks
1.	M/s. Ghazi Brothers, Karachi. / Manufactured & Product License Holder:- M/s. Hebei Yuanzheng Pharmaceutical Co. Ltd., No.16, Liuyuan Road, Chang'an District, Shijiazhuang City, Hebei Province, China.	Sinozene Powder for Injection Each 2.36 sachet contains:- Diminazene Diaceturate…..…1.05g Antipyrine (Phenazone)…….1.31g **(Through sub-committee constituted in M-237)**	2.36g	5 years	Approved.
3.	-do-	Isomedium Powder for parental administration Each 1g sachet contains:- Isometamedium Chloride Hydrochloride……1g **(M-251)**	1gm sachet	03years	Approved.

With reference to above products following details are submitted:

(i) In compliance, inspection of the manufacturer abroad M/s. Hebei Yuanzheng Pharmaceutical Co. Ltd., Shijiazhuang City, Hebei Province, China was carried out by the nominated panel comprising Mr. Abdul Sattar Soomro, Director, Drug Testing Laboratory, Karachi/Member Drug Registration Board &Mr. Khalid Mehmood, Federal Inspector of Drugs, DRAP, Islamabad on 04th& 05th April, 2017 and the panel rated the manufacturing facility as "**good"** (recommended), recommending only seven other veterinary drugs (liquid injectable & oral suspension) excluding the above mentioned sachet.

(ii) The panel further, reported that "both of the above products are not in free sale in the country of origin as admitted by the management. The panel stated to have inspected the sachet section as per mandate, recommending it only/if subject to provision of free sale certificate (FSC) of above products in the country of origin which has not been found on the day of inspection.

(iii) Now the firm has submitted fresh valid and legalized original CoPP/ Free Sale Certificate issued by Chinese Authorities for the above products for which inspection panel has reported to be not in free sale in country of origin. The observations on the CoPP submitted by the firm are mentioned in the remarks column of above table against each product.

(iv) The complete address of manufacturer and product license holder as per new CoPP submitted is as under.

M/s. Hebei Yuanzheng Pharmaceutical Co. Ltd., No.16, Liuyuan Road, Road, Chang'an District, Shijiazhuang City, Hebei Province, China.

(v) The finish product specifications for the above products are not mentioned in minutes. However the firm vide letter informed that the firm has claimed specification of innovator.

(vi) The local storage facility of M/s. Ghazi Brothers, Karachi has already been verified by the concerned area FID.

Decision of 287th meeting of Registration Board:

Registration Board in its 287th meeting deferred the case for obtaining clarification from the firm regarding the submitted CoPPs wherein the status regarding presence of product in market of exporting country i.e China is not mentioned/ confirmed. The firm has now provided fresh valid legalized CoPP showing free sale status in the country of origin.

Registration Board in its 297th meeting approved the products subject to inspection of manufacturer abroad for finished drugs as current inspection report does not cover sachet for parental administration.

Remarks:

Sterile sachet veterinary section was inspected by the panel of expert. Panel inspected the sachet section as per mandate, however recommends only/if/subject to provision of free sale certificate (FSC) in the country of origin which has not been found as of today. The Registration Board may take the decision with all legal & just. Errors & omissions accepted.

Decision:- Registration Board considered and deferred the product "Sinozene Powder for Injection"for consideration in next Board meeting along with clarification of both products as inspection abroad conducted on dated 04th & 05th April 2017 shows product is not available in free sale in exporting country but submitted CoPP dated 07th April 2017 show that product is available in exporting country.

Case No. 07:- Request of M/s. Star Laboratories (Pvt) Ltd., Lahore for Correction of Composition of registered product.

M/s. Star Laboratories (Pvt) Ltd., Lahore has requested for correction of composition of their following registered drug as per detail mentioned against each:-

S. No.	Regn. No.	Product Granted Composition	Demanded Composition	Remarks/ Diary No. R&I
I	II	III	IV	V
1.	031490	Nitoxil -34% Injection Each ml contains:- Nitroxynil B.P. (Vet)…..3.4mg	Nitoxil -34% Injection Each ml contains:- **Nitroxynil …….340mg**	Dy. No. 16098 dated 09-06-2017.

M/s. Star Laboratories (Pvt) Ltd., Lahore has deposited fee of Rs.5,000/- and submitted following supporting documents:-

(i) Copy of initial registration letter along with latest renewal status.

(ii) New Form-5 for each product wherein the demanded composition is mentioned.

The case was discussed in its 27th PRVC held on 25-04-2019 and the Committee evaluated the case and decided to place the case before Registration Board for its consideration after getting the following details;

a. Composition of originator brands/product.
b. Clarification from the firm regarding the composition of product they have manufactured with, since grant of registration of the said product.
c. Composition of the product mentioned by the firm at the time of submission of renewal of said product.

In response the firm has informed that;

- Composition of originator brand Fascionex 34% Injection manufactured by M/s. Kepro, Holland. Each ml contains: Nitroxynil 340mg
- Composition of product the firm have manufactured with since grant of registration of this product. In order to supply effective product to the market, only few batches were produced and supplied as 34% of Nitroxinil 34% Injection. Data attached.
- The firm has informed they received an export order for Nitoxil-34% Injection, therefore in order to supply to foreign customer, the corrected composition of this registered product is required.

Remarks:

Firm apply for correction of composition of API in accordance with 34%.

The case was discussed in its 66th Post Registration Variation Committee and the Committee evaluated the case and Chairman Registration Board, on the recommendations of the committee, decided to refer the case to Registration Board.

Decision:- Registration Board considered and approved the standardization of composition of already registered drug. Firm will deposit differential fee Rs. 25000/- before issuance of letter. The details are as under: -

S. No.	Regn. No.	Product Granted Composition	New Approved Composition
1.	031490	Nitoxil -34% Injection Each ml contains:- Nitroxynil B.P. (Vet)...3.4mg	Nitoxil -34% Injection Each ml contains:- Nitroxynil …….340mg

Case No.08:- Request of M/s. Selmore Pharmaceuticals (Pvt) Ltd., Lahore for Correction of Composition.

Registration Board in its 296th meeting approved drug of M/s. Selmore Pharmaceuticals (Pvt) Ltd., Lahore, registration letter withheld that confirmation of composition. Now the firm has requested for correction of composition of their following approved drug as per detail mentioned against each:-

S. No.	Product Approved in Minutes	Applied Composition As per Registration Dossier	Decision/ Pack Sizes
I	II	III	IV
1.	Vital Plus Powder Each Kg contains:- Vitamin A……...10MIU Vitamin D3……...…3MIU Vitamin E……5000MIU Vitamin K3…….3000MIU Vitamin C……..…30,000MIU	Vital Plus Powder Each Kg contains:- Vitamin A……...10MIU Vitamin D3…….……..3MIU Vitamin E……...5000IU Vitamin K3……...3000mg Vitamin C……30000mg	Approved with innovators' specifications. 500g 1Kg 2.5Kg

As per registration dossier received from PEC the correct composition mentioned in dossier mentioned in Column-III

Decision:- Registration Board considered and approved the correction of composition as per following details:

S. No.	Product Approved in Minutes	New Approved Composition	Approved Pack Size(s)
1.	Vital Plus Powder Each Kg contains:- Vitamin A……...10MIU Vitamin D3……..…..3MIU Vitamin E……5000MIU Vitamin K3…….3000MIU Vitamin C……30,000MIU	Vital Plus Powder Each Kg contains:- Vitamin A……..…10MIU Vitamin D3…….……3MIU Vitamin E……..5000IU Vitamin K3……..3000mg Vitamin C……...30000mg	500g 1Kg 2.5Kg

Case No.09:- Request of M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura for Change of Composition 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	Demanded Composition	Remarks/ Diary No. R&I
I	II	III	IV	VI
1.	071048	Avienro-C Liquid Each 100ml contains:- **Enrofloxacin……100gm** Colistin Sulphate…..50MIU	Avienro-C Liquid Each 100ml contains:- **Enrofloxacin……10gm** Colistin Sulphate….50MIU	Dy. No. 11465-R&I DRAP dated 15-04-2021

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-
4.	063652	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…….….0.06gm** **Oxfendazole……0.0226gm**	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…..….60gm** **Oxfendazole…..…22.6gm**	-do-
5.	071044	Link-200 Powder **Each 100gm contains:-** Lincomycin HCl……100gm Colistin Sulphate…..0.8MIU	Link-200 Powder **Each 1000gm contains:-** Lincomycin HCl……100gm Colistin Sulphate…..0.8MIU	-do-
6.	071046	Comox Oral Powder Each 100gm contains:- **Amoxyciline Tartrate…150gm** Colistin Sulphate……..50MIU	Comox Oral Powder Each 100gm contains:- **Amoxicilline Trihydrate……..…15gm** Colistin Sulphate…...50MIU	-do-
7.	063650	Avi-Bro Oral Liquid Each 1000ml contains:- **Bromohexine HCl……0.05gm**	Avi-Bro Oral Liquid Each 1000ml contains:- **Bromhexine HCl..…50gm**	-do-

M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura deposited fee of Rs.5000 x 7 = Rs.35000/- 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 312th meeting of Registration Board deferred for confirmation of already approved generic drugs and details of renewal.

The details of already approved generic drugs are as under:-

S. No.	Regn.No.	Product Granted Composition	Demanded Composition
I	**II**	**III**	**IV**
1.	071048	Avienro-C Liquid Each 100ml contains:- **Enrofloxacin……100gm** Colistin Sulphate…..50MIU **Generic is not available**	Avienro-C Liquid Each 100ml contains:- **Enrofloxacin……10gm** Colistin Sulphate….50MIU **Generic is available**
2.	063649	Avi-Dex Liquid Each 1000ml contains:- **Triclobendazole……..0.05gm** **Levamisole HCl……0.015gm** **Generic is available**	Avi-Dex Liquid Each 1000ml contains:- **Triclabendazole……..50gm** **Levamisole HCl…..…15gm** **Generic is not available**
3.	063654	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....0.025gm**	Albencena Plus Oral Liquid Each 1000ml contains:- **Albendazole…….....25gm**

		Sodium Selenite…...0.0015gm **Cobalt Sulphate….0.00382gm** **Generic is not available**	**Sodium Selenite..….1.5gm** **Cobalt Sulphate…..3.82gm** **Generic is not available**
4.	063652	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…….….0.06gm** **Oxfendazole……0.0226gm** **Generic is not available**	Boxer Liquid. Each 1000ml contains:- **Oxyclozanide…..….60gm** **Oxfendazole…..…22.6gm** **Generic is not available**
5.	071044	Link-200 Powder **Each 100gm contains:-** Lincomycin HCl……100gm Colistin Sulphate…..0.8MIU **Generic is not available**	Link-200 Powder **Each 1000gm contains:-** Lincomycin HCl……100gm Colistin Sulphate…..0.8MIU **Generic is available**
6.	071046	Comox Oral Powder Each 100gm contains:- **Amoxyciline Tartrate…150gm** Colistin Sulphate……..50MIU **Generic is not available**	Comox Oral Powder Each 100gm contains:- **Amoxicilline Trihydrate……...…15gm** Colistin Sulphate…...50MIU **Generic is available**
7.	063650	Avi-Bro Oral Liquid Each 1000ml contains:- **Bromohexine HCl……0.05gm** **Generic is not available**	Avi-Bro Oral Liquid Each 1000ml contains:- **Bromhexine HCl..…50gm** **Generic is available**

Decision:- Registration Board considered and Decided as under:

a. Deferred the product at sr. 2-4 for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.

b. Approved the standardization of composition of already registered drugs for products at Sr.No.1 & 5-7 of M/s. Avicenna Laboratories (Pvt) Ltd., Bhikki Distt., Sheikhupura. Firm will submit differential fee Rs. 25000/- per product before issuance of letter. The details are as under: -

S. No.	Regn.No.	Existing Name of Drug & Composition	New Approved Name of Drug & Composition
1.	071048	Avienro-C Liquid Each 100ml contains:- **Enrofloxacin……100gm** Colistin Sulphate…..50MIU	Avienro-C Liquid Each 100ml contains:- **Enrofloxacin……10gm** Colistin Sulphate….50MIU
2.	071044	Link-200 Powder **Each 100gm contains:-** Lincomycin HCl……100gm Colistin Sulphate…..0.8MIU	Link-200 Powder **Each 1000gm contains:-** Lincomycin HCl……100gm Colistin Sulphate…..0.8MIU
3.	071046	Comox Oral Powder Each 100gm contains:- **Amoxyciline Tartrate…150gm** Colistin Sulphate……..50MIU	Comox Oral Powder Each 100gm contains:- **Amoxicilline Trihydrate……..15gm** Colistin Sulphate…...50MIU
4.	063650	Avi-Bro Oral Liquid Each 1000ml contains:- **Bromohexine HCl……0.05gm**	Avi-Bro Oral Liquid Each 1000ml contains:- **Bromhexine HCl..…50gm**

HUMAN IMPORT

Case.No.01:- GRANT OF EXEMPTION FROM INSPECTION OF MANUFACTURER ABROAD ON THE BASIS OF PIC/S PARTICIPATING AUTHORITIES.

The various firms have applied for exemption from inspection of manufacturer abroad on the basis of PIC/S participating authority. In the light of above following documents are required for exemption:

i. Original legalized Certificate of a Pharmaceutical Product/Free Sales Certificate issued by PIC/S participating authority.
ii. Online verification link which shows that product is approved/registered by PIC/S participating authority.

Decision: Registration Board considered and noted the above information.

Case No.02 REQUEST OF M/S PFIZER PAKISTAN LTD, KARACHI FOR TRANSFER OF REGISTRATION TO THEIR NAME FROM M/S CARE PHARMA INTERNATIONAL (PVT) LTD, KARACHI.

M/s Pfizer Pakistan Limited, B-2, SITE, Karachi has submitted an application for Registration of following already registered product **from** M/s Care Pharma International (Pvt) Ltd, Karachi to their name along with change of name of product at sr. no. 2 &3 from Leucovarin Calcium to DBL Leucovarin Calcium. Detail of proposed product is as under:

S. No	Reg. No.	Name & Composition (as per transfer reg. letter 25-11-2008)	Existing approved Manufacturing Site (as per transfer reg. letter 25-11-2008)	New Proposed Site / Manufacturer/ Product License Holder (as per COPP)
1.	016147	DBL Leucovarin Calcium Injection 50mg/ 5ml Each 5ml contains: Folinic Acid 50mg as calcium salt	M/s Hospira Australia Pvt. Ltd	M/s Hospira Australia Pvt. Ltd. 1-5 7-23 and 25-39 Lexia Place MULGRAVE VIC 3170 Australia
2.	016148	Leucovarin Calcium Injection 100mg/ 10ml Each 10ml contains: Folinic Acid 100mg as calcium salt	M/s Hospira Australia Pvt. Ltd	M/s Hospira Australia Pvt. Ltd. 1-5 7-23 and 25-39 Lexia Place MULGRAVE VIC 3170 Australia
3.	016149	Leucovarin Calcium Injection 300mg/ 30ml Each 30ml contains: Folinic Acid 300mg as calcium salt	M/s Hospira Australia Pvt. Ltd	M/s Hospira Australia Pvt. Ltd. 1-5 7-23 and 25-39 Lexia Place MULGRAVE VIC 3170 Australia

The firm has submitted the following supporting documents: -

i. Fee of Rs.100,000 x 3 = 300,000/- dated 11-11-2020
ii. Applications on Form-5F
iii. Copy of initial registration letter 07-02-1995 and transfer of reg. letter dated 25-11-2008. Last Renewal submission dated 20-11-2018.
iv. Original & legalized COPPs issued by TGA for above products dated 25-05-2018, 27-04-2018, 25-05-2018 respectively showing the freely availability of product in exporting country and GMP compliant status of the product).
v. Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.
vi. Letter of Authorization from product license holder.

Decision: Keeping in view the above position, Registration Board considered and decided as follow;

a. Cancelled the registration of following products from the name of M/s Care Pharma International (Pvt) Ltd, Karachi.

S.No	Reg. No.	Name & Composition
1.	016147	DBL Leucovarin Calcium Injection 50mg/ 5ml Each 5ml contains: Folinic Acid 50mg as calcium salt
2.	016148	Leucovarin Calcium Injection 100mg/ 10ml Each 10ml contains:

		Folinic Acid 100mg as calcium salt
3.	016149	Leucovarin Calcium Injection 300mg/ 30ml Each 30ml contains: Folinic Acid 300mg as calcium salt

b. Approved the registration of above products in the name of M/s Pfizer Pakistan Limited, B-2, SITE, Karachi along with change of brand name of product at sr. 2 & 3 from Leucovarin Calcium to DBL Leucovarin Calcium as per policy for imported finished drug registration (in accordance with details of composition and manufacturer as per CoPP).

c. A reference shall be sent to Costing & Pricing Division for their comments regarding MRP of the said products.

Case No.03 REQUEST OF M/S NOVARTIS PHARMA (PAKISTAN) LTD, KARACHI FOR PERMISSION TO IMPORT INTERNATIONAL PACKS OF THEIR REGISTERED PRODUCTS.

M/s Novartis Pharma (Pakistan) Ltd, Karachi has stated that their principals have informed that due to very specific and limited quantity of Onbrez Breezhaler 150mcg inhalation powder hard capsules (Reg. No.069586) & Onbrez Breezhaler 300mcg inhalation powder hard capsules (Reg. No.069587), they are unable to provide this medicine in country specific packs.

The firm requested to allow them to print the following components on outer box of product locally at their licensed premises (DML No.000193, 15 West Wharf Road, Karachi) as per labeling and packaging rules 1986.

- Urdu text.
- Registration number.
- Maximum retail price.
- Name and address of sole agent.
- 2D matrix barcode.
- 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 letter
   issued on 22nd April, 2011
   Last renewal submitted on 08th March, 2021 (valid)

Decision: Registration Board considered and decided as under:

a. **Acceded to the request for import of already registered above products in standard export packs and locally printing of MRP, final Batch release and Registration Number along with Urdu text before sale of drug at their Licensed Premises of M/s Novartis Pharma (Pakistan) Limited, 15 West Wharf, Dockyard Road, Karachi (DML No.000193) to comply requirement as per Drugs (Labelling & Packing) Rules, 1986.**
b. **This permission shall be valid for two (02) years only.**
c. **The firm shall submit the future plan regarding the import of drugs as per Drugs (Labelling & Packing) Rules, 1986.**

Case No.04: REQUEST OF M/S GLAXOSMITHKLINE PAKISTAN LIMITED, KARACHI FOR EXTENSION IN EXEMPTION FROM DRUG (LABELLING AND PACKAGING) RULES, 1986 ON IMPORTED REGISTERED PRODUCTS.

M/S Glaxosmithkline Pakistan Limited, Karachi has submitted request for grant of extension of three years for labelling exemption for their registered products permission to import the products in General Export packs : -

S. No.	Product(s) Description	Reg.No.	Registered Source
1.	Seretide Diskus 50/100mcg Powder for Inhalation Each inhalation (single dose) contains:- Salmeterol (as xinafoate) 50mcg. Fluticasone propionate 100mcg	074726	France
2.	Seretide Diskus 50/250mcg Powder for Inhalation Each inhalation (single dose) contains:-	074727	France

	Salmeterol (as xinafoate) 50mcg. Fluticasone propionate 250mcg.		
3.	Seretide Diskus 50/500mcg Powder for Inhalation Each inhalation (single dose) contains:- Salmeterol (as xinafoate) 50mcg. Fluticasone propionate 500mcg.	074728	France
4.	Seroxat Tab 20mg Each tablet contains: - Paroxetine HCL….20mg	019501	Poland
5.	Avodart Capsule Each Capsule contains: - Dutasteride 0.5gm	041157	France
6.	Duodart Capsules. Each capsule contains:- Dutasteride…. …….0.5mg. Tamsulosin ……..0.4mg.	069515	Germany

The same permission was granted for a period of two years for above six products out of 12 products in M-291 dated 30th September, 2019 and firm has stated that they need more time to switch them over to market specific packs

The firm has stated that product registration number, MRP and Urdu text will be printed locally through laser jet printer at their licensed premises (i.e.F-268, SITE, Karachi DML No.000233 by way of formulation) prior to market the products for an initial period of 03 years.

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 letter with post registration variation and complete renewal trail.

Decision: Registration Board considered the case and decided as under:

a. **Acceded to the request for import of already registered above products in standard export packs and locally printing of MRP, final Batch release and Registration Number along with Urdu text before sale of drug at their Licensed Premises of M/s Glaxosmithkline Pakistan Limited, Karachi, F-268, SITE, Karachi (DML No.000233) to comply requirement as per Drugs (Labelling & Packing) Rules, 1986.**
b. **This permission shall be valid for two (02) years only.**
c. **The firm shall submit the future plan regarding the import of drugs as per Drugs (Labelling & Packing) Rules, 1986.**

Case No. 05: **Request of M/S Servier Research and Pharmaceuticals (Pakistan) (Pvt) Ltd, Lahore for Cancellation of Applied Registrations.**

M/s Servier Research and Pharmaceuticals (Pakistan) (Pvt) Ltd, Lahore has submitted request for cancellation of applied products as per following details: -

S. No.	Name of Drug(s) / Composition	Remarks
1.	Euvascor 40mg/10mg capsule Each capsule contains: Atorvastatin as calcium trihydrate…...40mg Perindopril Arginine…….10mg	Approved in M-297
2.	Euvascor 10mg/5mg capsule Each capsule contains: Atorvastatin as calcium trihydrate…...10mg Perindopril Arginine……..5mg	Approved in M-297
3.	Euvascor 10mg/10mg capsule Each capsule contains: Atorvastatin as calcium trihydrate…...10mg Perindopril Arginine……..10mg	Deferred in M-297
4.	Euvascor 40mg/5mg capsule Each capsule contains: Atorvastatin as calcium trihydrate…...40mg Perindopril Arginine……..5mg	Deferred in M-297

5.	Triveram 40mg/10mg/10mg Film coated tablets Each film coated tablets contains:- Atorvastatin (as Calcium Trihydrate) ……40mg Perindopril (as Arginine)……10mg Amlodipine (as Besilate)……..10mg	Approved in M-271
6.	Triveram 10mg/5mg/5mg Film coated tablets. Each film coated tablets contains:- Atorvastatin calcium trihydrate……10.82mg (Eq. to Atorvastatin….10mg) Perindopril Arginine……..…5mg (Eq. to Perindopril....3.40mg) Amlodipine beilate……..6.94mg (Eq. to amlodipine…...5mg)	Approved in M-289
7.	Triveram 20mg/10mg/10mg Film coated tablets. Each film coated tablets contains:- Atorvastatin calcium trihydrate…….21.64mg (Eq. to Atorvastatin….20mg) Perindopril Arginine……10mg (Eq.to Perindopril….6.79mg) Amlodipine beilate……..13.87mg (Eq. to amlodipine…..10mg)	Approved in M-289
8.	Triveram 20mg/5mg/5mg Film coated tablets. Each film coated tablets contains:- Atorvastatin (as Calcium Trihydrate) ……..…20mg Perindopril (as Arginine) ……..…5mg Amlodipine (as Besilate)….....5mg	Approved in M-271

The firm has stated that they are not interested in registration of these products and firm has submitted a fee of Rs.7500/- for each products for above subject: -

Decision: **Registration Board considered and deferred the case and advised to further deliberate the matter with availability committee and share the outcome with Registration Board for consideration.**

Case No. 06: **REQUEST OF M/S BATTLA ASSOCIATES, KARACHI FOR CANCELLATION OF MEDICAL DEVICES REGISTERED AS DRUGS.**

Additional Director (MDMC) has forwarded a letter on above subject and stated that firm has submitted request for cancellation of their following registered medical devices for import (registered as drugs): -

S.No.	Reg. No.	Name of Drug(s) & Composition	Name of Manufacturer
1.	074712	Q Flow I.V. Cannula Wing Type without Injection Port (14g, 16g, 18g, 20g, 22g, 24g, 26g)	M/s Qatari German Company for Medical Devices (QSC), PO Box 22556, Abu Hamour, Doha, Qatar
2.	074713	Q Flow I.V. Cannula Wing Type with Injection Port (14g, 16g, 18g, 20g, 22g, 24g, 26g)	-do-
3.	074714	Q Ject 3P Syringe Luer/Luer Lock. (1ml, 2ml, 3ml, 5ml, 10ml, 20ml)	-do-
4.	074715	Q Ject Disposable Leur Lock Insulin Syringe, 1ml	-do-

The case was placed before MDB in its 38th meeting held on 16th September 2021. The MDB discussed and decided to refer the case to Drug Registration Board for cancellation of Above-mentioned medical devices (registered as drug)

Decision: **Registration Board considered and cancelled registration of above products from Drug Registration status of M/s Battla Associates, No.4, Allah Wala Building, Kutchi Gali-1, Marriot Road, Karachi.**

Case No. 1 M/s. Getz Pharma Pvt, Limited 29-30/27 Korangi Industrial Area, Karachi

Sr. No	Reg. No.	Brand Name, Composition & Specifications	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	RRA status	Decision
M/s. Getz Pharma Pvt, Limited 29-30/27 Korangi Industrial Area, Karachi						
1.	026164	Leflox Tablet 250mg Each film coated tablet contains: Levofloxacin … 250mg	29-09-2000	Dy. No. 18752 dated 29-07-2020 Rs.10,000/-	USFDA	w.e.f. 29.09.2020 to 28.09.2025
2.	026163	Leflox Tablet 500mg Each film coated tablet contains: Levofloxacin … 500mg	29-09-2000	Dy. No. 20986 dated 21.08-2020 Rs.10,000/-	USFDA	w.e.f. 29.09.2020 to 28.09.2025
Remarks: Renewal of year 2015 was submitted on 29.09.2015 with 10000/- fee, the firm has now submitted differential fee 15000/- each for Leflox Tablet 250mg & 500mg vide Dy No.26187 dated 21.09.2021						

Case No.2: M/s. Glitz Pharma, Plot No 265 Industrial Triangle Kahuta Road Islamabad.

M/s Glitz Pharma has informed that they had submitted renewal applications of below products on 15-06-2015 instead on due date i.e. 14.06.2015 because on said date was Sunday (Gazetted holiday). The firm further informed that they had submitted the fee on 12.06.2015. Further QA&LT Division has also referred the various cases of clearance of raw materials of the firm for confirmation of renewal status for some of the products below and PE&R Division has informed that the renewal applications will be placed before the Registration Board for consideration of regularization.

Sr. No	Reg. No.	Brand Name, Composition & Specifications	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	RRA status	Decision/ Renewal Validity
M/s. Glitz Pharma, Plot No 265 Industrial Triangle Kahuta Road Islamabad. (DML No.000571)						
GMP Status: Panel inspection dated 22-01-2019, Good level of GMP compliance						
1.	038534	Glirox Tablet 250mg Each tablet contains: Ciprofloxacin (as HCl) …...250mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
2.	038535	Glirox Tablet 500 mg Each tablet contains: Ciprofloxacin (as HCl)…. 500mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.

3.	038536	Clatz Tablet 500mg Each tablet contains: Clarithromycin …….500mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
4.	038537	Clatz Tablet 250mg Each tablet Contains: Clarithromycin ……..250mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
5.	038538	Tiloryth Tablet 250 mg Each tablet contains: Erythromycin ……250 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet with salt form used and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
6.	038539	Tiloryth Tablet 500 mg Each tablet Contains: Erythromycin …….500 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet with salt form used and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
7.	038540	Getif Tablet 200mg Each tablet contains: Gatifloxacin ……200 mg	15.06.2005	Dy No.372-R&I 15-6-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Registration is cancelled as formulation is deregistered vide Registration Board decision in its 205th , 206th and 215th meetings due to safety issues (abrupt dysglycemic effects)
8.	038541	Getif Tablet 400mg Each tablet Contains: Gatifloxacin... 400 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Registration is cancelled as formulation is deregistered vide Registration Board decision in its 205th , 206th and 215th meetings due to safety issues (abrupt dysglycemic effects)

9.	038542	Lezov Tablet 250 mg. Each tablet Contains Levofloxacin (as Hemihydrate) …. 250 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
10.	038543	Lezov Tablet 500 mg Each tablet Contains: Levofloxacin (as Hemihydrate)..500 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
11.	038544	Mogiz Tablet 400mg Each tablet Contains: Moxifloxacin ……400 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
12.	038545	Nalid Tablet 500mg Each tablet contains: Nalidixic Acid ……500 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA (Discontinued)	Deferred for confirmation of formulation in RRA
13.	038546	Aliz Tablet 200 mg Each tablet contains: Albendazole…… 200 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
14.	038549	Gloft Tablet Each tablet contains: Iron (III) Hydroxide Polymaltose Complex Eq to Elemental Iron…...100 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	Iron formulation	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as chewable tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.

15.	038550	Gloft-F Tablet Each tablet Contains: Iron (III) Hydroxide Polymaltose Complex eq to elemental Fe……..100mg Folic Acid …….0.35mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	Iron formulation	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as chewable tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
16.	038551	Wormclo-6 Tablet 100mg Each tablet Contains: Clotrimazole …100mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as vaginal tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
17.	038552	Wormclo -1 Tablet 500mg Each tablet Contains: Clotrimazole….500 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as vaginal tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
18.	038553	Glif-K Tablet 75 mg Each tablet Contains: Diclofenac Potassium… 75 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Deferred for issuance of show cause notice with reference to Registration Board decision on the formulation.
19.	038554	Litz-40 Tablet Each tablet Contains: Famotidine …40 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
20.	038555	Tefend Tablet 120mg Each tablet contains: Fexofenadine HCl….. 120 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.

21.	038556	Tefend Tablet 180mg Each tablet Contains: Fexofenadine HCl… 180 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
22.	038559	ANG Tablet 0.5 mg Each tablet contains: Glyceryl Trinitrate….. 0.5 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
23.	038561	Glitfen Tablets 400 mg Each tablet contains: Ibuprofen ……400 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film/ sugar coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
24.	038562	Baver Tablets 135 mg Each tablet contains: Mebeverine HCl …135 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as sugar coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
25.	038563	Megit Tablet 15 mg. Each tablet contains: Meloxicam …….15 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
26.	038564	Megit Tablet 7.5 mg. Each tablet contains: Meloxicam …..7.5 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
27.	038565	Granid Tablet 400mg Each tablet contains: Metronidazole…. 400	15.06.2005	Dy No.372-R&I Dated 15-06-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet

		mg		2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
28.	038569	Pracmol Tablet Each tablet contains: Paracetamol…500 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
29.	038571	Glitlite Tablet 15 mg Each tablet Contains: Pioglitazone..15 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The salt form shall be corrected as Pioglitazone as HCl and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
30.	038572	Glitlite Tablet 30 mg Each tablet contains: Pioglitazone …… 30 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The salt form shall be corrected as Pioglitazone as HCl and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
31.	038573	Glitlite Tablet 45 mg Each tablet contains: Pioglitazone ……45 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The salt form shall be corrected as Pioglitazone as HCl and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
32.	038574	Quinine Tablet 300 mg Each tablet contains: Quinine bisulphate …..300 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
33.	038575	Tex-20 Tablet Each tablet Contains:	15.06.2005	Dy No.372-R&I	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The formulation shall be

		Tenoxicam …..20 mg		Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		corrected as film coated tablet and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
34.	038576	Goter Tablet 125mg Each tablet contains: Terbinafine HCl ….125 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
35.	038578	Anafril Tablet 10 mg Each tablet contains: Clomipramine ….10 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
36.	038579	Anafril Tablet 25 mg Each tablet Contains: Clomipramine…. 25 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
37.	038580	Esglit Tablet (10 mg) Each tablet Contains: Escitalopram (as Oxalate) ….10 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
38.	038581	Sera Tablet 1.5 mg Each tablet contains: Haloperidol ……1.5mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
39.	038582	Sera Tablet 5 mg. Each tablet Contains: Haloperidol…5mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
40.	038583	Graset 50mg Tablets Each tablet Contains: Sertraline …….50 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specification

				Dy. No. 11671 18.05.2020 Rs. 10000/-		for incorporation of the same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
41.	038584	Graset 100mg Tablets Each tablet Contains: Sertraline ……100 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as film coated tablet and firm shall also submit the reference of finished product specification for incorporation of same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
42.	038585	Azogil Capsule 250mg Each capsule contains: Azithromycin (as dihydrate) …..250 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
43.	038586	Gefdrox Capsule 500 mg Each capsule contains: Cefadroxil (as monohydrate) ….500 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
44.	038587	Glixim Capsule 400 mg. Each capsule contains: Cefixime ……400 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
45.	038588	Glifdin Capsule 250 mg. Each capsule contains: Cephradine …….250 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
46.	038589	Glifdin Capsule 500 mg. Each capsule contains: Cephradine …500mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
47.	038590	Eger Capsule 20 mg Each capsule contains: Esomeprazole Magnesium (as Enteric Coated Microgranules) …. 20 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit source of pellets and shall also submit the reference of finished product specification for incorporation of same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.

48.	038591	Tefend Capsule 60mg Each capsule contains: Fexofenadine HCl… 60 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Deferred for confirmation of formulation in RRA.
49.	038592	Glitzol 100 mg. Capsule Each capsule contains: Itraconazole …….100 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit source of pellets and shall also submit the reference of finished product specification for incorporation of same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
50.	038593	Zoglit 20 mg Capsule Each capsule contains: Omeprazole (Enteric coated pellets) ……...20 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit source of pellets and shall also submit the reference of finished product specification for incorporation of same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
51.	038594	Galaxy Capsule (20 mg.) Each capsule contains: Fluoxetine ……20 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Salt form shall be corrected as Fluoxetine as HCl and firm shall also submit the reference of finished product specification for incorporation of the same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
52.	038595	Wormclo Cream 1 % Contains: Clotrimazole…… 1%	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
53.	038597	Glitfen Cream Each 100gm Contains: Ibuprofen…...10gm	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
54.	038599	Goter Cream 1 % Contains: Terbinafine…. 1 %	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	w.e.f. 15.06.2020 to 14.06.2025 Salt form shall be corrected as Terbinafine HCl and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.

55.	038604	Benoxyl Gel Contains: Benzoyl Peroxide Gel. 5.0%	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
56.	038605	Lignocain Cream Contains: Lignocaine HCl ……..2.0%	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
57.	038606	Govid-Scrub Contains: Povidone-Iodine 7.5% in non Ionic detergent base solution	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as Povidone Iodine 7.5% w/w and firm shall also submit the reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
58.	038607	Govid Solution Contains: Povidone -Iodine aqueous solution ……...10.0%	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as Povidone Iodine 10% w/w and firm shall also submit the reference of finished product specification for incorporation of same in renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
59.	038609	Alloxid Syrup Each 5 ml contains: Aluminum Hydroxide 300 mg Magnesium Hydroxide…..150 mg Simethicone..125mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
60.	038611	Dryglit Cough Syrup Each 10 ml Contain: Aminophylline..32mg Diphenhydramine……..8mg Ammonium Chloride…30mg Menthol…….0.98mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	RRA	Deferred for confirmation of formulation in RRA.
61.	038612	Glitfen Suspension Each 5 ml Contains: Ibuprofen…100mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.

62.	038613	Pracmol Syrup Each 5 ml contains: Paracetamol……. 120 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
63.	038614	Progitz Syrup Each 5ml Contains: Promethazine HCl ...25 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
64.	038617	Granid Suspension Each 5 ml Contains: Metronidazole …200 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as Metronidazole as benzoate and firm shall also submit reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
65.	038618	Nalid Suspension Each 5 ml Contains: Nalidixic Acid ……..300 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Deferred for confirmation of formulation in RRA.
66.	038619	Glimox Dry Suspension Each 5 ml Contains: Amoxycillin Trihydrate eq. to Amoxycillin ….125 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Deferred for confirmation of manufacturing facility for Penicillins.
67.	038620	Glimox Fort Dry suspension Each 5ml Contains: Amoxycillin Trihydrate eq. to Amoxycillin…250mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Deferred for confirmation of manufacturing facility for Penicillins.
68.	038621	Clatz 125 mg Suspension Each 5ml Contains: Clarithromycin ……125 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 Firm shall submit the reference of finished product specification for incorporation of the same in renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
69.	038622	Glixim Suspension Each 5ml Contains: Cefixime ….100 mg	15.06.2005	Dy No.372-R&I 15-06-2015	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as Cefixime as trihydrate and

				Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		firm shall also submit reference of finished product specification for incorporation of the same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
70.	038623	Glixim 200 mg Suspension Each 5ml Contains: Cefixime …….200 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as Cefixime as trihydrate and firm shall also submit reference of finished product specification for incorporation of the same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.
71.	038624	Glifdin 125 mg Suspension Each 5ml Contains: Cephradine …125 mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-		Deferred for confirmation of formulation in RRA
72.	038625	Glifdin 250 mg Suspension Each 5ml Contains: Cephradine .250mg	15.06.2005	Dy No.372-R&I 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	MHRA	w.e.f. 15.06.2020 to 14.06.2025 The firm shall submit reference of finished product specifications for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
73.	038626	Tiloryth 200 mg Suspension Each 5 ml Contains: Erythromycin… 200 mg	15.06.2005	Dy No.372-R&I Dated 15-06-2015 Rs. 10000/- Dy. No. 11671 18.05.2020 Rs. 10000/-	USFDA	w.e.f. 15.06.2020 to 14.06.2025 Formulation shall be corrected as Erythromycin as ethyl succinate, further the frim shall submit the source of granules and shall also submit reference of finished product specification for incorporation of same in the renewal of registration as per decision of 295th meeting Reg. Board with prescribed fee.

Case No. 3 M/s Max Pharmaceuticals Plot No. 12 Street No. N-7 National Industrial Zone RCCI Rawat Rawalpindi (DML No. 000671)

Sr. No	Reg. No.	Brand Name, Composition & Specifications	Initial date of Registration PRV (If any)	Date of application (R&I) Fee submitted	RRA status	Decision/ Renewal Validity
1.	063002	Himalt F Syrup Each 5ml contains: Iron III Hydroxide Polymaltose complex eq. to elemental iron .. 50mg Folic Acid… 0.35mg (Max Specification)	23-2-2010	Dy. No. 1988 dated 19-02-2020 Rs. 10000\- Rs. 10000/- dated 23.02.2015	Iron formulation	w.e.f 23.02.2020 to 22.02.2025 Firm shall submit reference of finished product specification for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.

2.	063003	Maximalt Syrup Each 5ml contains: Iron III Hydroxide Polymaltose complex eq. to elemental iron .. 50mg (Max Specification)	23-02-2010	Dy. No. 1988 dated 19-02-2020 Rs. 10000\- Rs. 10000/- dated 23.02.2015	Iron formulation	w.e.f 23.02.2020 to 22.02.2025 Firm shall submit reference of finished product specification for incorporation of the same in the renewal of registration as per decision of 295th meeting Registration Board with prescribed fee.
3.	063004	Famoday Suspension Each 5ml contains: Famotidine… 10mg (USP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- dated 23.02.2015	USFDA (Dry Powder Suspension)	Deferred for confirmation of formulation whether liquid/ powder along with evidence of approval of manufacturing facility for oral dry powder.
4.	063005	Maztelium Suspension Each 5ml contains: Domperidone … 5mg (BP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- 23.02.2015	MHRA	w.e.f 23.02.2020 to 22.02.2025
5.	063006	Maxigyl Suspension Each 5ml contains: Metronidazole (as Benzoate) … 200mg (BP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- 23.02.2015	MHRA	w.e.f 23.02.2020 to 22.02.2025
6.	063007	Loralion Syrup Each 5ml contains: Loratadine… 5mg (USP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- dated 23.02.2015	MHRA	w.e.f 23.02.2020 to 22.02.2025
7.	063008	Maxzine Syrup Each 5ml contains: Cetirizine Dihydrochloride… 5mg (BP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- dated 23.02.2015	MHRA	w.e.f 23.02.2020 to 22.02.2025
8.	063009	Pretimol Suspension Each 5ml contains: Paracetamol… 120mg (BP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- 23.02.2015	MHRA	w.e.f 23.02.2020 to 22.02.2025
9.	063010	Micafen Syrup Each 5ml contains: Ibuprofen… 100mg (BP Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- 23.02.2015	MHRA	w.e.f 23.02.2020 to 22.02.2025
10.	063011	Master Cough Syrup Each 5ml contains: Aminophylline…. 32mg Diphenhydramine Chloride… 30mg Diphenhydramine… 8mg Menthol…. 0.98mg (Max Specification)	23-02-2010	Dy. No. 1988 19-02-2020 Rs. 10000\- Rs. 10000/- dated 23.02.2015	RRA	Deferred for confirmation of formulation in RRA.
11.	063012	Flumax Suspension Each 5ml contains:	23-02-2010	Dy. No. 1988 19-02-2020	RRA	Deferred for confirmation of formulation in RRA.

		Ibuprofen… 100mg Pseudoephedrine HCl… 15mg (Max Specification)		Rs. 10000\- Rs. 10000/- 23.02.2015		

Remarks:

Case was considered in 6th meeting of RRR Sub Committee and deferred for following:

1. Differential fee is required as the renewal application for the year 2015 is submitted late but within sixty days.
2. Latest GMP Inspection report.
3. Manufacturer specifications are mentioned on the initial registration of Flumax Suspension, Master Cough Syrup, Maximalt Syrup, and Himalt F Syrup If the drug is the included in any one of the Official Pharmacopeia as prescribed under Drug (Specification) Rules 1978, then reference of the same, along with 5000/- fee each shall be submitted for incorporation of the same in renewal of registration. Otherwise the product shall confirm to the Innovator company specifications.

Reply:

The firm has informed that on the due date i.e. 22.02.2015 was Sunday (Guzatted Holiday) and they submitted the application on 23.02.2015 hence they may be considered in time.

Case No.4 Confirmation of renewal of Pensulid Tablet (030197) of M/s Don Valley Pharmaceuticals Pvt Limited Lahore.

Registration Board in 312nd meeting cancelled the registration of Pensulid Tablets (030197) as firm fails to submit renewal application for the year 2013 and 2018. Details of the product are as under:

Reg. No.	Brand Name & Composition & Specification	Initial date of Registration	Date of application (R&I) Fee submitted
030197	Pensulid tablet Each tablet contains: - Nimesulide…….100mg	03.03.2003	06.05.2016 Rs.10000/- & 30.04.2021 Rs.10000/-

Proceeding in M-312 RB:

Remarks:

The PR-II section was requested to provide the evidence submission of renewal for year 2013 & 2018. Accordingly, they requested to firm vide letter No.F.3-1/2021-Deficency (AD) PR-II dated 02.07.2021. The firm submitted the reply which was forwarded to RRR section for evaluation the response of the firm as under:

"We have submitted application for transfer of our products along with fee challans and letter No.F.5-64/2021 DDC (R-V) dated 26th June 2013, which is a proof that we have submitted renewal application for 2013 as acknowledgment receipt and copy of fee challan has been misplaced for company data in shifting process. In 2016 DRAP has issued us transfer letter for all products except pensulid because at that time Nimsulide got banned internationally and DRAP was no issuing registration for Nimsulide containing products. However, in 2018 DRAP has allowed to grant registration for Nimsulide containing products. But our transfer letter is not issued yet"

Reply of the firm w.r.t decision of 312 RB Meeting:

The firm has informed that Registration Board in its 312nd meeting has cancelled the registration of Pensulid on behalf of absence of renewal status of 2013 and 2018. In this context the firm informed that they wrote a letter to DRAP for transfer of registration in 2012 at that time Pensulid registration status was valid. In 2013 DRAP has issued us a letter No.F.5-64/2012 DDC (R-V) in which they asked to submit differential fee of 12000/- for all products including Pensulid. They got the transfer letter for our products from DRAP in 2016 excluding Pensulid. They applied for transfer in 2013 but got the transfer letter in 2016 because as per DRAP they were asked correct the letter subject as transfer and renewal (as per policy), in that context they asked us to submit renewal, we submitted those renewal in 2016 (including Pensulid), after that we got the transfer letter excluding Pensulid. Pensulid transfer of registration got hold by DRAP and show cause notice (No7967/2016-DRAP (L-II) for cancellation of registration of Nimesulide containing drug product due to high risk vs benefit ratio was issued as FDA has banned the use to Nimesulide in 2007 that's why we did not follow up on Pensulid transfer letter.But in 2019 DRAP has issued and advisory stating that all the firms having registration of Nimesulide tablet 100mg can manufacture their products by mentioning indications, adverse events and contraindication on their leaflets. Which means that the cancellation of registration letter

which we got in 2016 (No.7967/2016-DRAP (L-II) will be invalid that's why we followed our renewal trail i.e from 2016-2021.

It is submitted that Registration Board its 252nd meeting considered the request of transfer of registration of Pensulid Tablets (030197) along with other registered products to their new site i.e. M/s. Don Valley Pharmaceuticals (Pvt) Ltd 31-km, Main Ferozepur Road, Lahore from its old site i.e. 39, Main Peco Road Lahore and deferred for decision on the molecule. Further Registration Board in its 269th meeting while considering approval status of Nimesulide 100mg tablet in EMA, approved the formulation of Nimesulide Tablets 100mg with a pack size of 15 tablets as per recommendations of EMA.

Hence as per above mentioned facts the application of M/s Don Valley Pharmaceuticals Pvt Limited Lahore for transfer of registration may be considered for renewal of 2013 and application of renewal submitted in 2016 may be considered towards renewal of 2018, the Board may review its earlier decision in 312nd meeting.

Decision: **Keeping in view the above stated facts Registration Board reviewed its earlier decision in 312nd meeting and acknowledged the application of M/s Don Valley Pharmaceuticals Pvt Limited Lahore for transfer of registration submitted in 2013 for renewal of 2013 and application of renewal submitted in 2016 towards renewal of 2018. Hence registration status of Pensulid Tablets (030197) is valid. PR-II section of PE&R Division may proceed for grant of registration to their new site i.e. M/s. Don Valley Pharmaceuticals (Pvt) Ltd 31-km, Main Ferozepur Road, Lahore.**

QUALITY CONTROL CASES

S No.	Case Title
I.	IMPORT OF REGISTERED PRODUCTS THROUGH FAKE/FORGED INVOICES BY M/S. BIOCURE PHARMACEUTICALS, LAHORE.
II.	CASE REFERED BY PQCB, PUNJAB REGARDING SUBMISSION OF FAULTY METHOD OF ANALYSIS OF PRODUCT CIFEROL TABLET SUBMITTED BY M/S MEDISAVE PHARMACEUTICALS, LAHORE.
III.	MANUFACTURE & SALE OF ADULTERATED AND SUB-STANDARD DRUG RHINEX P SYRUP, BATCH NO. 051 MANUFACTURED BY M/S. OPAL LABORATORIES PVT. LTD., KARACHI, - INSPECTION THEREOF.
IV.	MANUFACTURE & SALE OF SUB-STANDARD KAYMAX TABLET 75MG, BATCH NO. GHH1716, GH1729 AND GH1714 MANUFACTURED BY M/S. QUAPER (PVT.) LTD., SARGODHA.
V.	MANUFACTURE & SALE OF SUB-STANDARD PROTONIX 40MG TABLETS, BATCH NO. 052 BY M/S WILSHIRE LABORATORIES (PVT.) LTD., LAHORE.
VI.	MANUFACTURE & SALE OF SUB-STANDARD CLARINAVE SUSPENSION, REG.NO.078599, BATCH NO. D366, MANUFACTURED BY M/S NOVAE PHARMACEUTICALS, HATTAR.
VII.	CLOMFRANIL 25 MG SCT BATCH NO. HJOAAB AND HJOAAC OUT OF SPECIFICATION (OOS) OBSERVED IN DISSOLUTION TEST RESULTS OF 6 MONTHS TESTING POINT OF ACCELERATED STABILITY STUDY AT 40C/75% RH CONDITION AND BATCH NO. HJOAAB ON 9 MONTH TESTING POINT OF FOLLOW UP STABILITY STUDY AT 30C/65% RH.
VIII	INSPECTION AT M/S ATCO LABORATORIES, B-18, SITE, KARACHI STOCK ORDERED NOT TO DISPOSE OF ON FORM-1 UNDER SECTION 18(1) OF THE DRUGS ACT, 1976.
IX	HANDLING REQUESTS OF APPELLATE TESTING- GUIDANCE DOCUMENT FOR REGISTRATION BOARD
X	MANUFACTURE & SALE OF SUBSTANDARD LETIRIX SYRUP, REG. NO. 068438, BATCH NO. L2033, MFG. DATE 10-020, EXP. DATE 09-022, MANUFACTURED BY M/S. ALLIANCE PHARMACEUTICALS (PVT) LIMITED, PESHAWAR.
XI	MANUFACTURE & SALE OF SUBSTANDARD PANTOPEP TABLETS, BATCH NO. 911, REG. NO. 064137, MANUFACTURED BY M/S HASSAN PHARMACEUTICALS (PVT.) LTD., PESHAWAR.
XII	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.
XIII	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.
XIV	MANUFACTURE & SALE OF SUBSTANDARD PROTONIX 40MG TABLET, REG. NO. 030041, BATCH NO. 069, MFG. DATE JAN 2020, EXP. DATE JAN 2023, MANUFACTURED BY M/S. WILSHIRE LABORATORIES (PVT.) LIMITED, LAHORE.

Case No. I: **IMPORT OF REGISTERED PRODUCTS THROUGH FAKE/FORGED INVOICES BY M/S. BIOCURE PHARMACEUTICALS, LAHORE.**

Assistant Director (I&E), Lahore vide letter No.5247/2019/DRAP(AD-CD)(I&E) dated 15-04-2019 informed that Assistant Collector-II, Model Customs Collectorate of Appraisement-West, Karachi has asked for the verification of genuineness of following ADC invoices;

Sr. No	Invoice No. & Date	Diary No. & date	Dispatch No. & Date
1	SBF/EXP/23-2019, dated 21-02-2019	4699/2019 DRAP dated 15-03-2019	3769/2019-DRAP, dated 19-03-2019
2	SBF/EXP/24-2018, dated 15-03-2018	4569 dated 26-03-2018	4451/2018-DRAP, dated 29-03-2018
3	SBF/EXP/28-2017, dated 29-03-2017	5982 dated 27-04-2017	5647/2017-DRAP, dated 28-04-2017
4	SBF/EXP/127-2015, dated 28-10-2015	13579 dated 23-11-2015	18835/2015-DRAP, dated 26-11-2015
5	SBF/EXP/128-2016, dated 27-12-2016	1524 dated 26-01-2017	1396/2017-DRAP, dated 27-01-2017

AD (I&E), DRAP, Lahore further informed that the genuineness of the endorsement of said invoices is not verified from the office record. In response to the submission of AD (I&E), DRAP, Lahore the division of QA&LT directed the Area FID vide letter F. No.13-125/2019-(QC) dated 16-05-2019 to investigate the matter and after completing all the legal formalities, submit a comprehensive report including all the requisite documents along with documents from custom authorities, highlighting the nature of violation, fixing the responsibility (Names, Designations, complete addresses and copies of CNIC of accused person(s)) and comments/views on the response of accused, if any, on priority basis for consideration of the Board.

Area Federal Inspector of Drugs Lahore vide letter No.7011/2021-DRAP (L-IV) dated 07-05-2021 submitted the complete investigation report and the reply of accused as under:

"Please refer to Drug Regulatory Authority of Pakistan, Islamabad letter No. F. No. 13-125/2019 (QC) dated 16-05-2019 on the subject cited above, (copy attached Annex-1), and Model Custom Collectorate of Appraisement-West Custom House, Karachi letters Nos. SI/Misc/157/2017 Group-II dated 22-03-2019 and SI/Misc/157/2017 Group-II dated 01-04 2019 on the subject cited above (copies attached Annex-2&3), wherein it was informed that genuineness of the endorsement of commercial invoices (detail of which are below) was not verified from the office record of DRAP, Lahore (Copies of invoices are attached annex 4,5,6,7&8).

S. No.	*Invoice No & Date*	*Diary No. & date*	*Dispatch No, & Date*
1	*SBF/EXP/23-2019, dated 21-02-2019*	*4699/2019 DRAP dated 15-03-2019*	*3769/2019-DRAP, dated 19-03-2019*
2	*SBF/EXP/24-2018, dated 15-03-2018*	*4569 dated 26-03-2018*	*4451/2018-DRAP, dated 29-03-2018*
3	*SBF/EXP/28-2017, dated 29-03-2017*	*5982 dated 27-04-2017*	*5647/2017-DRAP, dated 28-04-2017*
4	*SBF/EXP/127-2015, dated 28-10-2015*	*13579 dated 23-11-2015*	*18835/2015-DRAP, dated 26-11-2015*
5	*SBF/EXP/128-2016, dated 27-12-2016*	*1524 dated 26-01-2017*	*1396/2017-DRAP, dated 27-01-2017*

2 Letter No. 12040/2019-DRAP (L-VI) dated, 17-09-2019, was sent from this office to M/s. Biocure Pharmaceuticals, Suite No. 211, 2nd Floor Khaleej Town, 38-A, Jail Road, Lahore, informing that genuineness of endorsement of said invoices was not verified from the office record and the firm was directed to explain their position in this regard (copy attached annex-9).

3 Reply received from M/s. Biocure Pharmaceuticals, Suite No. 211, 2nd Floor Khaleej Town, 38-A, Jail Road, Lahore vide letter No. Nil, dated Nil received office on 02-10-2019 (copy attached annex-10), wherein they have informed that after coming to know of the above they launched FIR against the clearing agent, whom they had hired some time ago (copy attached annex-11) The CEO of the firm further informed that he was shaken after knowing about this matter which caused severe tension, heart attack and cardiogenic shock. He has further requested that he may be granted relief on humanitarian basis. Previous import history of the firm as per this office record showing clearance certificates obtained from this office previously is also attached (copy attached annex-12). But as per available record of this office the above said invoices were not cleared by this office.

4 The available data of this office reveals that the firm did not get prior clearance to import their products Eridoksin Registration No. 059185 and Roxine 25% Registration No. 059186 which is the violation of the Drugs Act 1976/DRAP Act 2012, so, it is recommended that the registration of the drugs / product in question may be suspended or cancelled or any other action may be taken as deemed fit by the Competent Authorities.

Submitted for information and further necessary action please."

Area FID Lahore in the above-mentioned report has recommended the cancellation/suspension of registration of products namely Eridoksin powder containing Erythromycin 40mg and Doxycycline 20mg (Reg. No. 059185) and Roxine 25% oral solution containing Enrofloxacin 250g (Reg. No. 059186) or any other action as may deem fit by the Board.

Proceedings and Decision of 312th meeting:

The Board after thorough deliberations and considering the facts of the case and recommendations of the area Federal Inspector of Drugs decided to issue show cause notice to 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:

Jawad Ahmed (CEO) of M/s. Biocure Pharmaceuticals, Suite No. 211, 2nd Floor Khaleej Town, 38-A, Jail Road Lahore appeared before the Board and informed the Board that he had hired a clearing agent namely Muhammad Sadiq S/o Abdul Aziz R/o House No. 49-A, Street No. 139-C, Ittefaq street, Ghulam road, Ichhra Lahore who was responsible for submitting fake invoices to the custom authorities. Moreover, Mr. Jawad Ahmed also informed the Board that he was unaware of these illegal activities being carried out by his clearing agent and he also had lodged FIR against that clearing agent in Litton road Police Station Lahore.

The Board after thorugh deliberations, considering the facts of the case and submission of CEO of M/s. Biocure Pharmceuticals Lahore decided as under:

i. **Suspend the Registration of the products namely Eridoksin Powder (Reg. No. 059185) and Roxine 25% oral solution (Reg. No. 059186) till the decision of Registration Board.**
ii. **The division of QA&LT will conduct a detailed investigation of the matter and submit a comprehensive report before the Board within (02) months.**

Case No. II: **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 13-08-2020*	*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.

Case No. III: MANUFACTURE & SALE OF ADULTERATED AND SUB-STANDARD DRUG RHINEX P SYRUP, BATCH NO. 051 MANUFACTURED BY M/S. OPAL LABORATORIES (PVT) LTD, KARACHI-INSPECTION THEREOF.

The FID-VII, DRAP, Karachi visited the premises M/s Opal Laboratories (Pvt.) Ltd., located at plot No. LC-41, L.I.T.E, Landhi, Karachi wherein the sample of Rhinex P Syrup, Batch. No. 051, manufactured by M/S Opal Laboratories, (Pvt.), Ltd, Karachi was drawn along with other Drugs on 08-02-2018 under Schedule-V (1) (C) of DRAP Act, 2012 read with section 18 (1) (C) of the Drugs Act, 1976. Details are as under:

Name of Drug	Reg. No.	Batch No.	Mfg. Date	Exp. Date	Purported to be manufactured by
Rhinex - P Syrup	067409	051	02-2018	01-2020	M/s Opal Laboratories (Pvt.) Ltd., located at plot No. LC-41, L.I.T.E, Landhi, Karachi

The said sample was sent to the Government Analyst, Central Drugs Laboratory, Karachi vide memorandum No.DMT-07/2018- to 14/2018FID-VII (K) dated 09-02-2018 for the purpose of test /analysis.

The Federal Government Analyst, CDL, Karachi declared the aforementioned sample as of Adulterated & sub-standard quality vide test/analysis report No.KQ.87/2018, dated 11th April, 2018. Results are reproduced as under:

Description	*Brown colored syrup, containing black particles visible to the naked eye.* ***Does not comply with manufacturer's specifications***
Identification	*Promethazine and carbocystine identified*
pH determine	*6.21*
Limits	*5.8 – 6.3*
Assay of Carbocisteine	
Determined amount/5ml:	*98.1484mg*
Stated amount/5ml:	*100mg*
Percentage:	*98.1%*
Limits:	*90.0% to 110.0%*
Remarks	*The sample is of "Sub-Standard" quality under the Drug Act 1976*

In Light of the CDL, Karachi test report, FID-VII, DRAP, Karachi issued an explanation letter vide reference No.DMT-07/18-FID-VII (DRAP) dated 24-04-2018 to M/s Opal Laboratories (Pvt.) Ltd., located at plot No. LC-41, L.I.T.E, Landhi, Karachi but no reply was received. M/s Opal Laboratories (Pvt.) Ltd., located at plot No. LC-41, L.I.T.E, Landhi, Karachi was asked again to explain their position in this regard dated 25-02-2019.

M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi vide reference No. nil dated 05th March, 2019 & 14th March, 2019 submitted their reply wherein they have stated that QC tests were performed on their retention samples of Rhinex-P-Syrup, Batch No. 051and we are quite confident that all results (Physical & Chemical) are ok, complies & meet the specifications accordingly "Brown color Syrup" containing no traces of black particles.

They have recall 2565 packs from the market and also provided the destruction summary. The destruction was conducted without intimation to/permission from DRAP. Names of the management and technical persons provided by the firm vide letter dated 05-03-2019 are as under:

i. Iqbal Ahmad (Managing Director)
ii. Ikram Zubairi (G.M Plant operations)
iii. Rozina Babar (Head of Quality operations)

The Drugs licensing Division was requested to verify/provide the names provided by the firm and they provided the following:

Mr. Ali Afzal (Director) M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi	Mr. Jehanzeb (Director) M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi
Mrs. Rozina Babar (Q.C Incharge) M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi	Mr. Ikram Ahsan Zubairi (Production Incharge) M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi

The FID, DRAP, Karachi further added that M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi is involved in manufacturing & selling of Adulterated and Sub-Standard drug which is violation of section 23 (1) (a) (iv) & 23 (1) (a) (v) of the Drugs Act, 1976 and rules framed there under. Furthermore, she recommended that action may be taken as per section 42 of the Drugs Act 1976 and rules framed there under against M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi.

Show-cause notice has been issued to the technical staff/management of the firm for the following action (s) - U/S 7(11) of the Drugs Act, 1976 vide letter no. 03-28/2018-(QC) dated 24-01-2020.

i. Prosecution in the Drug Court.
ii. Cancellation/Suspension of Drug Registration.
iii. Any other action the Board may deem fit.

M/s Opal Laboratories (Pvt.) Ltd., plot No. LC-41, L.I.T.E, Landhi, Karachi submitted their reply to show-cause notice vide letter No. nil dated 31-01-2020 which is reproduced as under:

"Refer to your letter No. 03-28/2018-(QC) dated 24-01-2020, received on 30-01-2020 regarding substandard & Adulterated drug Rhinex-P syrup, B# 051, please note that we have submitted all the required documents on dated 05-03-2019 to DRAP Area FID-VII, DRAP, Karachi and copy to QC DRAP Islamabad. Furthermore, we have recalled all the remaining stock of complaint batch from Market through print media and through intimation given to all distributors.

In reference to your above-mentioned letter we would like to submit as under:

- *It is submitted that we have checked retained sample of the said batch and results have found ok within the limits and meets specifications "Brown color syrup" containing no traces of black particles. We are confident that all the chemical and physical tests are alright.*
- *Details of physical and chemical analysis along with test protocol are attached for your kind reference*

We will appreciate for meeting you for further elaboration in case of any clarification/information required"

Proceeding & Decision of 296th Meeting of Registration Board.

Mr. Iqbal Ahmad (42201-7917477-5), Managing Director & Rozina Babar of M/s Opal Laboratory appeared before the Board on behalf of M/s Opal Laboratory, karachi to plead the instant case. They submitted before the board that retained samples were checked and were found according to the specification. No black particles were seen in the retained samples. They further added that as the retained samples were according to the specifications, therefore, they didn't apply/requested for retesting of the said product.

Decision of 296th meeting of Registration Board.

Registration Board after detailed discussion and deliberations considering the test reports of CDL, Karachi decided as under:

i. Suspension of 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, product development data and verification of aforementioned points and Product Specific Inspection by following panel whichever is later.
   - Prof. Dr. Abdullah Dayo, Member Central Licensing Board.
   - Mr. Affan Ali, Assistant Director, CDL, Karachi.

- Dr. Krishan Das, Assistant Director, DRAP, Karachi.

Dr. Krishan Das, Assistant Director-V, DRAP, Karachi vide letter No. F. 1-5/2021-(AD) (K-V) dated 03.03.2021 submitted inspection report of M/s. Opal Laboratories (Pvt.) Ltd., situated at Plot No. LC-41/B, L.I.T.E., Landhi, Karachi. observations, recommendations and conclusion of the panel is given as under:

"Observations of Current Product Specific Inspection:

Panel members inspected the Change room, raw material store, packaging materials store, sampling area, dispensing area, transfer trolleys / staging area, Liquid section comprising manufacturing area, storage area, bottle blowing area, filling area, labeling and packing area and Finished goods store and observed good level of Good Manufacturing Practices at the time of inspection. Quality Control Laboratory was seen equipped with necessary analytical instruments and equipments for carrying out test / analysis of Liquid section. Quality assurance system was also seen in place.

b. Following documents were reviewed / verified by the panel member during the course of inspection process:

i. Root cause analysis (RCA) carried out by the firm after test report of CDL. (Annexure-F)

ii. Corrective and Preventive Action (CAPA) taken by the firm in order to avoid such occurrences in future. (Annexure-G)

iii. Respective utilities (HVAC) which may be the possible source of failure data was also reviewed and found satisfactory.

iv. The said product recall and disposal documents were found satisfactory. (Annexure-H)

Recommendations for further improvements:

The panel recommends the following for further improvements in the Liquid section of the firm to avoid future recurrences:

i. The optical checking frequency to be increased in the production system at each stage through production and Quality assurance personnel.

ii. Cartridge filters replacement in sugar syrup preparation, bulk filtration and filling area frequency to be increased.

iii. Testing protocols of sugar employed in manufacturing shall be revalidated.

iv. Updated training required for the technical personnel engaged in production, quality control and quality assurance activities.

v. Cleaning and process validation activity shall be revalidated.

Conclusion:

Based on the stated facts the panel concluded that the Adulteration may be due to the sugar sources procured from local sources resulting in increased chances of tiny black particles in few finished product bottles. Therefore, the panel advised the firm to further improve their systems as per above mentioned suggestions.

However, based on the actions taken by the firm and commitment towards further improvements in their system the panel has verified and is satisfied for the root cause analysis (RCA), corrective and preventive action (CAPA) and products development aspects under taken by the firm."

Proceedings & Decision of 307th Meeting of Registration Board

The case is deferred for next meeting due to paucity of time.

Proceedings & Decision of 308th Meeting of Registration Board

The Board after thorough deliberations, considering the facts of the case, report submitted by the panel decided that firm will submit compliance report for above recommendations of the panel for consideration of the Board.

Compliance report of Rhinex-P-Syrup, Batch # 051:

The report of compliance by M/s. Opal Laboratories has been received on 09-09-2021 which is reproduced as:

"We M/s. Opal has fulfilled and implemented all the recommendations given by the panel for further improvement in the Liquid section of the firm to avoid the recurrence of same in future batches. Details are given below;

S.#	Panel Recommendations for Further Improvement	Corrective Action / Implementation	Compliance Level
01	The optical checking frequency to be increased in the production system at each stage through production and Quality assurance personnel.	SOP for Optical checking of filled bottles has been revised and being implemented accordingly. As per SOP, Production and QA representative will perform in process checks after every half hour interval. Frequency of Optical checking has also been increased. Moreover; optical checker will be replaced after every 01 hour interval. Comprehensive refresher training has been given to all deputed optical checkers, QA & Production representative to avoid future recurrences. Training record is attached in '' Annexure I '' for your kind consideration. Eye test of all deputed workers and staff has been done successfully to ensure 100% performance.	Comply 100%
02	Cartridge filters replacement in sugar syrup preparation, bulk filtration and filling area frequency to be increased	SOP for '' Use / Replacement of Cartridge Filter in Liquid products '' has been revised and being implemented accordingly. As per SOP, cartridge filter will be replaced after every step & record will be maintained accordingly. Moreover; physical inspection of cartridge filter will be performed critically after filtration process for more confidence. Further; Filling Areas filter will be replaced on daily basis or as per requirement.	Comply 100%
03	Testing protocols of sugar employed in manufacturing shall be revalidated	Standard test method of Sugar has been revised and being implemented accordingly. Re-validation of test method of Sugar has been done successfully.	Comply 100%
04	Updated training required for the technical personnel engaged in production, quality control and quality assurance activities.	Comprehensive training has been given to all technical personnel of production, Quality Assurance & Quality Control. Training record is attached in '' Annexure II '' for your ready reference.	Comply 100%
05	Cleaning and process validation activity shall be revalidated.	Revalidation of cleaning procedure of all equipment involves in the Manufacturing & Filling of liquid products has been done	Comply 100%

		successfully. Moreover; revalidation of Rhinex-P-Syrup is incorporate in Master Validation Plan and will be performed accordingly on first three commercial batches after completion of suspension period of the product.	

Proceedings and Decision of 312th Meeting of Registration Board.

Registration Board after detailed discussion and deliberations considering the facts of the case advised Division to direct the firm for submission of complete data and supporting documents as mentioned in compliance report. The product shall remain suspended till decision of case by Registration Board.

The decision of Board has been communicated to the firm vide letter No. No.F.03-33/2021-QC (312-RB) dated 28-10-2021.

M/s. Opal Laboratories (Pvt) Ltd., Karachi vide letter no nil dated 05-11-2021 have submitted the data and supporting documents mentioned in compliance report.

Proceedings and Decision of 313th Meeting of Registration Board.

"The Board after considering the facts of the case and after thorough deliberations decided:

i. **To resume the production of Rhinex-P Syrup, Reg. No. 067409.**
ii. **Firm shall inform area FID, DRAP Karachi for taking sample from 1st three (03) commercial batches for test/analysis by CDL Karachi on the expense of the manufacturer to ensure the quality of the batches. Firm will sell the product after standard CDL reports."**

Case No. IV: **MANUFACTURE & SALE OF SUB-STANDARD KAYMAX TABLET 75MG, BATCH NO. GHH1716, GH1729 AND GH1714 MANUFACTURED BY M/S. QUAPER (PVT.) LTD., SARGODHA.**

A) Manufacture & Sale of Sub-Standard Kaymax 75mg Tablets, Batch No. GH1716, Manufactured by M/s Quaper (Pvt.) Ltd. Sargodha.

The Federal Inspector of Drugs-II, DRAP, Peshawar visited the premises of M/s Al-Ghani Medical Store, Wardaga Road, Sardheri, The. & Distt. Charsadda on 02-07-18 and taken the following sample of drug for the purpose of test/analysis on prescribed Form-3. Details are as under:

Name:	Kaymax 75 mg tablets
Composition:	Each Tablet contain 75mg Diclofenac Potassium
Registration No:	046202
Batch No:	GH1716
Manufacturing Date:	08-17
Expiry Date:	07-20
Manufactured By:	M/s Quaper (Pvt.) Ltd., Sargodha.

The FID-II, DRAP, Peshawar forwarded one sealed portion of sample to Government Analyst, Central Drugs Laboratory, Karachi for the purpose of test and analysis vide letter No.F.10-102/2018-Al-Ghani-DRAP-2620 dated 04-07-2018 as required under Section 19(3)(i) of the Drugs Act, 1976.

The sealed portion (manufacturer portion) was also sent to M/s Quaper (Pvt.) Ltd., Sargodha vide letter number No.F.10-102/2018-Al-Ghani-DRAP (P)-FID-II-2624 dated 04-07-2018

The Federal Government Analyst, CDL, Karachi declared the sample as of Sub-Standard quality on the basis of **Dissolution test** vide test/analysis report No.IP.238/2018, dated 30th July, 2018. Test results of the CDL, Karachi for the above product are reproduced as under;

Description:	*Brown colored, sugar coated tablets*
Identification:	*Diclofenac Potassium identified.*
Dissolution test:	***Does not comply.***
Uniformity of Dosage Units	

By Weight Variation. *Complies*

Assay for Diclofenac Potassium:

Determined amount/tablet: *75.3644mg*
Stated amount/tablet: *75mg*
Percentage: *99.2%*
Limits: *90.0% to 110.0% Complies.*
Remarks:- *The sample is of **"substandard"** quality under the Drugs Act. 1976.*

After the receipt of said test report of CDL Karachi, M/s Quaper (Pvt.) Ltd., Sargodha was show caused vide letter No.F.10-102/2018-Al-Ghani-DRAP-3175 dated 15-08-18 as to why a legal action may not be taken against you under the Drugs Act, 1976 for manufacturing and sale of substandard Kaymax 75mg Tablets with direction to recall the above said batch from the distributors and outlets. That M/s Quaper (Pvt.) Ltd., Sargodha submitted their reply vide Ref. No. QP/adm/818/008 dated 27-08-2018 wherein they have provided their clarification that they are not satisfied with the results of the CDL, as their product was tested according to the USP specifications while the product is registered according to the British Pharmacopeia specifications, hence they challenged the said test report under Section 22 (4) of the Drugs Act, 1976.
Sample was sent to Appellate laboratory, NIH, Islamabad for retesting under section 22 (5) of the Drugs Act, 1976.
The Appellate Laboratory, NIH, Islamabad declared the said sample as of **Substandard and Misbranded** quality vide test report No.024-M/2018 dated 21-01-2019.Results are reproduced as under;

Description: Reference of Pharmacopeia is mentioned only for the salt of Diclofenac Potassium, however reference of specification for the test and analysis of finished product Kaymax Tablets (Diclofenac Potassium 75mg) is neither mentioned on the immediate packing nor on the outer packing. Therefore USP 39 is followed for the test and analysis of the above product. Moreover, missing of reference of specification on the product is misleading and violation of packing and labeling Rules of the Drugs Act, 1976.quality

Dissolution Test:
Determined: 19.62% of the labeled amount **(Does not comply)**
Limits: Not less than 75% (Q) of the labeled amount.

Assay for Diclofenac Potassium:
Stated amount/Tablet: 75mg
Determined: 69.189mg/Tab (92.252%)
Limits: 90-110%
Remarks; The sample is of **substandard and Misbranded.**

The FID, DRAP, Peshawar has forwarded the names of responsible persons and submitted that the firm is involved in violation of Section 23 (1) (a) (iii) & 23 (1) (a) (v) of the Drugs Act, 1976. Names of responsible persons provided by FID, DRAP, Peshawar are as under;

i. Mr. Tauqeer Ali (CEO)
ii. Mr. Muhammad iftekhar (Director)
iii. Miss Fozia Naheed (Production manager)
iv. Mr. Muhammad Saleem (Quality Control Incharge)

It is submitted that the Drugs Licensing Division was requested to provide/verify the names of responsible persons of M/s Quaper (Pvt.) Ltd., Sargodha for Kaymax 75mg tablets, Batch No.GE1729 vide No.F.03-63/2018-QC and the Drugs Licensing division provided the following information:

Management as per Form-29 dated 31-10-2016	
i.	Muhammad Iftekhar s/o Muhammad Anwar Nadir, CNIC (33100-5773160-1)
ii.	Mr. Ali Touqeer s/o Touqeer Ahmad Taqi, CNIC No. (33100-2741642-3)

Quality Control Incharge
Mr. Abid Hussain s/o Muhammad Ramzan (33100-3349464-1) joined the firm as quality control Incharge on 10-10-2016 as per appointment and job acceptance letter and resigned from his post w.e.f. 31-08-2017 as per resignation letter. Muhammad Saleem s/o Allah ditta (32304-1682254-9) has joined the firm on 01-09-2017 as per job acceptance letter and serving the firm till date.
Production Incharge
Ms. Fozia Naheed D/o Muhammad Bashir (38403-6784627-2) has joined the firm as production incharge w.e.f. 06-01-2013 as per appointment and job acceptance letter and serving the firm till date.

Show-cause notice has been issued to the technical staff/management of firm – responsible persons U/S 7(11) of the Drugs Act, 1976 vide letter No.03-70/2018-(QC) dated 14-5-2019.

That M/s Quaper (Pvt.) Ltd., has submitted their reply vide letter No. QP/adm/519/002 dated 16th May, 2019 wherein they have stated that request was made to Director NIH, Islamabad for testing of their product as per BP specification and also provided the standard analytical procedure for the said product as well as product registration letter but even then their product was not tested according to BP specifications. BP requires only Disintegration test for coated tablets as mentioned in general monographs under the heading of "Coated tablets and their product adhere to the mentioned test. Moreover USP requires ***Enzyme (Pancreatin)*** *to be added to the test solution if the product contains gelatin in either its core or in coating to get the exact picture of drug dissolution profile while the dissolution test by NIH, Islamabad was carried out without that enzyme.*

They further stated that their product was declared misbranded for not bearing label of pharmacopeia specifications on the pack which is in fact complying to some extent with the registration letter which was approved by the DRAP and according to the Drugs Act, 1976 this objection is remediable and it has no dangerous effect on human health and we have informed our printing & packaging supplier to mention BP specs to the outer label in order to comply with the requirements of the Drugs Act, 1976.

They further submitted that on the basis of above mentioned facts they may be given a chance for personal hearing.

Proceeding of the 290th Meeting of Registration Board.

Mr. Muhammad Iftekhar, (Director) and Ali Tauqeer, CEO (33100-2741642-3) appeared on behalf of M/s Quaper (Pvt.) Ltd., Sargodha to plead the instant case of manufacture & sale of sub-standard Kaymax 75mg tablets, Batch No.GH1716, before the Board in its 290th meeting on 04th July, 2019.

Representatives of the firm stated that their product is registered as per B.P Specifications while both the labs tested the product as per USP specifications. They further stated that they have recalled all the stock and also destroyed the stock as per SOP's.

Decision of the 290th Meeting of Registration Board.

The Board after hearing the accused deliberated the matter in depth in the light of available record/ investigation report of FID decided as under:

- Suspension of the Registration of the said product for six (06) months or till the verification of root cause analysis and satisfactory report by the panel whichever is later.
- Corrective and preventive action by the firm.
- Product Specific Inspection including verification of product development data by the following panel:
    - Additional Director, DRAP, Lahore.
    - Area Federal Inspector of Drugs.

B) Manufacture & Sale of Sub-Standard Kaymax 75mg Tablets, Batch No. GH1729 Manufactured by M/s Quaper (Pvt.) Ltd. Sargodha.

The Federal Inspector of Drugs-III, DRAP, Islamabad visited the premises of M/s Global Chemist & Cosmetics, Kohsar Market, Kashmir Road, Bhurban Murree on 06-06-18 under Schedule V-(1) (C) of the DRAP Act, 2012 read with section 18 (1) (C) of the Drugs Act, 1976. Details are as under:

Name:	Kaymax 75 mg tablets
Composition:	Each Tablet contain 75mg Diclofenac Potassium
Registration No:	046202
Batch No:	GE1729
Manufacturing Date:	05-17
Expiry Date:	05-20
Manufactured By:	M/s Quaper (Pvt.) Ltd., Sargodha.

The FID-III, DRAP, Islamabad forwarded one sealed portion of sample to Government Analyst, Central Drugs Laboratory, Karachi for the purpose of test and analysis dated 08-06-2018 and other portions of the said samples were dispatched as per of DRAP Act, 2012 read with Drugs Act, 1976.

M/s Global Chemist & Cosmetics, Kohsar Market, Kashmir Road, Bhurban Murree was directed to submit the bill invoice with warranty and send the warrantor portion from whom they had purchased the said drug. M/s Global Chemist & Cosmetics, Kohsar Market, Kashmir Road, Bhurban Murree provided the bill invoice with warranty No. 7247 dated 19-01-2018 of M/s Quaper (Pvt.) Ltd., 26-A, SIE, Lahore Road, Sargodha in favor of said drug.

M/s Quaper (Pvt.) Ltd., 26-A, SIE, Lahore Road, Sargodha was directed vide letter dated 06-08-2018 to confirm the said bill invoice with warranty issued by them to M/s Global Chemist & Cosmetics, Kohsar Market, Kashmir Road, Bhurban Murree

The Federal Government Analyst, CDL, Karachi declared the sample as of sub-standard quality on the basis of **Dissolution test** vide test/analysis report No.IP.158/2018, dated 18th July, 2018. Test results of the CDL, Karachi for the above product are reproduced as under;

Description:	*Brown colored, sugar coated tablets*
Identification:	*Diclofenac Potassium identified.*
Dissolution test:	***Does not comply.***
Uniformity of Dosage Units By Weight Variation.	*Complies*
Assay forDiclofenac Potassium:	
Determined amount/tablet:	*79.2188mg*
Stated amount/tablet:	*75mg*
Percentage:	*105.6%*
Limits:	*90.0% to 110.0% Complies.*

Remarks:- *The sample is of **"substandard"** quality under the Drugs Act. 1976.*

Keeping in view of the above said test report of CDL, Karachi M/s Quaper (Pvt.) Ltd., Sargodha was directed vide letter No.F 5-2/2018-FID-III dated 15-08-2018 to stop the sale & recall the said drug and to explain their position on manufacturing and selling of the said substandard drug.

That M/s Quaper (Pvt.) Ltd., Sargodha submitted their reply vide Ref. No. QP/adm/818/007 dated 27-08-2018 wherein they have provided their clarification that they are not satisfied with the results of the CDL, as their product was tested according to the USP specifications while the product is registered according to the British Pharmacopeia specifications, hence they challenged the said test report under Section 22 (4) of the Drugs Act, 1976.

Sample was sent to Appellate laboratory, NIH, Islamabad for retesting under section 22 (5) of the Drugs Act, 1976 dated 18-09-2018.

The appellate Laboratory, NIH, Islamabd declared the said sample as **Misbranded** vide test report No.020-M/2018 dated 17-10-2018. Results are reproduced as under;

Description: *Brown colored circular, biconvex coated tablets packed in blister packing, further contained in an outer carton.*

Reference of Pharmacopeia BP is mentioned only for the salt of Diclofenac Potassium, however reference of specification for the finished product Kaymax Tablets (Diclofenac Potassium 75mg) is neither mentioned on the immediate packing nor on the outer packing. Therefore USP 39 is followed for the test and analysis of the above product. Moreover missing of reference of specification on the product is misleading and violation of packing and labeling Rules of the Drugs Act, 1976.

Identification: *Diclofenac Potassium identified.*

Dissolution Test:

Determined: *81.6% of the labeled amount of Diclofenac potassium is dissolved.*

Limits: *Not less than 75% (Q) of the labeled amount of Diclofenac potassium is dissolved.*

(Complies with USP 39)

Assay for Diclofenac Potassium:

Stated amount/Tablet: *75mg*

Determined: *70.95mg/Tab (94.60%)*

Limits: *90-110%*

(Complies with USP 39)

Remarks; *The sample is **Misbranded** as defined in the Drugs Act, 1976.*

The FID-III, DRAP, Islamabad has provided that the firm is involved in violation of section 23 (1) (a) (iii) read with section 27 (2) (b) & (4) of the Drugs Act, 1976. As a consequence the firm was directed to furnish the details of the recalled products and photocopy of newspaper as mentioned in their letters along with details of responsible persons. Names provided by the FID-III, DRAP, Islamabad are as under;

S.No	Name	CNIC NO.	Job Title
01	Mr. Tauqeer Ali	33100-2741642-3	CEO/Director
02	Mr. Muhammad Saleem	323041-882254-9	QC Manager
03	Ms. Fouzia Naheed	38403-6784627-2	Production Manager

The FID,-III, DRAP, Islamabad also proposed the following actions against the firm;

i. Prosecution in the Drug Court against the the Director, Production Incharge and Quality Control Incharge.
ii. Cancellation of DML.
iii. Cancellation of Registration.

The Drug Licensing Division was requested to verify the names provided by the FID, Islamabad and they provided the following names as per their available record;

Management as per Form-29 dated 31-10-2016
i. Muhammad Iftekhar s/o Muhammad Anwar Nadir, CNIC (33100-5773160-1)
ii. Mr. Ali Touqeer s/o Touqeer Ahmad Taqi, CNIC No. (33100-2741642-3)

Quality Control Incharge
Mr. Abid Hussain s/o Muhammad Ramzan (33100-3349464-1) joined the firm as quality control Incharge on 10-10-2016 as per appointment and job acceptance letter and resigned from his post w.e.f. 31-08-2017 as per resignation letter. Muhammad Saleem s/o Allah ditta (32304-1682254-9) has joined the firm on 01-09-2017 as per job acceptance letter and serving the firm till date.
Production Incharge
Ms. Fozia Naheed D/o Muhammad Bashir (38403-6784627-2) has joined the firm as production incharge w.e.f. 06-01-2013 as per appointment and job acceptance letter and serving the firm till date.

Show cause notice has been issued to the technical staff/management of firm – responsible persons U/S 7(11) of the Drugs Act, 1976 vide letter no. 03-63/2018-(QC) dated 06-03-2019.

That M/s Quaper (Pvt.) Ltd., has submitted their reply vide letter No. QP/adm/319/037 dated 11th March, 2019 wherein they have stated that their product was not declared substandard by the NIH, Islamabad as all the Physical and chemical testing parameters were as per standard instead of that product was declared Misbranded by NIH, Islamabad for not bearing label of pharmacopeia specifications for finished product Kaymax tablets (Diclofenac Potassium 75mg) on the immediate packing and outer packing whereas BP specifications were mentioned for salt of Diclofenac Potassium". Their packing was in fact complying with the letter which was approved by DRAP. It clearly mentions on the outer packing that each tablet contains Diclofenac Potassium 75mg.

That according to the Drug Act, 1976 this objection is remediable and it has no dangerous effect on human health. Recall of the product has been initiated through letters to our customers as per sales record as well as through newspapers. This minor error in printing was neither intentional nor deliberate rather we thought that specifications mentioned on the back of packing were sufficient and also corrected the packing material by mentioning the product specifications on Aluminum foil nor unit carton as per product registration letter. Keeping in view of the above-mentioned facts it is respectfully prayed that the case against us may please be dropped in the interest of justice.

Proceeding of the 290th Meeting of Registration Board.

Mr. Muhammad Iftekhar, (Director) and Ali Tauqeer, CEO (33100-2741642-3) appeared on behalf of M/s Quaper (Pvt.) Ltd., Sargodha to plead the instant case of manufacture & sale of sub-standard Kaymax 75mg tablets, Batch No.GH1729, before the Board in its 290th meeting on 04th July, 2019.

Representatives of the firm stated that their product is registered as per B.P Specifications while both the labs tested the product as per USP specifications. They further stated that they have recalled all the stock and also destroyed the stock as per SOP's.

Decision of the 290th Meeting of Registration Board.

The Board after hearing the accused deliberated the matter in depth in the light of available record/ investigation report of FID decided as under:

- Suspension of the Registration of the said product for six (06) months or till the verification of root cause analysis and satisfactory report by the panel whichever is later.
- Corrective and preventive action by the firm.
- Product Specific Inspection including verification of product development data by the following panel:
    - Additional Director, DRAP, Lahore.
    - Area Federal Inspector of Drugs.

C) Manufacture & Sale of Sub-Standard Kaymax 75mg Tablets, Batch No. GH1714, Manufactured by M/s Quaper (Pvt.) Ltd. Sargodha.

The Federal Inspector of Drugs-IV, DRAP, Islamabad visited the premises of M/s Al-Madina Pharmacy, Shop No.11 Saif Ullah Plaza, GT Road Rawat, Islamabad on 11.06.2018 and taken the following sample of drug for the purpose of test/analysis on prescribed Form-3 under schedule- V (1) (C) of DRAP Act. 2012 read with section 18 (1) (C) of the Drugs Act. 1976. Details are as under:

Name	Kaymax 75 mg tablets
Composition	Each Tablet contain 75mg Diclofenac Potassium
Registration No:	046202
Batch No:	GF1714
Manufacturing Date:	06-17
Expiry Date:	06-20
Claimed Manufacturer:	M/s Quaper (Pvt.) Ltd., Sargodha.

The Federal Inspector of Drugs-IV, DRAP, Islamabad forwarded one sealed portion of sample to Government Analyst, Central Drugs Laboratory, Karachi for the purpose of test and analysis dated 12-06-2018 2018 and other sealed portions of the said samples were dispatched as per of DRAP Act, 2012 read with section of the Drugs Act. 1976.

M/s Al-Madina Pharmacy, Shop No.11 Saif Ullah Plaza, GT Road Rawat, Islamabad provided the sale **invoice No.9786 dated 20-05-2018** with warranty issued to them by M/s Al-Makkah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi in favor of said drug.

M/s Al-Makkah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi, was directed to confirm the said sale invoice and provided subsequent bill invoice warranty of said drug, sent the warrantor portion to the distributor/manufacturer, attested copy of drug sale license and the distribution Authority as required Rule, l9(13-A) and Rule, 30(7-A) of Drugs Licensing, Registration &Advertising) Rules, 1976 wherein it is clearly mentioned that the only manufacturer and its authorized distributor can issue the warranty. M/s Al-Makah Pharmacy Mahran

MedicineNo.3, Shop No.6 College Road Rawalpindi has submitted photocopy of bill invoice with warranty No. 2255 dated 15-05-2018 issue to them by M/s Baber Trading Corporation D-506 Bab-e-Ali Rawalpindi of the drug, unreadable photocopy of their drug sale license but not informed about sending of warrantor portion to M/s Babar Trading Rawalpindi, also not sent original copy of bill invoice with warranty and authority letter of the manufacturer. Hence M/s Al-Makah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi violated Rule. 19(13-A) and Rule 30 (7-A) of Drugs (L.R. &Advertising) Rules, 1976 while obtaining bill invoice with warranty of the drug from another distributor rather than manufacturer.

M/s Babar Trading Corporation D-506 Bab-e-Ali Rawalpindi was directed vide letter of even number dated 9-8-2018 to confirm the said sale invoice and provided subsequent bill invoice warranty of said drug, attested copy of drug sale license and the distribution Authority as required Rule 19 (13-A) and Rule, 30 (7-A) of Drugs (L.R. &Advertising) Rules 1976 wherein it is clearly mentioned that the only manufacturer and its authorized distributor can issue the warranty where as they have issued the warranty to M/s Al-Makah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi Rule.l9(13-A) and Rule. 30 (7-A) of Drugs (L.R. & Advertising) Rules, 1976. M/s Babar Trading Corporation D-506 Bab-e-Ali Rawalpindi has submitted original bill invoice with warranty No. **7482**dated **14-03-2018,** issued by M/s Quaper (Pvt.) Ltd. 26-A, S.I.E. Lahore Road, Sargodha but not informed about sending of warrantor portion to manufacturer and authority letter of the manufacturer. Hence M/s Babar Trading Corporation D-506 Bab-e-Ali Rawalpindi violated Rule. 19 (13-A) and Rule. 30 (7- A) of Drugs (L.R. &Advertising) Rules, 1976 while issuing bill invoice with warranty of the drug to another distributor rather than manufacturer.

M/s Quaper (Pvt) Ltd. 26-A. S.I.TE. Lahore Road, Sargodha was directed vide letter dated to 24th August 2018 to confirm the said bill invoice with warranty issued by them to M/s Babar Trading Corporation D-506 Bab-e-Ali Rawalpindi. In reply M/s Quaper (Pvt.) Ltd. 26-A. S.I.T.E. Lahore Road, Sargodha has confirmed their bill invoice with warranty issued by them to M/s Babar Trading Corporation D-506 Bab-e-Ali Rawalpindi.

The Federal Govt. Analyst under section 22 of the Drugs Act, 1976 has submitted the test report of the sample. Copy of the test report is being submitted to the Firm under section 22 (2) of the Drugs Act, 1976. Deatails of the report are as under;

Description:	*Brown colored, sugar coated tablets*
Identification:	*Diclofenac Potassium identified.*
Dissolution test:	***Does not comply.***
Uniformity of Dosage Units	
By Weight Variation.	*Complies*
Assay for Diclofenac Potassium:	
Determined amount/tablet:	*75.4702mg*
Stated amount/tablet:	*75mg*
Percentage:	*100.6%*
Limits:	*90.0% to 110.0% Complies.*
Remarks:-	*The sample is of **"substandard"** quality under the Drugs Act. 1976.*

Keeping in view of the test report of Federal Government Analyst, Central Drugs Laboratory, Karachi the Firm has violated Section 23(1)(a)(v) of Drugs Act. 1976. The Firm was hereby required to stop the sale, recall the said drug and explain their position on manufacturing and selling the said "Substandard "drugs and to furnish following information within 07 days.

- Name of Chief Executive/Director along with attested copies of CNIC.
- Name of Production In-charge along with attested copies of CNIC.
- Name of Quality Control In-charge along with attested copies of CNIC.
- To provide batch history, production and quality control records along with the sale record.
- To confirm whether M/s Al-Makah Pharmacy Mehran Medicine No.3. Shop No.6 College Road Rawalpindi and M/s Bahar Trading Corporation D-506 Bab-e-Ali Rawalpindi, both are your authorized distributor.

In response to this office letter of even number dated 17-09-2018, M/s Quaper (Pvt.) Ltd, 26-A. SITE, Lahore Road, Sargodha has replied that their product Kaymax tablet 75mg is registered as per

BP specification whereas Government analyst CDL Karachi has applied the test according to USP specification hence challenge the said test report under section 22(4), 22(5) of drug Act 1976. It is further submitted that product specification are not mentioned on the pack by only the specification of Active Pharmaceutical ingredient.

Sample was sent to Appellate laboratory, NIH, Islamabad for retesting under section 22 (5) of the Drugs Act, 1976 dated 17-01-19.

The appellate Laboratory, NIH, Islamabad declared the said sample as of **Substandard** quality vide test report No.01-M/2019 dated 12-02-2019.Results are reproduced as under;

Description: Brown colored circular, biconvex coated tablets packed in blister packing, further contained in an outer carton.

Identification: Diclofenac Potassium Identified.

Dissolution Test:

Determined: 17.96% of the labeled amount.

Limits: Not less than 75% (Q) of the labeled amount.

(Does not comply)

Assay for Diclofenac Potassium:

Stated amount/Tablet: 75mg

Determined: 72.79mg/Tab (97.05%)

Limits: 90-110%

In the opinion of the undersigned the sample is of substandard quality as defined in the Drugs Act, 1976.

The test report of Appellate Laboratory was sent to the Firm with direction to explain their reason on violation of Section 23 (l) (a) (v) of Drugs Act, 1976 read with DRAP Act, 2012 and step taken as directed vide letter of even No. dated 17-9-2018. The copies of the test reports were sent to M/s Babar Trading Corporation D-506 Babe Ali Rawalpindi and M/s Al Makah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi with direction to explain the reason, to provide the information/ record as required under the Law but their reply is still awaited.

The Firm, M/s Quaper Pharmaceutical Pvt. Ltd Sargodha has explained the reasons on the said violations in which they have mentioned that the drug has manufactured and sold by them through their authorized agent M/s Babar Trading Corporation Rawalpindi, including authority letter issue to M/s Babar Trading Corporation Rawalpindi by their National Sales Manager on February 2018, and not informed about another distributor M/s Al-Makkah Pharmacy Rawalpindi.

M/s Al-Makah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi and M/s Babar Trading Corporation D-506 Bab-e-Ali Rawalpindi, both has issued bill invoice with warranty No.9786 dated 20-05-2018 and 2255 dated 15-08-201 8 respectively in favor of said drug but only M/s Babar Trading Corporation Rawalpindi is authorized agent whereas M/s Al-Makah Pharmacy Mehran Medicine No.3, Shop No.6 College Road Rawalpindi is not authorized agent to issue the bill invoice with warranty on behalf of the firm and also not cooperated in investigation of said substandard drug violated section 32(3)(b)(i)(ii) read with seetion 27 (3) (4) of Drugs Act, 1976 it is proposed that "Their cases be sent to Secretary Quality Control Board Rawalpindi, with recommendation of prosecution in the Drug Court against the proprietor and qualified person with cancelation of drug sale license."

Keeping in view the test report of Appellate Labs, the firm has violated Section 23(1)(a)(v) read with section 27 (2) (b) & (4) of Drugs Act, 1976. As a consequence, the firm was directed to furnish the details of recalled products and photo copy of Newspaper as mentioned in their letters along with details of responsible person, which have been received in this office, hence following action are being proposed against the said firm

i. Prosecution in the Drug Court against Directors, Production Incharge & QC incharge.
ii. Cancellation of DML
iii. Cancellation of Registration.

The FID-IV has provided the details of the responsible persons as follows;

Name	CNIC	Job Title
Mr. Ali Tauqeer	33100-2741642-3	CEO
Mr. Muhammad Iftikhar	33100-5773160-1	Director
Mr. Muhammad Saleem	32304-1882254-9	QC manager
Ms. Fouzia Naheed	38403-6784627-2	Production manager

It is submitted that the Drugs Licensing Division was requested to provide/verify the names of responsible persons of M/s Quaper (Pvt.) Ltd., Sargodha for Kaymax 75mg tablets, Batch No.GE1729 vide No.F.03-63/2018-QC and the Drugs Licensing division provided the following information:

Management as per Form-29 dated 31-10-2016
i. Muhammad Iftekhar s/o Muhammad Anwar Nadir, CNIC (33100-5773160-1) ii. Mr. Ali Touqeer s/o Touqeer Ahmad Taqi, CNIC No. (33100-2741642-3)
Quality Control Incharge
Mr. Abid Hussain s/o Muhammad Ramzan (33100-3349464-1) joined the firm as quality control Incharge on 10-10-2016 as per appointment and job acceptance letter and resigned from his post w.e.f. 31-08-2017 as per resignation letter. Muhammad Saleem s/o Allah ditta (32304-1682254-9) has joined the firm on 01-09-2017 as per job acceptance letter and serving the firm till date.
Production Incharge
Ms. Fozia Naheed D/o Muhammad Bashir (38403-6784627-2) has joined the firm as production incharge w.e.f. 06-01-2013 as per appointment and job acceptance letter and serving the firm till date.

Show-cause notice has been issued to the technical staff/management of firm – responsible persons U/S 7(11) of the Drugs Act, 1976 vide letter no. 03-62/2018-(QC) dated 14-06-2019.

That M/s Quaper (Pvt.) Ltd., has submitted their reply vide letter No. QP/adm/619/002 dated 19th June, 2019 wherein they have stated that request was made to Director NIH, Islamabad for testing of their product as per BP specification and also provided the standard analytical procedure for the said product as well as product registration letter but even then their product was not tested according to BP specifications. BP requires only Disintegration test for coated tablets as mentioned in general monographs under the heading of "Coated tablets and their product adhere to the mentioned test. Moreover USP requires ***Enzyme (Pancreatin)*** *to be added to the test solution if the product contains gelatin in either its core or in coating to get the exact picture of drug dissolution profile while the dissolution test by NIH, Islamabad was carried out without that enzyme. That on the basis of above mentioned facts we claim that our product contain Gelatin as binder in its sugar coating, it should have been tested with Enzyme (Pancreatin) for the exact dissolution profile and so the NIH report is false. They have initiated the recall process and received 2400 packs of the above said product and destroyed by following the SOP for destruction.*

They further submitted that on the basis of above mentioned facts they may be given a chance for personal hearing.

Proceeding of the 290th Meeting of Registration Board.

Mr. Muhammad Iftekhar, (Director) and Ali Tauqeer, CEO (33100-2741642-3) appeared on behalf of M/s Quaper (Pvt.) Ltd., Sargodha to plead the instant case of manufacture & sale of sub-standard Kaymax 75mg tablets, Batch No.GH1714, before the Board in its 290th meeting on 04th July, 2019.

Representatives of the firm stated that their product is registered as per B.P Specifications while both the labs tested the product as per USP specifications. They further stated that they have recalled all the stock and also destroyed the stock as per SOP's.

Decision of the 290th Meeting of Registration Board.

The Board after hearing the accused deliberated the matter in depth in the light of available record/ investigation report of FID decided as under:

- Suspension of the Registration of the said product for six (06) months or till the verification of root cause analysis and satisfactory report by the panel whichever is later.
- Corrective and preventive action by the firm.
- Product Specific Inspection including verification of product development data by the following panel:
    - Additional Director, DRAP, Lahore.
    - Area Federal Inspector of Drugs.

Product Specific Inspection Report:

In compliance to the decision of 290th Meeting of Registration Board, Mr. Ajmal Sohail Asif, FID, Lahore has submitted the PSI report of M/s. Quaper (Pvt.) Ltd., Sargodha vide letter No. 6965/2021-DRAP (FID-III) dated 07.05.2021. The inspection was carried out by the following panel of inspectors on 10.03.2021 for verification of product development data and confirmation of CAPA.

i. Mr. Ajmal Sohail Asif, FID, DRAP, Lahore.
ii. Dr. Akbar Ali, AD, DRAP, Lahore.

The panel inspection was focused on verification of CAPA and a thorough evaluation data for product development and stability studies of following product namely:

Sr. No.	Name / Composition of Drugs
01.	Each Tablet contains: Diclofenac Potassium……75mg (USP Specifications)

Detail of Investigation:

Q.No.	Contents	Remarks
1.	Do you have documents confirming the import of Diclofenac Potassium Including approval from DRAP?	The firm had imported Diclofenac Potassium raw material vide invoice no. EXP/1106/19-20 Dated 06/08/2019 From M/s. AARTI DRUGS LIMITED INDIA
2.	What was the rational behind selecting the particulars manufacturer of APS?	The firm selected M/s. AARTI DRUGS LIMITED INDIA for Diclofenac Potassium on their vendor evaluation mechanism.
3.	Do you have documents confirming the import of reference standard and impurity standards?	The firm imported Diclofenac Potassium reference standard from United states pharmacopoeia vide invoice no. 29899785 dated 09-Nov-17 and impurities standard from API supplier.
4.	Do you have certificate on analysis of the API, reference standards and impurity standards?	The firm had certificates of analysis for API, reference standard and impurity standards.
5.	Do you have GMP certificate of API manufacturer issued by regulatory authority of the country of origin?	The firm had provided valid GMP certificate of M/s. AARTI DRUGS LIMITED INDIA issued by Commissioner food and drugs administration Maharashtra state of India.
6.	Do you use API manufacturer method of testing for testing API?	The firm used API manufacturer's method of testing i.e. as per USP monograph.
7.	Do you have stability studies reports on API?	The firm had reports on API of raw material manufacturer.
8.	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	The API manufacturer had performed stability as per SIM method and degradation products had been quantified.
9.	Do you have method for quantifying the impurities in the API?	The firm had testing method to quantify the impurities as provided by API manufacturer.
10.	Do you have some remaining quantities of the API, reference standards and impurities standards?	The firm had remaining quantities of reference standard while no remaining quantity of API or impurities standards.
11.	Have you used pharmaceutical grade	The firm had used pharmaceutical grade excipients.

	excipients?	
12.	Do you have documents confirming the import of the used excipients?	The excipients were purchased from approved suppliers with all the necessary documents.
13.	Do you have test reports and other records on the excipients used?	The firm had certificates of analysis of the excipients used.
14.	Do you have written authorized protocols for development of Kaymax 75mg tablets.	The firm had written and authorized protocols for the development of Kaymax 75mg tablets.
15.	Have you performed drug -excipient compatibility studies?	The firm had performed drug-excipient compatibility studies under stress conditions of 60℃±2℃/75%±5% RH.
16.	Have you performed comparative dissolution studies?	The firm had performed comparative dissolution studies for Kaymax 75mg tablets with Beflam 75mg tablets manufactured by Batala pharma.
17.	Do you have Product development section (R & D)?	The firm had product development (R & D) section.
18.	Do you have necessary equipment available in product development section for development of Kaymax 75mg tablets?	Product development section had necessary equipment to develop Kaymax 75mg tablets.
19.	Are the equipment in product development section qualified?	The available equipment in product development section were qualified.
20.	Do you have proper maintenance / calibration / requalification program for the equipment used in product development section?	The firm had proper maintenance / calibration / requalification program for the equipment used in product development section.
21.	Do you have qualified staff in product development section with proper knowledge and training in product development?	Yes
22.	Have you manufactured three stability batches for stability studies of Kaymax 75mg tablets?	The firm had manufactured three stability batches for the stability studies of Kaymax tablets 75mg with batch numbers i.e. (DP/RD/T/75A, DP/RD/T/75B and DP/RD/T/75C) the accelerated studies were done in climatic test chamber (Model:SC-08, Make Dawn analytical) and long term studies were done in climatic test chamber (Model:SC-08, Make Dawn analytical)
23.	Do you have any criteria fixing the batch size of stability batches?	The firm had followed in-house SOP for fixing the batch size of stability batches in the light of DRAP guidelines.
24.	Do you have complete record of production of stability batches?	The firm had record of production of stability batches.
25.	Do you have protocols for stability testing of stability batches?	The firm had protocol for stability testing of stability batches.
26.	Do you have developed and validated method for testing of stability batches?	The firm adopted USP (2020) test method of Kaymax 75mg and validated the USP test method (QC/MVR/011) for testing of stability batches.
27.	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Not applicable.
28.	Do you have documents confirming the qualification of equipment / instruments used in test of Diclofenac Potassium API & Finished drug?	The firm had proper documents confirming the qualification of equipment / instruments being used in the test and analysis of Diclofenac Potassium API and the finished drug.
29.	Do your method of analysis stability indicating?	Yes
30.	Do your HPLC software 21 CFR compliant?	FPP testing had been conducted on HPLC which was 21CFR Compliant.
31.	Can you show Audit trail report on Diclofenac	The audit trail was active on the testing reports and

<table>
<tr><td></td><td>Potassium testing?</td><td>log of data was available in HPLC. The data was also confirmed through record, chromatograms and log books.</td></tr>
<tr><td>32.</td><td>Do you have some remaining quantities of degradation products and stability batches?</td><td>The firm had remaining quantities of stability testing.
<table>
<tr><th>Batch No.</th><th>Mfg. Date</th><th>Tablets used for stability studies</th><th>Remaining Quantity (Stability</th></tr>
<tr><td>DP/RD/T/75A</td><td>11-2019</td><td>208 tabs</td><td>92 tabs</td></tr>
<tr><td>DP/RD/T/75B</td><td>11-2019</td><td>208 tabs</td><td>92 tabs</td></tr>
<tr><td>DP/RD/T/75C</td><td>11-2019</td><td>208 tabs</td><td>92 tabs</td></tr>
</table></td></tr>
<tr><td>33.</td><td>Do you have stability batches kept on stability testing?</td><td>The firm had stability batches kept on stability testing.</td></tr>
<tr><td>34.</td><td>Do you have valid calibration status for equipment used in Kaymax tablets production and analysis?</td><td>The firm had valid calibration status for the equipment used in Kaymax 75mg tablets production and analysis.</td></tr>
<tr><td>35.</td><td>Do proper and continuous monitoring and control of stability chambers?</td><td>Adequate monitoring and control was available for stability chambers.</td></tr>
<tr><td>36.</td><td>Do related manufacturing area, equipment, personnel and utilities be rated as GMP Compliant?</td><td>Requisite facilities are satisfactory and GMP compliant (DRAP ref. no. 161/2019-DRAP(AD-732485-5132) dated 19-06-2019 valid for 3 years).</td></tr>
</table>

Verification:

(i) Firm had developed and conducted stability for three batches new batches DP/RD/T/75A, DP/RD/T/75B and DP/RD/T/75C and performed comparative dissolution studies with Beflam 75mg Tablets manufactured by M/s. Batala Pharma.

(ii) The CAPA has been examined and verified.

Recommendations:

Based on the area inspected, the technical personnel met and the documents reviewed, and considering the findings of inspection, Panel of inspectors verifies CAPA of M/s. Quaper (Pvt.) Ltd., 26-A, Small Industrial Estate, Lahore Road, Sargodha and firm have conducted product specific inspection including verification of product development and stability studies of the following products:

Sr. No.	Name / Composition of Drugs
01.	Each Tablet contains: Diclofenac Potassium……75mg (USP Specifications)

Proceedings & Decision of 307th Meeting of Registration Board

The case is deferred for next meeting due to paucity of time.

Proceedings & Decision of 308th Meeting of Registration Board:

The Board after thorough deliberations, considering the facts of the case, report submitted by the FID, DRAP, Lahore decided to issue show cause notice for cancellation of the subject cited drug to M/s. Quaper (Pvt.) Ltd., 26-A, Small Industrial Estate, Lahore Road, Sargodha. However, Mr. Adnan Rizvi Director DTL Karachi dis-agreed to aforementioned decision and opined for resumption of production of the product.

The decision has been communicated to the firm vide office letter of even number dated 08-9-2021.

M/s. Quaper (Pvt.) Ltd, Sargodha vide letter QP/admin/2021/00254 dated 15-09-2021 in response to *Letter No. F.03-25/2021-QC (309-RB) dated on 08th September, 2021. The reply of firm is reproduced as:*

"Reference to your Letter No. F.03-25/2021-QC (309-RB) dated on 08th September, 2021 on subject cited above the complete brief of the case is as under.

HISTORY:-

> It is submitted that following are facts of our case.. Three samples are taken by FIDs, Ms. Mahwish Ansari, Atiq ul Bari, and Hassan Afzal, from Islamabad, Peshawar, Murree.

> All these are declared substandard by CDL Karachi due to non-utilization of respective method using enzymes.
> After that we applied to NIH Appellate Laboratory and one got tested standard quality while other two declared substandard.
>After that DRAP has suspended our production of Kaymax 75mg Tablet for 6 months along with additional condition of verification through Panel vide Letter No. F.03-37/20219-QC (290th RB) dated 26-09-2019.
> After about 18th Months panel inspected our premises and verified the CAPA, Stability of three Batches of Tablet Kaymax 75mg and found satisfactory.

Technical Ground:-

1. This product is highly specific as we were using gelatin in coating (sugar) of it's production and in dissolution test the accurate results will be obtained only after addition of pancreatic enzyme as per USP claim regarding general conditions for tablet testing.
2. The product was declared of standard quality by DTL Peshawar vid Report No. 16/PDI/CHD.
3. One of the Batch of NIH was also declared standard quality.
4. Technically speaking in light of USP guidelines for products using gelatin in formulations dissolution test only give correct results if test is carried by addition of enzyme which causes the proper release of drug which gives accurate results, without enzyme the results will be jeopardize as false results will be produced and release kinetics of drug is changed will be change. USP Claim
5. Similarly, if our product was test in presence of pancreatic enzyme as defined by USP it will lead to standard product results as also been done by us in our lab and other private labs by using pancreatic enzymes.

Submission:-

It is submitted that we have been suspended the production activities of the product Kaymax 75mg tablet in response to DRAP letter No.F.03-37/2019 dated 26th September 2019 and till date we are not manufacturing our product as per restriction imposed by the Registration Board.
It is humbly requested that as the Board has already suspended the production of our product and its further action regarding cancellation of registration as decided in 30th meeting will lead to discrimination to our industry/firm regarding to 1st decision of the board.
Furthermore Board has decided to suspend the production of our product namely Tablet Kaymax 75mg and the same Board has decided to suspend the production in its 290th RB meeting till 6 months or verification of root analysis by panel, as both conditions have met, we shall be allowed to resume production of said product Kaymax 75mg tablet.
Further proceeding by board to cancel the registration of our product is against the board's decision in 290th meeting.
It is further submitted that if Board wants to cancel the registration of Diclofenac Potassium 75 mg, due to some other reasons, a uniform decision must be taken across the Board and same shall be applied to all the pharma industry to keep the spirit of justice alive, and till that date we be allowed to manufacture our already registered product Kaymax 75mg tablet."

The firm has been called for Personal Hearing.

Proceedings and Decision of 313th Meeting of Registration Board.

Mr. Ali Touqeer (C.E.O) and Mr. Mohammad Iftikhar (Director) of M/s. Quaper (Pvt.) Ltd, Sargodha appeared before the Board and stated their already submitted stance and requested them to allow resume the manufacturing of their product.

The Board after considering the facts of the case and after thorough deliberations decided:

i. **The firm had developed the product as per PSI report and resumption of production is due. However, as Registration Board in instant meeting has decided to issue show cause notice to all registration holders of Diclofenac potassium with 75mg and 100mg strengths for cancellation of these registrations therefore decision regarding resumption of product will be then considered accordingly.**

ii. **Dr. Munawar Hayat, Director DTL, Lahore disagreed to the abovementioned decision and opined for prosecution in the instant case.**

Case No. V: **MANUFACTURE & SALE OF SUB-STANDARD PROTONIX 40MG TABLETS, BATCH NO. 052 BY M/S WILSHIRE LABORATORIES (PVT.) LTD., LAHORE.**

The FID-VI, DRAP, Karachi visited the premises of M/s Marhaba Medicos, Shop No. 51, Bismillah Market, near New Sabzi Mandi Super Highway, Karachi on 25-04-18 and taken the following sample of drug along with other drugs for the purpose of test/analysis on prescribed Form-3. Details are as under:

Name:	Protonix 40mg Tablet
Composition:	Each tablet contain 40mg Pantoprazole
Registration No:	030041
Batch No:	052
Manufacturing Date:	09-17
Expiry Date:	08-20
Manufactured By:	M/s Wilshire Laboratories (Pvt.) Ltd, Lahore

The FID-VI, DRAP, Karachi has forwarded one sealed portion of sample to Government Analyst, Central Drugs Laboratory, Karachi vide memorandum No.ARS-32-35/2018-FID-VI (K) dated 26-04-2018 as required under Section 19(3)(i) of the Drugs Act, 1976.

The sealed portion of sample were also sent to Chairman, Registration Board vide letter number ARS-32-35/2018-FID-VI (K) dated 27-04-2018 as required under the provision of clause (b) (3) Schedule V of DRAP Act, 2012.

The sealed sample (manufacturer portion) of under reference drug was sent to M/s Wilshire Laboratories (Pvt.) Ltd., 124/1, Industrial Estate, Kot Lakhpat, Lahore vide letter number ARS-32-35/2018-FID-VI (K) dated 30-04-2018 as required under the provision of clause (c) (3) Schedule V of DRAP Act, 2012.

The Federal Government Analyst, CDL, Karachi declared the sample sub-standard quality on the basis of dissolution vide test/analysis report No.R.KQ.310/2018, dated 20th June, 2018 which is violation of section 23 (1) (a) (v) of the Drugs Act, 1976 and rules framed there under. The test report is reproduced as under:

Description:	*Yellow colored, circular shaped enteric coated tablets.*
Identification:	*Pantoprazole Sodium identified.*
Dissolution test:	***Does not comply.***
Uniformity of dosage unit	
By Weight Variation:	*Complies.*
Assay for Pantoprazole Sodium:	
Determined amount/tablet:	*38.2609mg*
Stated amount/tablet:	*40mg*
Percentage:	*95.7%*
Limits:	*90.0% to 110.0% Complies.*

Remarks: *The sample is of* ***"Substandard"*** *quality under the Drugs Act, 1976.*

The FID-VI, DRAP, Karachi vide reference No.ARS-32-45/2018-FID-VI (K) dated 26th June, 2018 served an explanation letter to M/s Wilshire Laboratories (Pvt.) Ltd., 124/1, Industrial Estate, Kot Lakhpat, Lahore for explaining their position in the manufacturing, selling & distributing of above mentioned substandard drug with direction to recall the above mentioned batch from the market.

In response to the above said explanation letter, M/s Wilshire Laboratories (Pvt.) Ltd., 124/1, Industrial Estate, Kot Lakhpat, Lahore submitted their reply vide letter No. WL/OC/S-221 dated

06th July, 2018 wherein they have stated that they received the sealed portion of their product Protonix 40mg Tablets (Samples quantity of 30 tablets) while Batch No/Mfg Date/Exp Date was not visible on sample pack. We also receive the sample after 41 days after picking the sample which is violation of Section 19 (3) of the Drugs Act 1976. As guidelines of the Drugs Act 1976 were not followed which is illegal and the said procedure is null and void in the eyes of law. The sample dispatched to us remained in transit during very hot months of May and June while no temperature and humidity conditions were maintained.

Storage conditions ar e not mentioned on the report where the sample was stored after receipt and we fail to understand as the sample remained untested for 54 days. We had provided reference standard to CDL but we are not sure whether our provided reference standard was used for testing or CDL arranged reference standard from some other source because USP 40 method was used. So, USP reference standard must have been used. Please provide a copy of reference standard of Pantoprazole USP. As per USP method of testing, 68 tablets are required while the sample sent to CDL, Karachi contain 30 tablets so how the required tests can be performed with provided sample.

The FID-VI, DRAP, Karachi was requested to provide the names of responsible persons vide letter No.03-49/2018-QC dated 07th August, 2018. The FID-VI, DRAP, Karachi vide letter No. ARS-32-45/2018-FID-VI (K) dated 09th August, 2018 submitted that updated names of responsible persons may be obtained from Directorate of Licensing Division, DRAP, Islamabad for further processing of the matter.

The Division of Drug Licensing, DRAP Islamabad was requested to provide the names of responsible persons and they provided the following names being responsible persons and technical persons.

M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore	Mr. Ghazanfar Ali Jawa (35202-7157858-5) M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore
Mr. Asad Ali Jawa (35202-2722600-3) M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore	Amjad Ali Jawa (35202-2722635-7) M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore
Ms. Tehseen Tahira (35202-2576262-2) M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore	Mr. Hafiz Nasrullah Khan (33301-1441883-5) M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore
Mr. Muhammad Faisal Javed (31103-1150494-1) M/s Wilshire Laboratories, 124/1, Industrial Estate, Kot Lakhpat Lahore	

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. 03-49/2018-(QC) dated 06-03-2019.

The firm submitted their reply with reference number WL/OC/S-267 dated 13th March, 2019 which is reproduced as under;

"We recievd letter No. F.ARS-32-35/2018-FID-VI (K) dated 14-05-18 received on 17-05-18 from Mr. Abdul Rsool Sheikh FID Karachi advising us to provide complete specifications/ working standard for our product Protoniz 40 mg Tablet directly to FGA CDL Karachi. This was the first intimation towards us for picking of samples of our products on 25-04-2018 but no sample portion was received by us, neither copy of Form nor place from where he sample was picked.

Being a responsible law abiding company we provided testing methods and working reference standard t FGA CDL vide letter No. WL/B/373-2018 dated 21-05-18.

We received letter No. F.ARS-32-35/2018-FID-VI (K) dated 30-04-18 posted by registered post without stamp received on 04-06-18 along with sealed sam0ple portion of the above said product (Quantity of 30 tablets) while batch No/ mfg date/ Expiry date was not visible on the sample pack. We received sample portion after 41 days which is violation of section 19(3) of the Drugs Act 1976. As guidelines of the Drugs Act 1976 were not followed which is illegal and the said procedure is null and void in the eyes of law.

We had not received any intimation until 17-05-18 and we have not received any copy of sample collection Form till date. The sample dispatched to us remained in transit during very hot months of May and June while no temperature and humidity conditions were maintained.
We received letter No. F. ARS-32-35/2018-FID-VI (K) dated 26-06-18 along with testing report No R.KQ.310/2018 dated 20-06-18 issued by CDL Karachi declaring our product substandard on the basis of non-compliance in dissolution test and it is also mentioned that bill/ warranty produced by M/s horizon Pharma, 108/J, Block-2, PECHS, Karachi is enclosed while it has not been found with the letter. While, no invoice/ warranty was provided with his previous letters as well, so how can we trace and ensure that the product picked by him is manufactured by Wilshire Labs?
We have found CDL test report No R.KQ.310/2018 as vague on the following grounds;

- *Storage conditions are not motioned on the report where the sample was stored after receipt and we fail to understand as the sample remained untested for 54 days.*
- *We had provided reference standard to CDL on 21-05-18 but we are not sure whether our provided reference standard was used for testing or CDL arranged reference standard from some other sourece because as mentioned by CDL, USP-40 method was used so, USP reference standard must have been used. Please provide copy of the primary standard of pentoprazole USP. We are also unaware of the grade and potency with standard solution preparation.*
- *As pr our provided method of testing at least 68 tablets are required for complete analysis while the sample sent to CDL contains 30 tablets so how the required tests can be performed with provided sample?*
- *As per USP-40 method of testing, at least 68 tablets are required (i.e 44 for assays and dissolution and 24 for disintegration and Hardness) while the sample sent to CDL contains 30 tablets so how the required tests can be performed with provided sample?*
- *Our DRAP Registration letter is with "MS Specifications" and same was mentioned on all packaging materials of Protonix 40 mg Tablet, Batch No. 052.*
- *We have provided the method of testing with manufacturers specifications and working standard with Manufacturers Specifications to FGA CDL Karachi vide letter No. WL/B/373 dated 21-05-18 but we are surprised to see that our product was tested as per USP-40.*
- *More over USP monograph requires USP Reference Standard while we had sent working standard with Manufactures Specifications. Reference standard with Manufacturers Specification was used to test the product according to USP-40 which is illegal and against the USP method of testing so the results are null and void.*
- *In Dissolution chapter <711> criterion for acidic stage (A1, A2, A3) and buffer stage (B1, B2, B3) is mentioned while the CDL report is lacking this information too.*
- *As per USP-40, mentioned column is 4.6-mm X 7.5-cm, 3-µm packing L1(C-18). While CDL test report shows column as (C-18) (5 microns with 0.25m-Length and 4.6 n diameter) it proves that wrong column was used for testing of the product.*
- *CDL report shows that column with (C-18) (5 microns) with 0.25m-Length and 4.6n Diameter was used which is astonishing that how a particle with 5 microns can be packed in 4.6n Diameter columns. If it exists, please share the source name and copies of invoices so that we are able to procure the same column and own a test to verify results.*
- *Injection volume mentioned in USP 40 is 10µl while CDL report shows injection volume as 20 µl which is violation of USP monograph.*
- *Chromatograms for assay and dissolution test are not provided along with CDL Report.*
- *As per USP Monograph, tailing factor and Relative Standard Deviation (RSD) are compulsory while in method provided along with CDL Report lacking this information.*
- *Testing Report No. R.KQ, 310/2018 dated 20-06-2018 declared our product as substandard due to failing in dissolution test. It shows only a phrase regarding dissolution i.e. "does not comply". Please note that dissolution test is a chemical test and for understanding it must be provided with numerical value for each tablet. While, in this report, no detailed/ numeric*

values are found which shows that dissolution test is performed as per physical observations.

- *No results for each tablet at acid stager are provided in CDL report. Further, no time and type of medium used, have been mentioned in report/ method.*
- *No, sample preparation and standard preparation and calculations are provided in CDL test method at acid stage.*
- *There is difference between quantitative analysis (mcg) of Sample preparation and working standard preparation. Moreover, no calculations re provided with the reports which confirms that the report as null and void.*
- *No results for each tablet at buffer stage are provided in CDL report. Further, the buffer 6.8 has no clarity for its preparation and salt information is missing whereas USP requires Phosphate buffer to be used.*
- *CDL Report shows assay results as 95.7% and we are surprised that how a product can be declared as substandard in dissolution test while the assay is well within the prescribed limit.*

In light of above mentioned submissions, it is respectfully requested that there are violations of The Drug Act 1976. Moreover, Central Drug Laboratory Report No. R.KQ, 310/2018 dated 20-06-2018 is null and void as numerous legal and technical faults are found in CDL Test Report issued for our product Protonix 40 mg Tablet. So, your letter may please be withdrawn and stop further proceeding. Moreover, as many technical aspects are involved in this case so we request you to please give us a chance for appearing in person for detailed briefing in this regard.

Proceeding of the 289th Meeting of Registration Board.

Hafiz Nasrullah, Senior QCM (11101-1441883-5) and Mr. Shoaib Hakeem, Technical Director (35202-2954794-1) of M/s Wilshire Laboratories (Pvt.) Ltd., Lahore appeared on behalf of M/s Wilshire Laboratories (Pvt.) Ltd., Lahore to plead instant case of Substandard drug Protonix 40mg Tablets, Batch No.052, before the Board in its 289th meeting on 16th May, 2019.

Representatives of the firm re-iterated points already mentioned in their letter as recorded above. After deliberation, the firm requested for retesting of drug product.

Decision: *Registration Board after hearing the accused deliberated the matter in depth in the light of available record/ investigation report of FID decided that the Board's portion of the sample shall be retested from appellate laboratory, NIH, Islamabad.*

The subject cited sample was received in Appellate laboratory, NIH, Islamabad on 17-07-2019 as per decision of the Registration Board in its 289th meeting.

Chief, Drugs Control & Traditional Medicine Division, National Institute of Health, Islamabad vide F.No.1-20/017-M/2019-DC&TMD dated 16th September, 2019 has also declared the sample of Protonix 40mg Tablets, Batch No. 052 by M/s Wilshire Laboratories (Pvt.) Ltd Lahore as of "**Sub-standard"** quality vide their test report No. 017-M/2019 **on the basis Dissolution test**. Results are reproduced as under:

Description:	Light yellow, circular, biconvex enteric coated tablets plain on both sides packed in blister packing further contained in an outer carton.
Identification:	Pantoprazole sodium identified.
Wt. Variation:	Complies with USP 39

Dissolution test:	**Determined.**	**Limit:**
Acid stage	12.7% of label amount	Not more than 10% (Q) of the label amount.
Buffer stage	36.32% of the label amount	Not more than 75% (Q) of the label amount.

(Does not comply with USP 39)

Assay:	**Stated:**	**Found:**	**Limit:**	**Percentage:**
Pentoprazole sodium Sesquihydrate	40mg/tablet	41.40mg/tablet	90-110%	103.51%

(Complies with USP 39)

In the opinion of the undersigned the sample is of sub-standard quality as defined in the Drug Act, 1976 for the reason(s) given below.

Dissolution test:	**Determined.**	**Limit:**
Acid stage	12.7% of label amount	Not more than 10% (Q) of the label amount.
Buffer stage	36.32% of the label amount	Not more than 75% (Q) of the label amount.

(Does not comply with USP 39)

Show cause notice has been served to the technical staff/management of the firm – responsible persons U/S 7(11) of the Drugs Act, 1976 vide letter no. 03-49/2018-(QC) dated 12-11-2019.

M/s Wilshire Laboratories (Pvt.) Ltd., Lahore vide reference No.WL/OC/S-344 dated 18th November, 2019 submitted their reply and is reproduced as under:

- *Our DRAP registration letter for Protonix 40mg tablet is with "MS Specification" and same was mentioned on all packing materials of Protonix 40mg tablets, B# 052. We have provided method of testing with "**Manufacturer Specification**" to NIH but we are surprised to learn that our product has been tested on USP-39.*
- *In USP monograph of pantoprazole sodium delayed release tablets, label cliaim is pantoprazol ($C_{16}H_{15}F_2N_3O_4S$) and identification test is derived on the basis of retention time of peaks from assay, while in both CDL and NIH reports the identification test claim is pantoprazole sodium which is violation of USP claim.*
- *In CDL report assay test result is 95.7% while in NIH report assay test result is 103.51% which deviate more than 5% of ICH stability limit.*
- *In dissolution test, Test1 is not mentioned in NIH report.*
- *Acid stage failure is not mentioned in CDL report while the NIH declared the product fail on both stages.*
- *In calculation formula applied on both stages is not precisely mentioned for given six batches as reading deviates from individual reports as well average results.*
- *In tolerance of dissolution acid stage Pantoprazole Sodium is written which further entitles that there is calculation errors in this report.*
- *As per our continuous improvement policy, we have already worked regarding dissolution of our product. We have complete product development and stability data available with us and can be provided in personal hearing.*

  In light of the above mentioned submissions, it is respectfully and humbly prayed that the report by CDL and NIH be held to be based upon misreading and non reading of evidence and consequently a nullity in the eyes of the law; Furthermore, the show cause notice dated 12-11-2019 be held to be not based upon the law and facts and be withdrawn/dismissed;

  You are most humbly requested to provide us with a right of hearing; any other relief as deemed just, appropriate and equitable by the learned Board may also most graciously be granted.

Proceedings of 293rd meeting of the Registration Board.

Hafiz Nasrullah, Senior QCM (11101-1441883-5) and M.Amir (35202-7321753-9 for Faisal Javed) appeared on behalf of M/s Wilshire Laboratories (Pvt.) Ltd., Lahore for instant case and stated that they still have concerns on the analytical method of NIH, Islamabad. Furthermore they have made necessary improvements and shifted their product from manufacturer's specifications to Pharmacopoeal specifications. They further requested to analyze their product from individual laboratory.

Decision of 293rd meeting of Registration Board.

The case was presented before the Registration Board in its 293rd meeting held on 08th January, 2019 and the Board after detailed discussion and deliberations considering the test reports of CDL & NIH, Islamabad unanimously decided as under:

i. Suspension of the Registration of the said product for six (06) months or till the verification of root cause analysis and satisfactory report by the panel whichever is later.
ii. Corrective and preventive action (CAPA) by the firm and product development data.
iii. Product Specific Inspection including verification of product development data and confirmation of CAPA by the following panel:
    - Mr. Iftikhar Ahmad Member Registration Board.
    - Area Federal Inspector of Drugs.
    - Hafiz Ahsan AD, PEC.

In compliance to the decision of 293rd Meeting of Registration Board, Ms. Aisha Irfan, FID, DRAP, Lahore has submitted the PSI report of M/s. Wilshire Labs (Pvt.) Ltd., 124/1, Industrial Estate, Kot Lakhpat, Lahore vide letter No. 6477/2021-DRAP (L-V) dated 30.04.2021. The inspection was conducted by the panel of inspectors on 15.03.2021 with reference to DRAP letter No. F. 03-65/2019-QC dated 21.04.2020 for verification of root cause analysis, corrective and preventive action (CAPA) and product development data of their product Protonix 40mg Tablet containing Pantoprazole sodium sesquihydrate. Observations, recommendations and conclusion of the report are given as under:

"Protonix 40mg Tablet, Batch No. 052 was declared as substandard by Central Drug Laboratory, Karachi vide Testing Report No. R.KQ,310/2018 dated 20.06.2018. The company informed that they had given advertisement for the recall of their product Protonix 40mg Tablet, Batch No. 052 in two national newspapers i.e. Daily Nation and Roznama Khabrain dated 18.12.2019 and had written letter to sole distributor High Land Pharma Marketing (Pvt.) Ltd for recall. The distributor informed that all the stock was consumed in pharmacies and no recall stock was available.

During inspection it was found that company had been practicing for testing of its said product as per "Manufacturer's Specification" which was mentioned on their registration letter but now company has updated its testing method as per USP. However, firm had not submitted any request for change of specifications as per pharmacopoeia to concerned section of DRAP, Islamabad.

The firm was asked to provide the batch manufacturing records (BMRs) of both old formulation and new formulation after product suspension, root cause analysis report, product development data, corrective and preventive action (CAPA), taken by the firm after detection of root cause analysis. The firm provided only manufacturing order of formulation without mentioning enteric and film coating excipients necessary to control dissolution of this delayed release formulation. The BMRs of trial batches were also not available. The batch size mentioned on manufacturing order was 13436 while that mentioned on stability data sheets was 2500 tablets (T005-A, T005-B each). Moreover, root cause analysis for the said formulation were not provided by the firm. In the CAPA conducted by firm only in-house (MS) testing method was shifted to pharmacopial testing method (USP) the reason for dissolution failure was not provided. The firm claimed that they have thoroughly worked for product development after their product suspension and now their product complies as per USP, however complete product development data including BMR were not provided and could not be verified.

Firm was asked to provide samples of batches of their Protonix 40mg Tablet which were manufactured after Batch No. 052. Firm informed that they

have manufactured batches of Protonix 40mg Tablet till Batch No. 069 and no batch was produced after suspension of product. The FID randomly took samples on Form-3, for test / analysis purpose by Central Drugs Laboratory, Karachi.

Conclusion:

Based on the inspection proceedings, such as verification of documents, interaction with management e.t.c the panel concludes that the company has not given root cause analysis and rectified their dissolution problem through product development process. The firm only shifted their testing method from Mfg spec to UPS. However, the management made commitment and also agreed to make necessary improvements in procedures.

Recommendation:

Keeping in view the above observations the panel could not verify the product development process and root cause analysis conducted by the firm at this stage. However, the final conclusion would be based upon the test report results received from the Central Drugs Laboratory, Karachi.

Hence the panel recommend that the decision of the Drug Registration Board for suspension of registration of Protonix 40mg Tablets may remain intact.

Proceedings & Decision of 307th Meeting of Registration Board

The case is deferred for next meeting due to paucity of time.

Proceedings of 308th Meeting of Registration Board

Ms. Aisha Irfan, FID, DRAP, Lahore has submitted a letter with reference to Letter No. 6477/2021-DRAP (L-VII) dated 15-06-2021 wherein the inspection report of M/s. Wilshire Labs (Pvt.) Ltd., 124/1, Industrial Estate, Kot Lakhpat, Lahore was submitted. She stated that:

"In the said report, panel could not verify the product development process and RCA conducted by the firm for Protonix 40mg tablet. However, samples of Protonix 40mg tablet, batch no 069 were taken and sent to CDL for test/analysis. Now the test report received from CDL has declared the sample as Sub-Standard. Hence, the case of suspension of registration of Protonix 40mg tablet may be placed before Registration Board for further necessary action. Moreover, as now the two batches of the same drug were declared substandard repeatedly, hence the firm may be asked to withdraw all the batches of the drug Protonix 40mg tablet from the market as a precautionary measure."

Decision of 308th Meeting of Registration Board

The Board after thorough deliberations, considering the facts of the case, report submitted by the FID, DRAP, Lahore decided as

i. The suspension of registration of Protonix 40mg Tablet remain intact.
ii. The Comparative Dissolution Profile of the product with innovator's product will be submitted by the firm for consideration of the Board

Decision has been communicated to the firm vide office letter of even number dated 08-09-2021.

M/s. Wilshire Labs (Pvt.) Ltd., Lahore vide Ref # WL/OC/S-597 dated 14-09-2021 where in they submitted the reply of office letter of even number dated 08-09-2021; reproduced below:

"Reference your letter no. F.03-18/2021-QC (308-RB) dated 08-09-2021 received on 09-09-2021 regarding the subject mentioned above, please note that we have following to say:-

>Our Panel Inspection was carried out on 15-03-2021 with reference of DRAP Letter no. F.No.03-65/2019-QC (293rd RB) dated 21-04-2020 for verification of root cause analysis, Corrective and Preventive Action (CAPA) and product development data of our product Protonix 40mg Tablet containing Pantoprazole Sodium Sesquihydrate by following panel:-

1. Mr. Iftikhar Ahmad, Member Registration Board
2. Ms. Ayesha Irfan, Area Federal Inspector of Drugs, DRAP, Lahore
3. Hafiz Ahsan, Assistant Director, Product Evaluation Cell, DRAP, Islamabad

>During inspection it was informed to the panel that company had been practicing for testing of its said product as per "Manufacturer's Specification" which was mentioned on their registration letter but now company has updated and revised its testing method/pharmacopoeial specification as per USP and found compliance of their product on Dissolution Test 2.
>Both formulations, old and new were provided by the firm. It was also told to the panel that we have thoroughly worked for product development after their product suspension and now their product complies as per USP (Dissolution Test 2).
>Stability data was also provided by us which was analyzed and verified by the panel from log books.
>We informed the panel that we have taken two trial batches after rectification of dissolution problem identified by Central Drug Laboratory, Karachi. Data for trial batches was verified from Manufacturing Order, Stability Data, Testing Raw Data, Chromatograms and Log Books.
>We also told that it was not our practice to maintain proper complete BMR (like commercial batches of trial batches but now we have started to maintain complete BMRs of trial batches as well.
>We informed to the panel that we have manufactured batches of Protonix 40mg Tablet till Batch No. 069. Samples were provided which were verified that these batches were manufactured before suspension of their product on 21-04-2020. It was also verified that we have not produced any batch after suspension of product.
>The panel checked the samples and randomly selected from these batches for sending to Central Drugs Laboratory, Karachi for testing,
>We use Dissolution Test 2 for testing of our product. We have provided Test Method to the office of FID for onward submission to CDL along with samples.
>We also provided our Test Method (USP) with Dissolution Test 2 to CDL vide our letter no WLB 958-2021 dated 04-08-2021.
>Then we came to know that our product Protonix 40mg Tablet, Batch No. 069 has been declared as substandard by Central Drugs Laboratory, Karachi vide its test report no. LHR. IS 2021 dated 21-05-2021 with following remarks: -
1. S is not required as 09 tablets out of 12 tablets are already found below 60% (Q-15) in S2
2. The sample is of "substandard" quality under the Drugs Act, 1976.
>We have checked retention samples of the said batch and found our product to be standard in all respects.
>The we received your letter no. F.03-18/2021-QC (308-RB) dated 08-09-2021 with following decision of Registration Board:-
"The Board after thorough deliberations, considering the facts of the case, report submitted by the FID, DRAP Lahore, decided as
i. The suspension of registration of Protonix 40mg Tablet remain intact.
ii. The Comparative Dissolution Profile of the product with innovator's product will be submitted by the firm for consideration of the Board."
>Reference remarks of CDL for declaring our product substandard on the basis of Dissolution Test and decision by the Registration Board mentioned above, please note that as per Dissolution Parameter of USP Test II, there are two stages of Dissolution Test which are: -
- Acid Stage
- Buffer Stage
>CDL report does not mention results of Acid Stage.
>CDL report mentioned parameter on Buffer Stage which were followed by analyst, are absolutely different from USP: -

Dissolution at Buffer stage	
Parameter in USP	***Parameter followed by CDL***
RPM: 100	*RPM: 75*
Time 45 minutes	*Time 30 minutes*
Analysis mode: UV mode	*Analysis mode: HPLC mode*

>Without prejudice to the reservations of us regarding legality of the CDL declaration, please
note that we have already recalled the said batch publically in the larger public interest.
>For your ready reference and as required by you, following documents are enclosed with
- Comparative Dissolution Profile of our product Protonix 40mg Tablet, Batch No. 069 (the same declared as substandard by CDL) with Protium 40mg Tablet, Batch No. 484330 of M/s Abbott Laboratories.
- Testing Method as per USP with Dissolution Test 2
- Recall Record of Batch No. 069

You are most humbly requested to provide us with a right of hearing any other relief as deemed just, appropriate and equitable by the learned Board may also most graciously be granted."

Proceedings and Decision of 313th 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. Wilshire Labs (Pvt.) Ltd., Lahore and called them for personal hearing before Registration Board.

CASE No. VI: MANUFACTURE & SALE OF SUB-STANDARD CLARINAVE SUSPENSION, REG.NO.078599, BATCH NO. D366, MANUFACTURED BY M/S NOVAE PHARMACEUTICALS, HATTAR.

The Federal Inspector of Drugs, DRAP Peshawar visited the premises of M/s Novae Pharmaceuticals, on 19-12-2019 where in the following drug was taken for the purpose of test/analysis on prescribed Form-3. Details are as under:

Name of Drug	Registration No.	Batch No.	Mfg. Date	Exp. Date	Mfg. By
Clarinave suspension	078599	D366	10-19	09-21	M/s. Novae Pharmaceuticals, Hattar

The Federal Inspector of Drug, DRAP, Peshawar visited the premises of M/s Novae Pharmaceuticals, Plot no. 123, phase V, Industrial Estate, Hattar on 16-10-2019 wherein the sample of Clarinave suspension, Batch No. D366, Manufactured by M/s. Novae Pharmaceuticals, Hattar was drawn under Schedule-V (1) (C) of DRAP Act, 2012 read with section 18 (1) (C) of the Drugs Act, 1976 for the purpose of test/analysis. Details are as under;

S. N0.	Name of Drug	Registration No.	Batch No.	Mfg. Date	Exp. Date	Mfg. By
01	Clarinave suspension	078599	D366	10-19	09-21	M/s. Novae Pharmaceuticals, Hattar

The said sample was sent to the Government Analyst, Central Drugs Laboratory, Karachi vide memorandum No.F.10-213-215/2019-DRAP(P)6304 dated 17-10-2019. The Federal Government Analyst, CDL, Karachi vide their test report No.IP.112/2019 dated 19-12-2019 declared the above said sample as of **"Sub-Standard"** quality. Test results of the CDL, Karachi are reproduced as under:

Description: *White powder which reconstitute into off white suspension on mixing with water.*
Identification: *Clarithromycin identified.*

pH Determined: *6.15*
Limits: *4.0 to 5.4* ***Does not comply.***
Assay for Clarithromycin:
Determined amount/5ml: *85.8384mg*
Stated amount/5ml: *125mg*
Percentage: *68.7%*
Limits: *90.0% to 115.0%* ***Does not comply.***

Note:- *Instead of coated granules (suspension grade) tablet grade API (fine powder) has been used in the product, which shows total inability of the formulator and lack of product development knowledge and practice.*

Remarks:- *The sample is of **" substandard"** quality under the Drugs Act, 1976.*

The FID-III, DRAP, Peshawar further submitted that firm vide letter No.NP/DRAP/20/001 dated 20-01-2020 stated that they do not agree with the results mentioned in test report No. IP.112/2019 dated 19-12-2019 and has requested for re-analysis of the subject mentioned product from Appellate Laboratory, NIH, Islamabad. On the request of the firm, sample was sent for retesting from Appellate laboratory, NIH, Islamabad dated 17-04-2020 under section 22(4) & (5) of the Drugs Act, 1976. The Appellate laboratory, NIH, Islamabad vide their test report No. 05-M/2020 dated 15-07-2020 has also declared the sample as of substandard quality. Results of the Appellate laboratory, NIH, Islamabad are reproduced as under:

Description: *White granular powder contained in ambered colored labeled glass bottle produces white suspension after reconstitution with distilled water further packed in an outer carton.*
Identification: *Clarithromycin identified.*
pH: ***Determined:*** *6.2* ***Limit:*** *4.0 – 5.4*
Does not comply with USP 39.
Volume: ***Determined:*** *60ml* ***Limit: 60****ml*
Complies with volume stated on the label.
Assay of Clarithromycin:

Stated:	***Found:***	***Limit:***	***Percentage:***
125mg/5ml.	*101.62mg/5 ml.*	*90-110%*	*81.29%*

Does not comply with USP 39.

In the opinion of the undersigned the sample is of substandard quality as defined in the Drug Act, 1976for the reasons given below:

Description: *White granular powder contained in ambered colored labeled glass bottle produces white suspension after reconstitution with distilled water further packed in an outer carton.*
Identification: *Clarithromycin identified.*
pH: ***Determined:*** *6.2* ***Limit:*** *4.0 – 5.4*
Does not comply with USP 39.
Volume: ***Determined:*** *60ml* ***Limit: 60****ml*
Complies with volume stated on the label.
Assay of Clarithromycin:

Stated:	***Found:***	***Limit:***	***Percentage:***
125mg/5ml.	*101.62mg/5 ml.*	*90-110%*	*81.29%*

Does not comply with USP 39.

FID-III, DRAP, Peshawar submitted vide letter No.F.10-213-215/19-Novae-DRAP (P) 46 dated 05th January 2021 that the firm contravened Section 23(1)(a)(v) of the Drug Act, 1976 and the case is submitted for consideration of the Drug Registration Board by FID.

Names of responsible provided by the firm to FID, DRAP Peshawar are as under and also verified by the Licensing Division:

Names of the CEO/Directors	**Name of Technical Persons**
Muhammad Ayub	Muhammad Samie (Production Manager)
Raja Safeer Hussain	Ghulam Ghaus (QC Incharge)

Muhammad Ilyas	----------

Show cause notice was issued to the firm and responsible persons along with the copies of CDL, Karachi and NIH, Islamabad test reports under section 7 (11) of the Drugs Act, 1976 vide letter No.F.03-11/2018-QC dated 06-07-2020 for the following actions:

i. Prosecution in the Drug Court.
ii. Cancellation/Suspension of Drug Registration.
iii. Any other action the Board may deem fit.

No reply has been received till date. The firm has been called for personal hearing before the board.

Proceedings of 307th Meeting of Registration Board.

Mr. Ameer Tahir Raja, Regulatory Affairs (37405-8835584-3) and Mr. Liaquat Ali, Quality Control Manager (13302-8115291-1) appeared before the Board on behalf of M/s. Novae Pharmaceuticals Hattar to plead the instant case. He reiterated the points already recorded above. Registration Board after detailed discussion and considering the facts of the case decided that the firm shall submit root cause analysis (RCA) for the matter along with Corrective and preventive action (CAPA) taken up by them. Aforementioned documents will be forwarded to following panel for verification and conduction of product specific inspection. Product shall remain suspended for 6 months or decision of Registration Board after consideration of aforementioned report whichever is later.

- Dr. Khalid Javed, Director DTL, Peshawar
- Area Federal Inspector of Drugs."

FID-I, DRAP, Peshawar submitted a follow up inspection report of the firm in compliance to office letter of even number dated 19-04-2021 wherein he inspected the premises of M/s. Novae Pharmaceuticals, Hattar on 02-06-2021. Following information was mentioned by FID:

Batch size	1200 bottles
Final yield	1176 bottles (1166 to FG store +10 QC retained samples
Firm recalled	745 packs out of 1166 packs while 01pack was found in QC retained samples.

FID-I, DRAP, Peshawar informed dated 22-09-2021 that Dr. Khalid Javed, Director, DTL, Peshawar has been retired from his post. The panel for said inspection may be revised for disposal of matter.

Proceedings and Decision of 313th Meeting of Registration Board.

The Board after thorough deliberations and considering the facts of the case revised the Panel;

i. **Dr. Qurban Ali, Board Member.**
ii. **Area Federal Inspector of Drugs.**

However, the product shall remain suspended till decision by Registration Board.

Case No. VII: CLOMFRANIL 25 MG SCT BATCH NO. HJOAAB AND HJOAAC OUT OF SPECIFICATION (OOS) OBSERVED IN DISSOLUTION TEST RESULTS OF 6 MONTHS TESTING POINT OF ACCELERATED STABILITY STUDY AT 40C/75% RH CONDITION AND BATCH NO. HJOAAB ON 9 MONTH TESTING POINT OF FOLLOW UP STABILITY STUDY AT 30C/65% RH.

M/s. Novartis Pharma (Pakistan) Limited submitted an Out of specification (OOS) results observed regarding the subject cited above and is reproduced as under:

a. *"As you will acknowledge that Novartis Pharma (Pakistan) Limited is a quality conscious healthcare company and have robust quality management systems in place, which are constantly active to ensure product quality and patient safety throughout the product lifecycle.*
b. *We would like to inform you of an Out of specification (OOS) results observed in the dissolution dissolution testing of Clomfranil 25 mg SCT Batch Number HJOAAB and HJOAAC, out of specification (OOS) observed in dissolution test results of 6 months test point of accelerated stability study at 40C/75%RH condition and batch number HJOAAB on 9 months test point of follow up stability*

study at 30C/65% RH (results were 65.5% against NLT 75% after 45 minutes).

c. *Extensive technical investigations were performed and root-cause identified and attributed to the use of lactose excipient with atypical particle size distribution (PSD). It was evidenced that the issue is limited to Clomfranil 25 mg SCT Batch Numbers HJOAAB and HJOAAC respectively, other Clomfranil 25mg batches were manufactured from typical lactose PSD.*
d. *The 2 batches HJOAAB and HJOAAC achieved 89.2% &82.9% respectively when tested for dissolution after 60 minutes in a dissolution profile testing. Based on the biopharmaceutical properties of clomipramine, the deviation observed at 45 minutes may result in lower Cmax. Nevertheless, since after 90 minutes clomipramine is completely dissolved, AUC may be similar as other batches. Therefore, though the Cmax may be lower, the overall exposure of clomipramine may not be significantly affected, and therefore have no significant clinical impact.*
e. *Furthermore, after the review of available data from the Novartis global safety database, it is considered unlikely that the OOS represents a safety concern related to the administration of clomipramine 25mg SCT from batches HJOAAB and HJOAAC. Use of the product from these batches is not expected to cause adverse health consequences.*
f. *Novartis will continue to closely monitor the batches in scope through re-testing and will update the DRAP with the results and corresponding impact assessment.*
g. *The batches were manufactured on May 2018 and has 60 months shelf-life and will expire on April 2023. Retain samples analysis complied with the specification. Internal review of stocks status conclude no stocks available at distributor level, and based on historical trend released batches may have been fully consumed in the market.*
h. *The above-mentioned product was manufactured for Novartis Pharma (Pakistan) Limited by a third party i.e. GlaxoSmithKline OTC Pvt. Ltd located at Petaro Road, Jamshoro."*

Keeping in view of above, a Recall Alert was issued to the firm vide letter F.No.13-192/2019-(QC) dated 04-11-2019 along with suspension of production until Root cause analysis and CAPA data was verified by the Drug Registration Board.

M/s Novartis Pharma Pakistan Pvt. Ltd., vide reference No.Nil dated 20-11-2019 regarding the subject cited above, submitted Root Cause Analysis and detail of Corrective Preventive Action Plan (CAPA) and is reproduced as under:

"Root Cause Investigation (RCA):

a. *We once again confirm that extensive technical investigations were performed and the root-cause was identified and attributed to the use of lactose excipient having atypical particle size distribution (PSD).*
b. *It was evidenced that the issue is only limited to Batch Numbers HJOAAB and HJOAAC manufactured with above variant of this excipient.*
c. *Other Clomfranil 25mg batches were manufactured from routine, typical lactose PSD and no deviations were observed in other produced batches. We have obtained satisfactory dissolution results for the retained samples of these batches.*
d. *Based on the Medical Risk Assessment Report, there is no safety concern with use of these batches. As per biopharmaceutical properties of clomipramine, the overall exposure of clomipramine may not be significantly affected, and therefore have no significant clinical impact.*
e. *Use of the product from these batches is not expected to cause any unusual adverse health consequences for patient.*

Corrective and Preventive Actions:

a. *As directed by you, production of this product is already suspended at this point in time.*
b. *Furthermore, we have manufactured 03 validation batches (BN# LX4V, LX4X & LX5A) to revalidate the use of referred excipient.*

As per our internal quality protocols and your directives, the release production of these batches said product will remain on hold until completion of six months accelerated stability studies

c. *Novartis is also initiating a precautionary Class II recall of mentioned batches at Retail Level. Pharmacies supplied with these batches will be immediately informed to return the unconsumed quantities of these batches.*

As there is no safety concern, we will not be issuing public safety alert at this stage. We anticipate your understanding and support in the recall process. However, should you have additional queries, please feel free to contact."

M/s. Novartis was directed to comply with the recall guidelines available at www.dra.gov.pk and submit recall assessment & reconciliation along with RCA and CAPA vide letter F.No.13-192/2019-(QC) dated 23-12-2019. M/s Novartis Pharma Karachi vide reference No. Nil dated 22nd September 2020 submitted that as per directives and compliance with the recall guidelines, the stability of Clonfranil 25mg has completed and result as satisfactory at end to 06th month testing point of accelerated stability studies. They further submitted that following document/ information are being submitted for reference and record.

i. Recall assessment and reconciliation form along with complete requisite information.
ii. Root cause analysis and CAPA data.

They further requested to please grant them approval for releasing the batches to the market and resume the production.

Keeping in view of the above reply, it was observed that neither Recall assessment & reconciliation form along with complete requisite information nor root cause analysis and CAPA has been provided by the firm. Therefore, a letter was issued to the firm vide letter F.No.13-192/2019-(QC) dated 07-10-2020 to submit the requisite information.

In response, M/s Novartis Pharma (Pakistan) Limited vide reference No. nil dated 28-10-2020 regarding the subject cited above, wherein they have referred DRAP, Islamabad letter No.F.13-192/2019-QC and informed that they have already submitted the required information. However, they are the same again along with 06 months accelerated stability studies.

Root cause analysis and CAPA provided by the firm were as under:

a. "Root Cause Investigation:

i. *After thorough investigation, Root-Cause of this deviation was identified and attributed to the use of lactose excipient having atypical particle size distribution (PSD).*
ii. *It was evidenced that the issue is only limited to Batch Numbers HJOAAB and HJOAAC manufactured with above variant of this excipient.*
iii. *Other Clomfranil 25mg batches were manufactured from routine, typical lactose PSD and no deviations were observed in other produced batches. We have obtained satisfactory dissolution results for the retained samples of these batches.*
iv. *Based on the Medical Risk Assessment Report, there is no safety concern with use of these batches. As per biopharmaceutical properties of clomipramine, the overall exposure of clomipramine may not be significantly affected, and therefore have no significant clinical impact.*
v. *Use of the product from these batches is not expected to cause any unusual adverse health consequences for patient.*

b. Corrective Actions and Preventive Actions:

i. Further manufacturing of this product is already suspended at this point in time.

ii. *Precautionary Class 11 recall of mentioned batches at Retail Level initiated. Pharmacies supplied with these batches informed to return the unconsumed quantities of these batches.*
iii. *03 validation batches (BN# LX4V, LX4X & LX5A) have been manufactured to re-validate the use of referred excipient.*
iv. *As per our internal quality protocols, the release production of these batches said product will remain on hold until completion of six months accelerated stability studies.*
v. *Lactose excipient having atypical particle size distribution (BSD) will no longer be used for this product."*

M/s Novartis Pharma (Pakistan) Limited vide reference no Nil dated 23-12-2020 regarding the subject cited above. They have submitted stability studies in response to office letter F.No.13-192/2019-(QC) dated 07-10-2020. They also submitted vide reference no Nil dated 14-01-2021 regarding the subject "Submission of initial time point test reports, manufacturing process validation and testing time points justification for Clomfranil 25mg tablet".

On evaluation of the receipt it was observed that dissolution and assay results were in specified limit. However, firm had mentioned in the Deviation Investigation Report that the referred excipient was taken as loan from GSK site area; while the supplier was not approved for Jamshoro site.

The firm was directed to stop production of the said product by Director QA&LT. Further, the firm has submitted their recall data along with CAPA. Firm has also submitted their accelerated stability studies.

Decision of 307th Meeting of Registration Board

Registration Board after detailed discussion and deliberations considering the facts of the case advised QA Division to again review the case as per relevant rules and present the case in next meeting if required.

The case has been reviewed and discussed with Chairman Registration Board and firm has directed to submitted following information/documents:

i. Particle size of Lactose excipient, approved sources and the source of lactose excipient having atypical particle size distribution with certificate of analysis.
ii. The validation study results of 03 batches as mentioned in CAPA
iii. Current recall status as per format of two subject mentioned batches.
iv. FAST study results of other affected batches of products where lactose excipient having atypical particle size distribution was used.

The firm submitted the documents as directed.

The firm was directed to stop production of the said product vide office letter of even number dated 04-11-2021, the firm have already been submitted the requisite information/ data.

Proceedings and Decision of 313th Meeting of Registration Board.

"The Board after considering the facts of the case and after thorough deliberations decided:

i. To resume the production of Clomfranil 25mg tablet.
ii. Area FID Karachi will take sample from 1st commercial batch for test/analysis by CDL Karachi on the expense of the manufacturer. Firm will sell the product after standard report from CDL.

CASE No. VIII: INSPECTION AT M/S ATCO LABORATORIES, B-18, SITE, KARACHI STOCK ORDERED NOT TO DISPOSE OF ON FORM-1 UNDER SECTION 18(1) OF THE DRUGS ACT, 1976.

Mr. Awais Ahmed Juno, FID-IX, DRAP, Karachi vide letter No.F.03-03/2019-FID-IX (K) dated 17-09-2020 on subject cited above wherein the officer has stated that he inspected the premises of M/s Atco Laboratories, B-18, SITE, Karachi on 12th September, 2020 to check compliance of already issued order regarding suspension of lotion manufacturing in an unauthorized area dedicated for manufacturing of ointment. He has further state that during the course of inspection, the firm was found involved in manufacturing of lotion and enema in ointment manufacturing area.

The officer further informed that the detailed GMP inspection report has already been forwarded to QA section. The following Stock of manufactured lotion and dispensed material for enema has been ordered "Not to Dispose of" on Form-1 under section 18(1) of the Drugs Act, 1976 for 28 days initially for which FID has requested for extension in the period of order made "Not to Dispose of".

S. No.	Name of Drug	Reg. No	Batch No.	Quantity	Mfg. Date	Exp. Date	Purported to be Manufactured by
1.	Betaderm Lotion	027954	JV 192	3286	09-2020	09-2022	M/s Atco Laboratories, B-18, SITE, Karachi
			JV 193	3271	09-2020	09-2022	-do-
2.	Scabion Lotion	012229	GL216F	6534	09-2020	09-2023	-do-
			GL213F	4742	09-2020	09-2023	-do-
			GL214F	6532	09-2020	09-2023	-do-
3.	Clobederm Lotion	024516	CC033F	12250	09-2020	09-2023	-do-
4.	Acsolve Lotion	067528	JJ025F	4742	09-2020	09-2022	-do-
			JJ023F	4742	09-2020	09-2022	-do-
5.	Conaz Lotion	024518	KY159F	4084	09-2020	09-2022	-do-
			KY160F	4084	09-2020	09-2022	-do-
			KY158F	4084	09-2020	09-2022	-do-
6.	Micronema dispensed material	012651	NA051F	228Kg	-	-	-
			NA052F	228Kg	-	-	-

A letter to FID had been issued to take samples from the stock for test/analysis so that any quality defects in the products may be identified vide letter F. No. 13-43/2020-QC dated 23-10-2020.

The request of FID for extension in the period of "Stock ordered not to dispose of" has been acceded by the Chairman, Registration Board being authorized by the Registration Board under Section 18(1)(i) of the Drugs Act, 1976 till 11th December, 2020, communicated vide letter F. No. 13-43/2020-QC dated 23-10-2020, which has already been expired. No further extension was requested by FID in the matter.

A letter of Ms. Hira Bhutto, Area FID received dated 08-07-2021 was received in the office wherein she stated that the samples taken by the then FID declared as of Standard quality by Federal Government Analyst, CDL. She also mentioned that M/s. Atco Laboratories requested to pursue the subjected issue, the firm informed that most of the hold products have shelf life of 02 years and have already lost more than 25% shelf life of those batches before dispatch to market.

S. No.	Name of Drug	Batch No.	CDL Results
1	CONAZ LOTION	KY159F	Standard
2	CONAZ LOTION	KY160F	Standard
3	SCABION LOTION	GL213F	Standard
4	SCABION LOTION	GL214F	Standard
5	SCABION LOTION	GL216F	Standard
6	BETADERM LOTION	JU192F	Standard
7	BETADERM LOTION	JV 193F	Standard
8	ACSOLVE LOTION	JJ025F	Standard
9	ACSOLVE LOTION	JJ023F	Standard
10	CLOBEDERM LOTION	CC033F	Standard

FID requested to submit clear cut recommendations as per law vide letter of even number dated 14-09-2021.

Mr. Abdul Rasool Shaikh, Area FID replied as:

> *"[…] After thorough review of the case and CDL reports thereof it seems that no apparent violations were noted hence it is recommended that order passed by the then FID for "Not to dispose of" may kindly be revoked and the firm may be allowed to consume the goods in larger interest of public."*

In view of above, according to Schedule V (1)(i) of the DRAP Act, 2012, FID can order not to disposed of for a reasonable period not exceeding 04 weeks or such further period which shall not be more than 03 months with the approval of the Board concerned.

Furthermore, Schedule V (5)(a) of the DRAP Act, 2012 read with Section 19 (5) (a) of Drug Act 1976; FID as soon as practicable ascertain whether or not the therapeutic good contravenes any of the provisions of this Act and, it is ascertained that the drug does not so contravene, he shall forthwith revoke the order passed under the said section under intimation to the Board concerned.

The current status of Lotion Section and Enema section have been asked from QA section and Licensing Division. QA section submitted that the Lotion (General) Section has been approved vide letter no. F.2-5/85-Lic (Vol-II) dated 18-03-2021. While Licensing Division has informed that no formal approval letter of Enema Section has been issued from CLB, only Layout Paln was regularized vide letter dated 20-07-2017.

The case is placed in light of CDL reports, sections status and with the FID's recommendations i.e. 'to revoke the orders.'

Proceedings and Decision of 313th Meeting of Registration Board.

The Board after thorough deliberations and considering the facts of the case decided as

i. **Direct the area FID to proceed as per Law.**
ii. **Production of Registered Products of Enema Section (General) will be suspended till the formal approval of Enema Section (General) from Central Licensing Board.**

CASE No. IX: HANDLING REQUESTS OF APPELLATE TESTING- GUIDANCE DOCUMENT FOR REGISTRATION BOARD

The firms requested for Appellate Testing from NIH and cases have been received time to time. 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 cases are submitted for consideration of Board. Therefore, a guidance document is designed for smooth functioning with the title "Handling the requests of Appelate testing- Guidance document for Registration Board.

Proceedings and Decision of 312th meeting:

The Board after thorough deliberations on the mater decided to defer the case whilst instructing the division of QA&LT to develop a comprehensive guidance document/protocol and present the said document in the forthcoming meeting of the Board.

A guidance document has been designed. (Annexure-A)

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.**

CASE No. X: MANUFACTURE & SALE OF SUBSTANDARD LETIRIX SYRUP, REG. NO. 068438, BATCH NO. L2033, MFG. DATE 10-020, EXP. DATE 09-022, MANUFACTURED BY M/S. ALLIANCE PHARMACEUTICALS (PVT) LIMITED, PESHAWAR.

The Federal Inspector of Drug, DRAP, Peshawar visited the premises of M/s Alliance Pharmaceuticals (Pvt) Limited, 112-A, Hayatabad Industrial Estate, Peshawar on 16-10-2020 wherein the sample of Letirix Syrup, Batch No. L-0233, Manufactured by M/s. Alliance Pharmaceuticals (Pvt) Limited, Peshawar was drawn under Schedule-V (1) (C) of DRAP Act, 2012

read with section 18 (1) (C) of the Drugs Act, 1976 for the purpose of test/analysis. Details are as under;

S. N0.	Name of Drug	Reg. No.	Batch No.	Mfg. Date	Exp. Date	Mfg. By	Basis of Sub-Standard
01	Letirix Syrup	068438	L2033	10-020	09-022	M/s. Alliance Pharmaceuticals (Pvt) Limited, Peshawar	Assay does not comply

The said sample was sent to the Government Analyst, Central Drugs Laboratory, Karachi vide memorandum No.F.10-269-271/2020-Alliance-DRAP-4005 dated 19-10-20. The Federal Government Analyst, CDL, Karachi vide their test report No.IP.130/2020 dated 04-01-2021 declared the above said sample as of substandard quality. Test results of the CDL, Karachi are reproduced as under:

S.No.	Test	Specification	Result	Reference
01.	Description	Clear, colourless syrup which is free from black particles.	Complies.	Mfg. Specs.
02.	Identification	Identification test must identify Levocetrizine Hydrochloride.	Complies	Mfg. Specs.
03.	pH	3.0 to 5.0	3.90-Complies	Mfg. Specs.
04.	**Assay** **Levocetrizine 2HCl (Label claim 2.5mg/5ml)**	90.0% to 110.0%	**69.5%** **Does not comply.**	Mfg. Specs.

Remarks: *The sample is **"Sub-Standard"** under the Drugs Act, 1976.*

The firm didn't agree to the results of CDL, Karachi and requested for retesting under Section 22(4) of the Drugs Act, 1976 and rules framed there under.

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 307th Meeting of Registration Board:

Registration Board after detailed discussion and considering the facts of the case decided to direct the firm to submit justification/scientific grounds for Appellate testing within 7 days.

The decision has been communicated to the firm vide office letter of even number dated 29-9-2021.

M/s. Alliance Pharmaceuticals (Pvt) Ltd, Peshawar vide Ref. No. AL/QC/021/014 dated 07-09-2021 in response to the decision letter of 307th meeting of Registration Board dated 03-09-2021. The stance of the firm is as follows:

> *"With reference to your letter No.F.03-15/2021-QC (307-RB) dated 3rd Sep, 2021, in which we M/S Alliance Pharmaceuticals (Pvt) Ltd are directed to submit justification/scientific ground for Appellate testing by the Drugs Registration Board.*
>
> *The Assay performed by Central Drugs Testing Laboratory of the cited above syrup on HPLC method while we M/S Alliance Pharmaceuticals (Pvt) Ltd adopted an extraction followed by UV/Visible Spectroscopic method, which is a valid method. (Method validation report attached).*
>
> *Alter CDL Karachi Report we M/S Alliance Pharmaceuticals (pvt) Ltd retested the retain samiple and market return of the same batch cited above on both HPLC and Extraction followed by UV and we observed interference in the retention time of API by an excipient on HPLC metlhod.*
>
> *As our product is of internal specifications and not included in any pharmacopeia, so we adopted Extraction followed by UV method. It is kindly requested to please consider our request for Appellate testing and perform the Assay of the batch cited above through extraction followed by UV method (Method and its results attached)."*

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 Substandard quality.

Case No. XI: <u>MANUFACTURE & SALE OF SUBSTANDARD PANTOPEP TABLETS, BATCH NO. 911, REG. NO. 064137, MANUFACTURED BY M/S HASSAN PHARMACEUTICALS (PVT.) LTD., PESHAWAR.</u>

The Federal Inspector of Drugs, DRAP visited the premises of M/s Hassan Pharmaceuticals (Pvt.) Ltd., Peshawar on 10-09-2020 where in the following drug was taken for the purpose of test/analysis on prescribed Form-3. Details are as under:

S. N0.	Name of Drug	Registration No.	Batch No.	Mfg. Date	Exp. Date	Mfg. By	Basis of Sub-Standard
01	Pantopep Tablet	064137	911	10-19	09-21	M/s. Hassan Pharmaceuticals (Pvt.) Ltd., Peshawar.	Dissolution test does not comply

The sealed sample of the above said drug was sent by the FID, DRAP, Peshawar to FGA, CDL, Karachi for the purpose of test/analysis vide memorandum No.F**.**10-264-265/2020-Hassan-FID-I/III-DRAP-3433 dated 14-09-2020. The Federal Government Analyst, CDL, Karachi vide their test report No.IP.100/2020 dated 26-11-2020 declared the above said sample as of substandard quality. Test results of the CDL, Karachi are reproduced as under:

S.No.	Test	Acceptance Criteria	Results	Reference
1	Description	Light brown biconvex enteric coated tablets having word "Hassan" on one side	Complies.	Mfg. Specs
2	Identification	The identification test must identify Pantoprazole Sodium.	Complies.	USP 43
3	Dissolution	Each unit is not less than 75% (Q)	**Does not Comply**	USP 43
4	Uniformity of dose units by weight variation	Acceptance value should be less than or equal to L1 (L1 is 15)	14.73. Complies.	USP 43
5	**Assay** Pantoprazole Label claim is 40mg/tablet.	90% to 110%	107.1%. Complies.	USP 43

<u>REMARKS:</u> *The sample is of substandard quality under the Drugs Act, 1976.*

M/s Hassan Pharmaceuticals (Pvt.) Ltd., Peshawar was asked by the FID, DRAP, Peshawar to explain their position via letter No. F.11-15/2020-Hassan-DRAP-5 dated 23-12-2020. M/s Hassan Pharmaceuticals (Pvt.) Ltd., Peshawar submitted their reply vide letter No. nil dated nil wherein they have requested for retesting of the above said drug from NIH, Islamabad. The FID, DRAP, Peshawar established that firm has contravened the section 23(I)(a)(v) of the Drug Act, 1976 and concluded that portion of the sample lying with the Board may be got retested from Appellate Laboratory, NIH, Islamabad as requested by the firm.

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.

<u>Decision of 307th Meeting of Registration Board</u>

Registration Board after detailed discussion and deliberations considering the facts of the case decided to direct the firm to submit justification/scientific grounds for Appallate testing within 7 days.

The decision has been communicated to the firm vide office letter of even number dated 29-09-2021.

M/s. Hassan Pharmaceuticals Peshawar in reference to office letter of even number dated 29-09-2021 submitted the test reports along with chromatograms and challenged the CDL report.

<u>Proceedings and Decision of 313th Meeting of Registration Board.</u>

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 Hassan Pharmaceuticals (Pvt.) Ltd., Peshawar and called them for personal hearing before Registration Board.

CASE NO. XII: **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	-
02	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.

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.**

CASE NO. XIII: **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.

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.**

Case No. XIV: Manufacture & Sale of Substandard Protonix 40mg Tablet, Reg. No. 030041, Batch No. 069, Mfg. Date Jan 2020, Exp. Date Jan 2023, Manufactured by M/s. Wilshire Laboratories (Pvt.) Limited., Lahore.

FID Lahore inspected the premises of M/s. Wilshire Laboratories (Pvt) Limited., Lahore wherein following sample of drug was 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 **"Sub-Standard"** quality vide their test report No. No. LHR.18/2021 dated 21-05-2021

S. No.	Name of Drug	Reg. No	Batch No.	Mfg. Date	Exp. Date	Mfg. By	Result of CDL	Basis of Result
01	Protonix tablet	030041	069	01/2020	01/2023	M/s. Wilshire Laboratories (Pvt) Limited., Lahore	Sub-standard	Dissolution

Results of CDL on the basis of which sample under reference has been declared as Substandard quality are reproduced as under:-

S.No.	Test	Acceptance Criteria	Result	Reference
1.	Description	Yellow colored circular enteric coated tablet.	Complies.	Mfg. Specs.
2.	Identification	The identification test must identify Pantoprazole Sodium.	Complies.	USP 43
3.	Dissolution	S1: Each unit is not less than 75% (Q). S2: Average of 12 units (S1+S2) is equal to or greater than Q (75%) and no unit is less than Q-15 (75-15=60%)	**Does not comply.** **Does not comply.**	USP 43 USP 43
4.	Uniformity of Dosage units by weight variation.	Acceptance value should be less than or equal to L1 (L1 to L15)	11.694-Complies.	USP 43
5.	**Assay.** Pantoprazole. (Label claim 40mg/tablet)	90.0% to 110.0%	106.6%-Complies	USP 43

Remarks:
1) S3 is not required as 09 tablets out of 12 tablets are already found below 60% (Q-15) in S2.
2) The sample is **"Sub-Standard"** under the Drugs Act, 1976.

FID submitted the firm's request for retesting of sample from NIH.

Proceedings and Decision of 313th Meeting of Registration Board.

i. **The Product 'Protonix 40mg Tablet' has already been suspended by Registration Board in its 293rd meeting on the basis of Sub-standard report of CDL and NIH.**
ii. **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.**
iii. **Federal Government Analyst, Karachi will provide OOS investigation and complete testing record of such reports.**

Item No. IV Division of Biological Evaluation & Research

Sr. No.	Details of application	No. of Cases
A	Emergency Use Authorization of COVID-19 Vaccines	09
B	Imported Human Biologicals from Reference Countries/WHO prequalified	04
C	Imported Human Biologicals from Non-Reference Countries	07
D	Imported Veterinary Biologicals from Non-Reference Countries	10
E	Locally Manufactured Veterinary Biologicals	01
F	Miscellaneous/ Deferred Cases	23
Additional Agenda		05
Total		59

Sr. No.	Assistant Director	Designated No.	No. of Cases
1.	Mr. M. Zubair Masood	AD-I	28
2.	Mr. Saadat Ali Khan	AD-II	15
3.	Ms. Haleema Sharif	AD-III	16

A: Emergency Use Authorization of COVID-19 Vaccines

1. Covid-19 Vaccine applied by M/s Sind Medical Store, Karachi.

1.	**Name and address of Importer**	M/s Sindh Mdical Store, Sector 13B/B-10, Block 6, PECHS, Karachi.
	Detail of DSL	Copy of DSL No. 1296 dated 14-07-2020 valid till 01-07-2022.
	Name and address of Manufacturer	M/s Bharat Biotech International Limited, Sy. No. 230, 231, & 235, Genome Valley, Telangana State, Turkapally (V), Shamirpet (M), Medchal- Malkajgiri (Dist.) 500078, India.
	Brand Name +Dosage Form + Strength	Covaxin Whole Virion, Inactivated Corona Virus Vaccine
	Diary No. Date of R& I & fee	Dy. No. 15614, 17158, 19775 (R&I) Dated 04-06-2021, 21-06-2021, 14-07-2021 Rs. 75,000/- Dated 02-06-2021
	Composition	Each dose of 0.5ml contains: Whole Virion, Inactivated Corona Virus antigen Strain NIV-2020-770…….6mcg
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	36 months (2^0C-8^0C)
	Document Details	• Notarized Copy of FSC No. 57829/TS/2021 dated 01-04-2021 valid till 01-04-2022 • Notarized copy of sole authorization letter dated 25-05-2021 valid for 24 months.
	Pack size	1's Vial (0.5mL)
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	SARS-CoV-2 Vaccine (Vero Cell), Inactivated Vial (Reg. No. 107887) of M/s NIH, Islamabad.

2.	**Name and address of Importer**	M/s Sindh Mdical Store, Sector 13B/B-10, Block 6, PECHS, Karachi.
	Detail of DSL	Copy of DSL No. 1296 dated 14-07-2020 valid till 01-07-2022.
	Name and address of Manufacturer	M/s Bharat Biotech International Limited, Sy. No. 230, 231, & 235, Genome Valley, Telangana State, Turkapally (V), Shamirpet (M), Medchal- Malkajgiri (Dist.) 500078, India.
	Brand Name +Dosage Form + Strength	Covaxin Whole Virion, Inactivated Corona Virus Vaccine
	Diary No. Date of R& I & fee	Dy. No. 15614, 17158, 19775 (R&I) Dated 04-06-2021, 21-06-2021, 14-07-2021 Rs. 75,000/- Dated 02-06-2021
	Composition	Each dose of 0.5ml contains: Whole Virion, Inactivated Corona Virus antigen Strain NIV-2020-770…….6mcg
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	36 months (2^0C-8^0C)
	Document Details	• Notarized Copy of FSC No. 57829/TS/2021 dated 01-04-2021 valid till 01-04-2022 • Notarized copy of sole authorization letter dated 25-05-2021 valid for 24 months.
	Pack size	1's Vial (5mL)
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	SARS-CoV-2 Vaccine (Vero Cell), Inactivated Vial (Reg. No. 107887) of M/s NIH, Islamabad in pack size of 1 dose.
3.	**Name and address of Importer**	M/s Sindh Mdical Store, Sector 13B/B-10, Block 6, PECHS, Karachi.
	Detail of DSL	Copy of DSL No. 1296 dated 14-07-2020 valid till 01-07-2022.
	Name and address of Manufacturer	M/s Bharat Biotech International Limited, Sy. No. 230, 231, & 235, Genome Valley, Telangana State, Turkapally (V), Shamirpet (M), Medchal- Malkajgiri (Dist.) 500078, India.
	Brand Name +Dosage Form + Strength	Covaxin Whole Virion, Inactivated Corona Virus Vaccine
	Diary No. Date of R& I & fee	Dy. No. 15614, 17158, 19775 (R&I) Dated 04-06-2021, 21-06-2021, 14-07-2021 Rs. 75,000/- Dated 02-06-2021
	Composition	Each dose of 0.5ml contains: Whole Virion, Inactivated Corona Virus antigen Strain NIV-2020-770…….6mcg
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	36 months (2^0C-8^0C)
	Document Details	• Notarized Copy of FSC No. 57829/TS/2021 dated 01-04-2021 valid till 01-04-2022 • Notarized copy of sole authorization letter dated 25-05-2021 valid for 24 months.
	Pack size	1's Vial (10mL)
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	SARS-CoV-2 Vaccine (Vero Cell), Inactivated Vial (Reg. No. 107887) of M/s NIH, Islamabad in pack size of 1 dose.

DRAP Authority in its 101st meeting held on 06-01-2021, while exercising its power under Rule 26 of Drugs (LRA) Rules amended via SRO 713 (I)/ 2018 dated 08-06-2018, allowed to submit registration application on Form-5/ Form 5-A/ Form 5-D instead of Form 5F for registration of COVID-19 vaccines **till 06-06-2021.**

Moreover, Policy Board of DRAP in its 35thmeeting exempted the inspections of manufacturing sites abroad for COVID-19 vaccines and drugs for a period of one year.

Assessment by the Division of Biological Evaluation and Research

i. WHO has granted EUL to above products on 03-11-2021 with 9 months shelf life and age group of 18 and above.
ii. The weblink of WHO EUL is as follows:
https://extranet.who.int/pqweb/vaccines/who-recommendation-bharat-biotech-international-ltd-covid-19-vaccine-whole-virion
iii. Details of stability data provided by the firm is as follows:

Sr. No.	Name of Product	Pack Size	Real Time	Accelerated
1.	Covaxin	0.5mL Vial	6 months	3 months
2.		5mL Vial	3 months	3 months
3.		10mL Vial	3 months	3 months

iv. Recommendations from Clinical Expert Committee are not yet received.

2. COVID-19 vaccine applied by M/s 2 World Traders Pakistan, Karachi.

1.	**Name and address of Importer**	M/s 2 World Traders Pakistan, Plot No. 55/2, Main Khayaban-e-Hafiz Phase-V, DHA, Karachi.
	Detail of DSL	Copy of DSL No. 316 dated 19-03-2021 valid till 15-03-2023
	Name and address of Manufacturer	M/s Wuhan Institute of Biological Products Co., Ltd., No.1, Huangjin Industrial Park Road, Zhengdian, Jiangxia, District, Wuhan, Hubei Province, China
	Brand Name +Dosage Form + Strength	Covilo Inactivated antigen of SARS-CoV-2 WIV04 strain
	Diary No. Date of R& I & fee	Dy. No. 21444 (R&I) Dated 05-08-2021 Rs. 75000/- dated 05-08-2021
	Composition	Each human dose (0.5mL) contains: Inactivated SARS-CoV-2 antigen…….200WU
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	12 months (2^0C-8^0C)
	Document Details	Copy of Drug License issued by NMPA accessed on official NMPA at http://app1.nmpa.gov.cn/data_nmpa/face3/base.jsp?tableId=25&tableName=TABLE25&title=%B9%FA%B2%FA%D2%A9%C6%B7&bcId=152904713761213296322795806604
	Pack size	1's Vial
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	SARS-CoV-2 Vaccine (Vero Cell), Inactivated Vial (Reg. No. 107887) of M/s NIH, Islamabad.
2.	**Name and address of Importer**	M/s 2 World Traders Pakistan, Plot No. 55/2, Main Khayaban-e-Hafiz Phase-V, DHA, Karachi.
	Detail of DSL	Copy of DSL No. 316 dated 19-03-2021 valid till 15-03-2023
	Name and address of Manufacturer	M/s Wuhan Institute of Biological Products Co., Ltd., No.1, Huangjin Industrial Park Road, Zhengdian, Jiangxia, District, Wuhan, Hubei Province, China
	Brand Name +Dosage Form + Strength	Covilo Inactivated antigen of SARS-CoV-2 WIV04 strain
	Diary No. Date of R& I & fee	Dy. No. 21445 (R&I) Dated 05-08-2021

		Rs. 75000/- dated 05-08-2021
	Composition	Each human dose (0.5mL) contains: Inactivated SARS-CoV-2 antigen…….200WU
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	12 months (2^0C-8^0C)
	Document Details	Copy of Drug License issued by NMPA accessed on official website of NMPA at http://app1.nmpa.gov.cn/data_nmpa/face3/base.jsp?tableId=25&tableName=TABLE25&title=%B9%FA%B2%FA%D2%A9%C6%B7&bcId=152904713761213296322795806604
	Pack size	1's PFS
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	SARS-CoV-2 Vaccine (Vero Cell), Inactivated PFS (Reg. No. 107879) of M/s NIH, Islamabad.

Assessment by the Division of Biological Evaluation and Research

i. Details of stability data provided by the firm is as follows:

Sr. No.	Name of Product	Real Time	Accelerated
1.	Covilo Vial	3 months	1 month
2.	Covilo PFS	6 months	3 months

ii. Recommendations from Clinical Expert Committee are not yet received.

3. COVID-19 vaccine applied by M/s Macter International, Karachi.

1.	**Name and address of Importer**	M/s Macter International Limited, F-216, S.I.T.E., Karachi.
	Detail of DSL	Copy of valid DSL is not submitted.
	Name and address of Manufacturer	M/s Anhui Zhifei Longcom Biopharmaceutical Co., Ltd., No. 100 Fushan Road, Hefei High-tech Development Zone, Anhui Province, China.
	Brand Name +Dosage Form + Strength	Zifivax Recombinant Novel Coronavirus Vaccine (CHO Cell)
	Diary No. Date of R& I & fee	Dy. No. 21571, 22928 (R&I) Dated 06-08-2021, 23-08-2021 Rs. 75000/- dated 30-07-2021
	Composition	Each vial (0.5mL) contains: NCP-RBD Protein…….25µg
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	24 months (2^0C-8^0C)
	Document Details	
	Pack size	1's Vial
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	Not Available

Assessment by the Division of Biological Evaluation and Research

A. Following documents not provided by the firm.
   i. Copy of valid Drug Sale License.
   ii. Original OR Notarized copy of Distribution Agreement as submitted document is MOU indicating that distribution rights shall be licensed to importer after EUA in formal commercial agreement.
   iii. Notarized copy of EUA issued by NMPA China along with web link of official website.
   iv. Notarized copy of EUA issued by Uzbekistan along with web link of official website.

v. Details of environment and water control processing.

B. Following documents not provided by the firm.

vi. Real time stability data provided is of 06 months.
vii. Accelerated stability data of six (06) months is provided.
viii. Recommendations from Clinical Expert Committee are not yet received.

4. COVID-19 vaccine applied by M/s Innovative Medical Solutions, Karachi.

1.	**Name and address of Importer**	M/s Innovative Medical Solutions, P60-A, SMCHS, Karachi
	Name and address of Manufacturer	M/s Sinovac Biotech Limited, Peking University Biological City, 39 Shangdi West Road, Haidian District, Beijing, PR China.
	Brand Name +Dosage Form + Strength	CoronaVac Covid-19 Vaccine (Vero Cell), Inactivated
	Diary No. Date of R& I & fee	Dy. No. 19197 (R&I) Dated 08-07-2021 Rs. 150,000/- Dated: 02-07-2021
	Composition	Each dose (0.5ml) contains: Inactivated SARS-CoV-2 as an antigen…….600SU
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	24 months (2^0C-8^0C)
	Document Details	Notarized copy of EUA from Philippines is submitted. https://www.fda.gov.ph/wp-content/uploads/2021/03/Package-Insert-v.10.pdf
	Pack size	1's Vial
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	Product is already registered in name of M/s Varitron, Lahore.

Assessment by the Division of Biological Evaluation and Research

A. Following documents not provided by the firm.

i. Initially the firm applied the import from Sinovac Biotech while the Coronavac is of M/s Sinovac Life Sciences. Later, the firm submitted the letter of authorization from Sinovac Life sciences However, **revised Form-5A is not submitted.**
ii. Pakistan Notarized copies of registration/ emergency use authorization certificates from country of origin is not submitted.
iii. Clinical trial data.
iv. Real time and accelerated stability data of vaccine.
v. Step wise details of manufacturing method.
vi. A full description of finished product specifications and analytical methods.
vii. Details of persons and equipment involved in product and quality control of drug product.
viii. Details of environment control and water processing facility.
ix. Recommendations from Clinical Expert Committee are not yet received.

5. Extension of the existing indication from "individuals 18 years of age and older" to "individuals 3 years of age and older" applied by M/s Varitron, Karachi for already registered COVID Vaccine *Coronavac.*

The Emergency use authorizations (EUAs) for COVID vaccine Coronavac of M/s Varitron were approved in 304th & 305th meetings of Registration Board and registration (EUA) letters were issued on 08-04-2021 & 07-05-2021 vide Registration numbers 107897 & 107931. EUA was granted for use in individual of age 18 years and above

The firm has now applied for Extension of the existing indication from "**individuals 18 years of age and older" to "individuals 3 years of age and older"** for their vaccines on the basis of recommendations of China.

In support the firm has submitted following documents.

i. Notarized copy of approval letter of 3 to 17 years age from Joint Prevention and Control Mechanism of the State Council Science & Research Technology Experts Team of Vaccine dated 15-07-2021.

Assessment by the Division of Biological Evaluation and Research

- News dated 17-09-2021 available on official website of NMPA indicates that China has administered more than 170 million doses to people aged 12 to 17 years.
- Another news dated 26-10-2021 available on official website indicates that many provinces had started vaccinating children aged 3 to 11 years.
- However, the evidence of the specific vaccine which is being used by China for above vaccination is not available on official website.

Submitted for consideration of Board please.

6. Approval of Sinopharm Vaccination for 12-18 years

M/s National Institute of Health, Islamabad vide letter dated 10-11-2021 received on 12-11-2021 submitted the following:

"It is intimated that Sinopharm Vaccine has been utilized for adults in Pakistan after EUA. Now the Ministry of Health is keen to get the EUA for children aged 12-18 years.

Your office is kindly requested to process the case."

Decision: Registration Board deferred all the above cases (related to COVID-19 vaccine) for recommendations of Expert Committee on evaluation of Clinical Trials.

B: Imported Human Biologicals from Reference countries/ WHO prequalified products.

1.	Name, address of Applicant / Importer	M/s Amson Vaccines& Pharma (Pvt.) Ltd., Plot No. 115, Industrial Triangle, Kahuta Road, Islamabad.
	Details of Drug Sale License of importer	License No: 920-ICT/2013 **Address** Plot No. 115, Industrial Triangle, Kahuta Road, Islamabad. Validity: 31-07-2022
	Name and address of marketing authorization holder (abroad)	M/s LG Chem, Ltd., 129, Seogam-ro, Iksan-si, Jeollabuk-do, Republic of Korea.
	Name, address of manufacturer(s)	M/s LG Chem, Ltd., 129, Seogam-ro, Iksan-si, Jeollabuk-do, Republic of Korea.
	Name of exporting country	South Korea
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted legalized CoPP (No. 2020-A1-0740) dated 27-03-2020 issued by Ministry of Food and Drug Safety, Korea. 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 manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Director, Exports of **M/S LG Chem, Ltd.** According to the letter, the firm **M/S LG Chem, Ltd** authorizes "M/s Amson Vaccines & Pharma (Pvt.) Ltd. for the purpose of registration, import, promotion, marketing, quoting in private & public (Government) tenders and negotiation with Ministry of Health, Pakistan & Hospitals for the 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	32047 (R&I) Dated: 02-12-2021
	Details of fee submitted	Rs: 100,000/- Dated: 02-12-2020
	The proposed proprietary name / brand name	**Euvax B™ Inj. 0.5 ml (10 µg),** **Single dose Vial (Recombinant), IM Use Only**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 0.5 ml vial contains: Purified Hepatitis B Surface Antigen 10 µg
	Dosage form of applied Drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Human Recombinant Vaccine
	Reference to Finished product specifications	Ph. Eur
	Proposed Pack size	1's Vial /0.5 ml
	Proposed unit price	As per SRO
	Shelf Life	36 months
	Storage Conditions	2-8 ˚C
	The status in reference regulatory authorities	Poland, South Africa, Romania, Argentina
	For generic drugs (me-too status)	Engerix-B Inj 10 µg /0.50 ml 1 Vial by GSK
	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	M/s LG Chem, Ltd., Iksan Plant # 129, Seogam-ro, Iksan-si, Jeollabuk-do, 54588, South Korea.
	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 recombinant Hepatitis B vaccine at real time conditions and Ongoing stability study with one batch of drug substance was performed according to the ICH Guideline. The real time stability data is conducted at 5 ± 3˚C for 18 months and Ongoing stability is conducted at 25±2˚C for 30 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 details of analytical method validation.
	Container closure system of the drug product	• 0.5/1.0 ml clear, colorless untreated borosilicate Type I Glass • Grey Chlorobutyl elastomer, PH21/50 • Aluminum seal / Polypropylene flip-off cap.
	Stability study data of drug product, shelf life and storage	Firm has submitted stability study data of 3 batches of Euvax B at accelerated and real time conditions. The real time stability

	conditions	data is conducted at 5 ± 3˚C for 42 months and accelerated stability is conducted at 25±2˚C for 06 months
	Module-IV Non-Clinical	Non clinical study In order to confirm the safety profile of the product, three toxicology studies is conducted. Single-dose toxicity in rats, repeat-dose toxicity in rats, and Reproductive and developmental toxicity study in rats was conducted.
	Module-V Clinical	**Phase III clinical trial:** A Blind observer Randomised Parallel group Active controlled Study to Assess the Immunogenicity and Safety of the product Compared to Engerix B in Healthy Children 0 Months to 15 Years of Age (198 subjects) Post-marketing safety study conducted in Korea
	Remarks	The product is WHO prequalified and prequalification status is accessed on 12-11-2021. The weblink is as follows: https://extranet.who.int/pqweb/content/euvax-b-1
Decision: Keeping in view WHO Prequalification and valid 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.	Name, address of Applicant / Importer	M/s Amson Vaccines& Pharma (Pvt.) Ltd., Plot No. 115, Industrial Triangle, Kahuta Road, Islamabad.
	Details of Drug Sale License of importer	License No: 920-ICT/2013 Address Plot No. 115, Industrial Triangle, Kahuta Road, Islamabad. Validity: 31-07-2022
	Name and address of marketing authorization holder (abroad)	M/s LG Chem, Ltd., 129, Seogam-ro, Iksan-si, Jeollabuk-do, Republic of Korea.
	Name, address of manufacturer(s)	M/s LG Chem, Ltd., 129, Seogam-ro, Iksan-si, Jeollabuk-do, Republic of Korea.
	Name of exporting country	South Korea
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted legalized CoPP (No. 2020-A1-0740) dated 27-03-2020 issued by Ministry of Food and Drug Safety, Korea. 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 manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Director, Exports of **M/S LG Chem, Ltd.** According to the letter, the firm **M/S LG Chem, Ltd** authorizes "M/s Amson Vaccines & Pharma (Pvt.) Ltd. for the purpose of registration, import, promotion, marketing, quoting in private & public (Government) tenders and negotiation with Ministry of Health, Pakistan & Hospitals for the 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	32046 (R&I) Dated: 02-12-2020
	Details of fee submitted	Rs: 100,000/- Dated: 02-12-2020
	The proposed proprietary name /	Euvax B™ Inj. 1.0 ml (20 µg),

	brand name	Single dose Vial (Recombinant), IM Use Only
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1.0 ml vial contains: Purified Hepatitis B Surface Antigen 20 µg
	Dosage form of applied drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Human Recombinant Vaccine
	Reference to Finished product specifications	Ph. Eur
	Proposed Pack size	1's Vial /1.0 ml
	Proposed unit price	As per SRO
	Shelf Life	36 months
	Storage Conditions	2-8 ˚C
	status in reference regulatory authorities	Poland, South Africa, Romania, Argentina
	For generic drugs (me-too status)	Engerix-B Inj 20 µg /1.0 ml 1 Vial by GSK
	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	M/s LG Chem, Ltd., Iksan Plant # 129, Seogam-ro, Iksan-si, Jeollabuk-do, 54588, South Korea.
	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 Recombinant Hepatitis B vaccine at real time conditions and Ongoing stability study with one batch of drug substance was performed according to the ICH Guideline. The real time stability data is conducted at 5 ± 3˚C for 18 months and Ongoing stability is conducted at 25±2˚C for 30 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 details of analytical method validation.
	Container closure system of the drug product	• 0.5/1.0 ml clear, colorless untreated borosilicate Type I Glass • Grey Chlorobutyl elastomer, PH21/50 • Aluminum seal / Polypropylene flip-off cap.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of Euvax B at accelerated and real time conditions. The real time stability data is conducted at 5 ± 3˚C for 42 months and accelerated stability is conducted at 25±2˚C for 06 months
	Module-IV Non-Clinical	Non clinical study In order to confirm the safety profile of the product, three toxicology studies is conducted. Single-dose toxicity in rats,

		repeat-dose toxicity in rats, and Reproductive and developmental toxicity study in rats was conducted.
	Module-V Clinical	**Phase III clinical trial:** A Blind observer Randomised Parallel group Active controlled Study to Assess the Immunogenicity and Safety of the product Compared to Engerix B in Healthy Children 0 Months to 15 Years of Age (198 subjects) Clinical trials of recombinant hepatitis B vaccine produced by LG Chem. Ltd. (Brand Name : Euvax-B) were performed in 107 adults and 103 children, successfully finished the clinical tests, from September, 1995 to March, 1997 during 19 months. Post-marketing safety study conducted in Korea
	Remarks	The product is WHO prequalified and prequalification status is accessed on 12-11-2021. The weblink is as follows: https://extranet.who.int/pqweb/content/euvax-b-1
Decision: Keeping in view WHO Prequalification and valid 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, address of Applicant / Importer	M/s Pfizer Pakistan Limited, 12 Dockyard Road West Wharf, Karachi.
	Details of Drug Sale License of importer	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 Europe MA EEIG Boulevard de la Plaine 17, 1050, Bruxelles, Belgium
	Name, address of manufacturer(s)	M/s Pfizer Manufacturing Belgium NV Rijksweg 12, Puurs, 2870, Belgium
	Name of exporting country	Belgium
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted original, legalized CoPP (No. 08/20/149787) dated 14-10-2020 valid for five years issued by European Medicine Agency Belgium. 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	Firm has submitted Letter of product specific authorization from Senior Director Global Regulatory Affairs of *M/s Pfizer Europe MA EEIG Boulevard de la Plaine 17, 1050, Bruxelles, Belgium*. According to the letter, the firm *M/s Pfizer Europe MA EEIG* 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 07-09-2020.
	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. 2779: 25-01-2021
	Details of fee submitted	PKR 100,000/-: 14-01-2021
	The proposed proprietary name / brand name	RUXIENCE (rituximab) Concentrate for solution for Infusion 100mg
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Rituximab……100mg
	Dosage form of applied drug	Concentrate for solution for infusion
	Pharmacotherapeutic Group of (API)	Antineoplastic agents, monoclonal antibodies
	Reference to Finished product specifications	As per Innovator.
	Proposed Pack size	1's Vial
	Proposed unit price	Not Provided.
	Shelf Life	24 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	EMA, Belgium
	For generic drugs (me-too status)	Ristova Solution for Infusion 100mg/10ml by Roche Pakistan
	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 Boehringer Ingelheim Pharma GmbH & Co KG, Birkendorfer Straße 65, 88397 Biberach an der Riss Germany
	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 6 batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at -40^0C±10^0C is for 60 months for 3 batches and for 24 months for 03 batches. The real time stability data conducted at -20^0C±5^0C is for 60 months for 3 batches and for 24 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 the analytical procedures is performed to ensure the characteristics, identity, purity, biological activity, product-related impurities, and safety of drug product met the requirements described in ICH Q2 (R1): Validation of Analytical Procedures: Text and Methodology, and the current USP Verification of Compendial Methods. Compendial analytical procedures used for release and stability studies are appearance (after reconstitution, which includes visible particulates, clarity, and coloration), particulate matter, pH, osmolality (release only), moisture content, uniformity of dosage units (release only), sterility, and endotoxin. These analytical procedures were verified and confirmed suitable for their intended use. Non-compendial analytical procedures used for batch release and stability studies and which are common to both the drug substance and drug product
	Container closure system of the drug product	• Vial - Type I borosilicate glass (clear and colorless) • Stopper - Chlorobutyl stopper with fluoropolymer film (ETFE, ethylene tertafluoroethylene) and cross-linked silicone coating. • Seal - Aluminum with a polypropylene tamper-evident flip-off cap that has no embossing.
	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 30±2^{O}C/75±5%RH for 12 months. The real time stability study data is conducted at 5±2^{O}C for 60 months.
	Module-IV Non-Clinical	Summarized in Biosimilarity data.
	Module-V Clinical	Summarized in Biosimilarity data.
4.	Name, address of Applicant / Importer	M/s Pfizer Pakistan Limited, 12 Dockyard Road West Wharf, Karachi.
	Details of Drug Sale License of importer	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 Europe MA EEIG Boulevard de la Plaine 17, 1050, Bruxelles, Belgium
	Name, address of manufacturer(s)	M/s Pfizer Manufacturing Belgium NV Rijksweg 12, Puurs, 2870, Belgium
	Name of exporting country	Belgium
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	• Firm has submitted original, legalized CoPP (No. 08/20/149787) dated 14-10-2020 valid for five years issued by European Medicine Agency Belgium. 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	Firm has submitted Letter of product specific authorization from Senior Director Global Regulatory Affairs of *M/s Pfizer Europe MA EEIG Boulevard de la Plaine 17, 1050, Bruxelles, Belgium*.

		According to the letter, the firm *M/s Pfizer Europe MA EEIG* 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 07-09-2020.
	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. 2780: 25-01-2021
	Details of fee submitted	PKR 100,000/-: 14-01-2021
	The proposed proprietary name / brand name	RUXIENCE (rituximab) Concentrate for solution for Infusion 500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Rituximab ……500mg
	Dosage form of applied drug	Concentrate for solution for infusion
	Pharmacotherapeutic Group of (API)	Antineoplastic agents, monoclonal antibodies
	Reference to Finished product specifications	As per Innovator.
	Proposed Pack size	1's Vial
	Proposed unit price	Not Provided.
	Shelf Life	24 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Belgium
	For generic drugs (me-too status)	Ristova Solution for Infusion 100mg/10ml by Roche Pakistan
	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 Boehringer Ingelheim Pharma GmbH & Co KG, Birkendorfer Straße 65, 88397 Biberach an der Riss

		Germany
	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 6 batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at -400C±100C is for 60 months for 3 batches and for 24 months for 03 batches. The real time stability data conducted at -200C±50C is for 60 months for 3 batches and for 24 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 the analytical procedures is performed to ensure the characteristics, identity, purity, biological activity, product-related impurities, and safety of drug product met the requirements described in ICH Q2 (R1): Validation of Analytical Procedures: Text and Methodology, and the current USP Verification of Compendial Methods. Compendial analytical procedures used for release and stability studies are appearance (after reconstitution, which includes visible particulates, clarity, and coloration), particulate matter, pH, osmolality (release only), moisture content, uniformity of dosage units (release only), sterility, and endotoxin. These analytical procedures were verified and confirmed suitable for their intended use. Non-compendial analytical procedures used for batch release and stability studies and which are common to both the drug substance and drug product
	Container closure system of the drug product	• Vial - Type I borosilicate glass (clear and colorless) • Stopper -Siliconized bromobutyl stopper • Seal - Aluminum with a polypropylene tamper-evident flip-off cap that has no embossing.
	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 30 ± 2^0C & 40 ± 2^0C /75±5%RH for 48 months & 6 months respectively. The real time stability study data is conducted at 5 ± 3^0C for 24 months.
	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. Verification of Rituximab Amino Acid Sequence via LC/MS – Subunit Analysis b. Verification of Rituximab Amino Acid Sequence via De Novo Sequencing

	c. Characterization of Molecular Mass, Primary Structure and Posttranslational Modifications d. HILIC/MS – N-Linked Glycan Mapping e. Total Afucosylation and Terminal Galactosylation and Individual N-linked Glycoforms • **Charge Heterogeneity** a. LC/MS Characterization of Charge Isoforms b. Additional Characterization of Basic Species c. Characterization by Carboxypeptidase B Treatment • **Disulfide Bonds** a. Elucidation of Disulfide Bonds and 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, Fluorescence d. Thermal stability of higher order structure by Differential Scanning Calorimetry (DSC)
Biological Activity & Immunochemical properties	Recorded in Primary Pharmacodynamics
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) d. SDS-PAGE (Reducing) and Western Blotting
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** a. Characterization of Complement Dependent Cytotoxicity (CDC) Function b. Characterization of Antibody-Dependent Cellular Cytotoxicity (ADCC) Function c. Characterization of Antibody Dependent Cellular Phagocytosis Function (ADCP) d. Additional Fc□ Receptor Binding SPR Assays e. FcRn Binding SPR Assay **Pharmacokinetic Studies** a. ELISA Assay Validation Report-Determination of Rituximab in Cynomolgus Monkey Serum By ELISA. b. Validation of an ECL Assay for the Detection of Anti-Drug Antibodies (ADA) Directed Against Mabthera (Rituximab-EU) in Monkey Serum c. Validation of an ECL Assay for the Detection of Anti-Drug Antibodies (ADA) Directed Against PF-05280586 (Rituximab-Pfizer) in Monkey Serum d. Single-Dose Intravenous Toxicokinetic and Tolerability Study with Rituximab-Pfizer and Rituximab-EU in cynomolgus Monkeys with a 13-Week Observation Period e. 4-Week Intravenous Injection Toxicity and Toxicokinetic Study with Rituximab-Pfizer and Rituximab-EU in Cynomolgus Monkeys with a 13-Week Recovery Phase f. Investigative Report: Single Nucleotide Polymorphisms in Cynomolgus Monkeys Receiving Rituximab-Pfizer and Rituximab-ER in Studies 11GR111 and 11GR112
Clinical Comparison	1. A Randomized, Double-Blind, Study Comparing the Pharmacokinetics and Pharmacodynamics, and Assessing the Safety of PF-05280586 and Rituximab in

	Subjects with Active Rheumatoid Arthritis on a Background of Methotrexate who have had an Inadequate Response to One or More TNF Antagonist Therapies. 2. A Phase 3, Randomized, Double-Blind Study of PF-05280586 versus Rituximab for the First-Line Treatment of Patients with CD20-Positive, Low Tumor Burden, Follicular. 3. Extension Study Evaluating Treatment with Pf-05280586 Versus Rituximab in Subjects with Active Rheumatoid Arthritis Who Have Participated in Other Pf-05280586 Clinical Trials
Remarks of Evaluator:	
Decision: Keeping in view legalized CoPPs indicating products availability in country of origin and approval of EMA (Reference Regulatory Authority); Registration Board approved the products subject to compliance of current Import Policy for finished drugs.	

C: Imported Human Biologicals from Non-reference countries

1.	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. 4584/E1/2019-18) dated 08-01-2020 valid till 22-10-2022 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)

	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. 33877 (R&I): 21-12-2020
	Details of fee submitted	PKR 100,000/-: 26-12-2020
	The proposed proprietary name / brand name	Bevaas 400mg (Bevacizumab 400mg/16mL)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 16mL vial contains: Bevacizumab……..400mg
	Dosage form of applied drug	Concentrate for Solution for Injection
	Pharmacotherapeutic Group of (API)	Anti-neoplastic agent
	Reference to Finished product specifications	As per Innovator.
	Proposed Pack size	1's Vial
	Proposed unit price	Not Provided.
	Shelf Life	24 months
	Storage Conditions	2^0C-8^0C
	The status in reference regulatory authorities	Abevmy 25mg/ml of M/s Mylan Products Limited, UK.
	For generic drugs (me-too status)	Bazumab 400mg of M/s Hilton (Reg. No. 107942)
	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 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 6 batches of Drug Substance at accelerated and real time conditions. The real time stability data conducted at -20^0C±5^0C is for 36 months for 6 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 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	• 20ml Vial - Type I borosilicate glass clear with crimp neck finish and flat bottom. • 20mm Grey Color Chlorobutyl rubber stopper. • 20mm Flip Off Aluminium Seal.
	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±2ºC for 6 months. The real time stability study data is conducted at 5±3ºC for 24 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	• **Identity/ Content** a. Protein Identity by Capillary Electrophoresis b. Protein Identity by SDS-PAGE (Non-reducing) c. Protein Concentration by UV 280 d. Protein Specificity by Western Blot • **Primary Structure** a. Peptide Mapping b. Intact Mass Analysis c. Amino Acid Sequencing by LC-MS/MS d. C-Terminal Sequencing e. N-Terminal Sequencing f. Glycan Site Identification • **Purity** a. SDS-PAGE b. Size Exclusion Chromatography • **Posttranslational Modifications** i. Far UV CD Spectroscopy ii. Fluorescence Spectroscopy (Extrinsic & Intrinsic) iii. Glycan Analysis iv. Hinge Region Identification v. Free Thiol Estimation vi. Charge Variant Distribution by Cation Exchange Chromatography (CEX) vii. Isoaspartic content Estimation viii. Sialic Acid Estimation (RP-UPLC)

Biological Activity & Immunochemical properties	a. VEGF Binding b. VEGF neutralization assay to measure biological efficacy c. FcRn Binding d. C1q Binding e. FcγR Binding
Impurities	• **Product Purity** a. LMW Impurities by SDS-PAGE (Non-reducing) b. Non-Glycosylated Heavy Chain (Reducing) c. HMW Impurities by SEC • **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	**Primary Pharmacodynamic Studies** Already detailed in Biological Activity. **Toxicology Studies** a. Single dose Toxicity studies in Swiss Albino Mice b. Single dose Toxicity studies in Wistar Rats c. 4 weeks Sub-Acute Toxicity Study in Wistar Rats (Repeat-dose) d. 4 weeks Sub-Acute Toxicity Study in New Zealand White Rabbits (Repeat-dose) e. Local Tolerance (Monkey) f. Skin Sensitization study 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 Bevacizumab with RMP. (n=137) 2. Open Label, Prospective, Multicentric Post-Marketing Study in patients of solid malignancies.

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.

2.	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: 1296 Address: Sector 13B/B-10, Block-6, PECHS, Karachi Address of go-down: N/A Validity: 01-07-2022 Status: License to sell drugs by way of Distributor
	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.2021-A0-076) dated **15-01-2021** 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. 8789, 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	SK Albumin 20% Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 50ml contains: Human Serum Albumin……10g
	Dosage form of applied drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Human Albumin
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's Vial (50mL)
	Proposed unit price	As per DPC
	Shelf Life	39 months
	Storage Conditions	$30^0C \pm 2^0C$
	The status in reference regulatory authorities	Alburex 20 of M/s CSL Behring UK Limited.
	For generic drugs (me-too status)	AlbuRx 20% of M/s Hakimsons (Reg. No. 083695)
	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 of Analytical Procedures: Identification Total Protein Protein Composition Molecular Size Distribution Haem Prekallikerin Activator Potassium Sodium Aluminium Sterility Ethanol residue N-acetyl-dl-tryptophan contents Sodium caprylate
	Container closure system of the drug product	Glass vial Colorless Type II glass Chlorobutyl rubber type I stopper 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 40^OC for 6 months. The real time stability study data is conducted at 30^OC$\pm 2^0$C for 24 months.
	Module-IV	No non-clinical studies are performed.
	Module-V	No non-clinical studies are performed.
	Periodic Safety Update Report	Report of 5 years from 2010 to 2015.
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: 1296 Address: Sector 13B/B-10, Block-6, PECHS, Karachi Address of go-down: N/A Validity: 01-07-2022 Status: License to sell drugs by way of Distributor
	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.2021-A0-076) dated 15-01-2021 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. 8788 (R&I), 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	SK Albumin 20% Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Human Serum Albumin……20g
	Dosage form of applied drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Human Albumin
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	1's Vial (100mL)
	Proposed unit price	As per DPC
	Shelf Life	39 months
	Storage Conditions	$30^0C \pm 2^0C$
	The status in reference regulatory authorities	Alburex 20 of M/s CSL Behring UK Limited.
	For generic drugs (me-too status)	AlbuRx 20% of M/s Hakimsons (Reg. No. 087404)
	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 20C-80C 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 of Analytical Procedures: Identification Total Protein Protein Composition Molecular Size Distribution Haem Prekallikerin Activator Potassium Sodium Aluminium Sterility Ethanol residue N-acetyl-dl-tryptophan contents Sodium caprylate
	Container closure system of the drug product	Glass vial Colorless Type II glass Chlorobutyl rubber type I stopper 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 40OC for 6 months. The real time stability study data is conducted at 30OC±20C for 24 months.
	Module-IV	No non-clinical studies are performed.
	Module-V	No non-clinical studies are performed.
	Periodic Safety Update Report	Report of 5 years from 2010 to 2015.
Remarks of the evaluator: The firm has demanded shelf life of 39 months while provided stability data is of 24 months only. Moreover, the firm has not performed any non-clinical or clinical studies. It is evident from public assessment reports of different products approved in RRAs like Australia, Germany that these products were authorized on the basis of well-established use and no new non-clinical or clinical studies were performed.		
Decision: Keeping in view public assessment reports of Australia & Germany and legalized CoPPs indicating products availability in country of origin; Registration Board approved the products subject to compliance of current Import Policy for finished drugs.		
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/ Product License Holde (abroad)	M/s Centurion Ilac. San. Ve Tic AS Gayretteple MAH. Hossohbet Sok. No:6 Besiktas/Istanbul
	Name, address of manufacturer(s)	M/s Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	Name of exporting country	**Turkey**
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** • Firm has submitted original, legalized CoPP (No.2021/2799) dated 20-09-2021 valid upto 20-09-2023 issued by Turkish Medicines and Medical Devices Agency, Ministry of Health, Republic of Turkey. 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) **GMP:** • The firm has also submitted EudraGMP No. NL/H 18/2008748 inspection of this manufacturer was conducted on 2018-11-09 by the competent authority of Netherlands for Biological medicinal products (list of product types) i.e. Blood products. The EudraGMP has also been verified online on 05-07-2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Member of Board of M/s Centurion, Besiktas/Istanbul According to the letter, the firm M/s Centurion, Besiktas/Istanbul certify that "M/s Himmel Pharmaceuticals (Pvt.) Ltd," with address "793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan" is their exclusive agent to register and market blood bloods including Albuman 20%, 50ml & 100ml vial in the territory of Pakistan. The letter was issued on 27-02-2020.
	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 25904 Dated 02-10-2020, Dy. No 14837 Dated 31-05-2021 & Dy. No 28708 Dated 20-10-2021,
	Details of fee submitted	Rs. 100,000/- Dated 11-09-2020
	The proposed proprietary name / brand name	**Albuman 20%,** 50ml vial Solution for Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient	Each 1000ml contains: Human Albumin (95%) ……200g

	(API) per unit	
	Dosage form of applied drug	A vial contains 10 g/50 ml of human albumin. The solution is clear, slightly viscous; it is almost colourless, yellow, amber or green.
	Pharmacotherapeutic Group of (API)	Plasma substitutes and plasma protein fractions
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	Pack Size: 1's (50ml glass vial)
	Proposed unit price	Retail price as per SRO
	Shelf Life	36 months
	Storage Conditions	Below 30 °C
	The status in reference regulatory authorities	The product itself approved by The *Medicines Evaluation Board (MEB) The Netherlands* (https://english.cbg-meb.nl/) Albutein 200 g/l (50ml vial), (EMC UK) Human Albumin Grifols 200 g/l (50ml vial) (EMC UK)
	For generic drugs (me-too status)	Human Albumin 20% 50ml by M/s Eastern Trade & Distribution Co. (Pvt) Ltd. & M/s Hakimsons Impex (Pvt) Ltd.
	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 Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	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 hold time of the Drug Substance of 5 days at 15 - 25°C is supported by hold time studies as per following details; In hold time studies three batches of Drug Substance 200 g/l and one batch of Drug Substance 40 g/l for verification are used to demonstrate at lab scale the stability of Drug Substance. Furthermore, testing one batch of Drug Substance 200 g/l in production is used the stability of Drug Substance 200 g/l at manufacturing scale. The study has been done for 5 days with time frequency of 0,3& 5 days at 20 ^{O}C -25 ^{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.
	Analytical method validation/verification of product	The specifications of the drug product are in compliance with the monograph on Human Albumin Solutions, Ph. Eur. 01/2008:0255 For all other characteristics the specification is the same as in the Ph. Eur.

		monograph except for aluminium, which specifications are lower for batch release but the same as in Ph. Eur. at the end of shelf life. This is a due precautionary measure which confirms the full compliance of the drug product with the Ph. Eur. specifications at the end of the shelf life Test methods related to the drug product specifications are presented in the dossier only for the test method that is not included in Ph. Eur. And validation data of the test methods are also included. The test methods and validations are provided for followings; Determination of Aluminum content with ICP-OES Aluminium-assay, linearity, limit of quantitation and limit of detection Quantitative measurement of caprylate & Caprylate assay Endotoxin-assay
	Container closure system of the drug product	Albuman 200 g/l is supplied in 50ml glass vials (transparent vials of type II glass, Ph. Eur.,) with Siliconised bromobutyl rubber stopper,(Type I closure, Ph. Eur. & silicone oil meets the reequipments of Ph. Eur.) and aluminium seal.
	Stability study data of drug product	Firm has submitted stability study data of 3 batches. The real time stability study data is conducted at 28 – 32 °C, 65%RH ± 5% RH for 36 months. The accelerated stability study data is conducted at 38 – 42 °C, 75%RH ± 5% RH for 6 months.
	Module-IV	In module 4 the firm has submitted that that Nonclinical data is not applicable for Albumin 40 mg/ml and Albumin 200 mg/ml, for this purpose they have referred the guideline on the core SPC for Human Albumin Solution (CPMP/PhVWP/BPWG/2231/99 rev.2), the following is stated regarding preclinical safety data (part 5.3): "Human albumin is a normal constituent of human plasma and acts like physiological albumin. In animals, single dose toxicity testing is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models. To date, human albumin has not been reported to be associated with embryo-foetal toxicity, oncogenic or mutagenic potential. No signs of acute toxicity have been described in animal models."
	Module-V	In module 5 the firm has submitted that Albumin was first approved by the FDA in 1942, and it was licensed in the USA in 1954. By the time albumin was included in the European definition of a medicinal product, in the early 1990's, albumin had been in clinical use for half a century. The pharmacological and physiological effects of albumin are well-established in humans, and clinical studies to demonstrate further safety and efficacy have not been deemed necessary with Albuman. Data are derived from the literature, among others from the albumin reviews. Albumin has been in clinical use for many decades and over time the use has evolved and a large number of clinical trials has been performed comparing the outcome of treatment with different volume expanders. Systematic reviews on these trials are submitted. Albuman 40 g/l and 200 g/l and its predecessors have been on the market since 1985. Post-marketing data have been collected by the MAH (originally by FRC BS) and over the entire marketing period, only 3 adverse events have been reported in association with the use of Albuman. The firm has also submitted Periodic Safety Update Reports & Phase IV data.

	Remarks:	i. Non-clinical & clinical trial data have not been submitted by the firm. And the firm has submitted justification from their manufacturer wherein it has been mentioned that non-clinical & clinical studies are not applicable for the said product as per following justification. *"Albumin is a normal component of human plasma acts like physiological albumin, Albumin products derived from human plasma have been used as medicinal products for many years and therefore known as "preparations with well-established use".* ***Non-clinical studies*** *In the EMA (European) guideline on the core SPC for Human Albumin Solution (EMA/CHMP/BPWP/494462/2011/Rev.3), the following is stated regarding preclinical safety data (part 5.3):* *"Human albumin is a normal constituent of human plasma and acts like physiological albumin.* *In animals, single dose toxicity testing is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models.* *To date, human albumin has not been reported to be associated with embryo-foetal toxicity, oncogenic or mutagenic potential.* *No signs of acute toxicity have been described in animal models."* **Clinical studies:** *Albumin has been clinically used for restoring colloidal osmotic pressure for more than 50 years. Therefore, the classical clinical development program has not been* *conducted with Albumin products. Data from literature studies indicate that albumin is safe and effective in the intended indication. Therefore, clinical data presented in* *Module 5 section of our registration dossier are within the scope of Literature references which is accepted in EU and Turkey authorities.*
Decision: Keeping in view legalized CoPP indicating product availability in country of origin and approval of Netherlands (Reference Regulatory Authority); Registration Board approved the products subject to compliance of current Import Policy for finished drugs.		
5.	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/ Product License Holde (abroad)	M/s Centurion Ilac. San . Ve Tic AS Gayretteple MAH. Hossohbet Sok. No:6 Besiktas/Istanbul
	Name, address of manufacturer(s)	M/s Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands.
	Name of exporting country	Turkey
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** • Firm has submitted original, legalized CoPP (No.2021/2800) dated 20-09-2021 valid upto 20-09-2023 issued by Turkish Medicines and Medical Devices Agency, Ministry of Health, Republic of Turkey.

		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) **GMP:** • The firm has also submitted EudraGMP No. NL/H 18/2008748 inspection of this manufacturer was conducted on 2018-11-09 by the competent authority of Netherlands for Biological medicinal products (list of product types) i.e. Blood products. The EudraGMP has also been verified online on 11-12-2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Member of Board of M/s Centurion, Besiktas/Istanbul According to the letter, the firm M/s Centurion, Besiktas/Istanbul certify that "M/s Himmel Pharmaceuticals (Pvt.) Ltd," with address "793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan" is their exclusive agent to register and market blood bloods including Albuman 20%, 50ml & 100ml vial in the territory of Pakistan. The letter was issued on 27-02-2020.
	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 25904 Dated 02-10-2020, Dy. No 14838 Dated 31-05-2021 & Dy. No 28711 Dated 20-10-2021
	Details of fee submitted	Rs. 100,000/- Dated 11-09-2020
	The proposed proprietary name / brand name	**Albuman** 20%, 100ml vial Solution for Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1000ml contains: Human Albumin (95%) ……200g
	Dosage form of applied drug	A vial contains 20 g/100 ml of human albumin. The solution is clear, slightly viscous; it is almost colourless, yellow, amber or green.
	Pharmacotherapeutic Group of (API)	Plasma substitutes and plasma protein fractions
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	Pack Size: 1's (100ml glass vial)
	Proposed unit price	Retail price As per SRO
	Shelf Life	36 months
	Storage Conditions	Below 30 °C
	The status in reference regulatory authorities	The product itself approved by The *Medicines* Evaluation *Board (MEB) The Netherlands* (https://english.cbg-meb.nl/) Albutein 200 g/l (100ml vial), (EMC UK)

		Human Albumin Grifols 200 g/l (100ml vial) (EMC UK)
	For generic drugs (me-too status)	Human Albumin 20% 100ml by M/s Eastern Trade & Distribution Co. (Pvt) Ltd. & M/s Hakimsons Impex (Pvt) Ltd.
	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 Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	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 hold time of the Drug Substance of 5 days at 15 - 25°C is supported by hold time studies as per following details; In hold time studies three batches of Drug Substance 200 g/l and one batch of Drug Substance 40 g/l for verification are used to demonstrate at lab scale the stability of Drug Substance. Furthermore, testing one batch of Drug Substance 200 g/l in production is used the stability of Drug Substance 200 g/l at manufacturing scale. The study has been done for 5 days with time frequency of 0,3& 5 days at 20-25 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.
	Analytical method validation/verification of product	The specifications of the drug product are in compliance with the monograph on Human Albumin Solutions, Ph. Eur. 01/2008:0255. For all other characteristics the specification is the same as in the Ph. Eur. monograph except for aluminium, which specifications are lower for batch release but the same as in Ph. Eur. at the end of shelf life. This is a due precautionary measure which confirms the full compliance of the drug product with the Ph. Eur. specifications at the end of the shelf life Test methods related to the drug product specifications are presented in the dossier only for the test method that is not included in Ph. Eur. And validation data of the test methods are also included. The test methods and validations are provided for followings; Determination of Aluminum content with ICP-OES Aluminium-assay, linearity, limit of quantitation and limit of detection Quantitative measurement of caprylate & Caprylate assay Endotoxin-assay
	Container closure system of the drug product	Albuman 200 g/l is supplied in 100ml glass vials (transparent vials of type II glass, Ph. Eur.,) with Siliconised bromobutyl rubber stopper, (Type I closure, Ph. Eur. & silicone oil meets the reequipments of Ph.

		Eur.) and aluminium seal.
	Stability study data of drug product	Firm has submitted stability study data of 3 batches. The real time stability study data is conducted at 28 – 32 °C, 65%RH ± 5% RH for 36 months. The accelerated stability study data is conducted at 38 – 42 °C, 75%RH ± 5% RH for 6 months.
	Module-IV	In module 4 the firm has submitted that that Nonclinical data is not applicable for Albumin 40 mg/ml and Albumin 200 mg/ml, for this purpose they have referred the guideline on the core SPC for Human Albumin Solution (CPMP/PhVWP/BPWG/2231/99 rev.2), the following is stated regarding preclinical safety data (part 5.3): "Human albumin is a normal constituent of human plasma and acts like physiological albumin. In animals, single dose toxicity testing is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models. To date, human albumin has not been reported to be associated with embryo-foetal toxicity, oncogenic or mutagenic potential. No signs of acute toxicity have been described in animal models."
	Module-V	In module 5 the firm has submitted that Albumin was first approved by the FDA in 1942, and it was licensed in the USA in 1954. By the time albumin was included in the European definition of a medicinal product, in the early 1990's, albumin had been in clinical use for half a century. The pharmacological and physiological effects of albumin are well-established in humans, and clinical studies to demonstrate further safety and efficacy have not been deemed necessary with Albuman. Data are derived from the literature, among others from the albumin reviews. Albumin has been in clinical use for many decades and over time the use has evolved and a large number of clinical trials has been performed comparing the outcome of treatment with different volume expanders. Systematic reviews on these trials are submitted. Albuman 40 g/l and 200 g/l and its predecessors have been on the market since 1985. Post-marketing data have been collected by the MAH (originally by FRC BS) and over the entire marketing period, only 3 adverse events have been reported in association with the use of Albuman. The firm has also submitted Periodic Safety Update Reports & Phase IV data.
	Remarks:	i. Non-clinical & clinical trial data have not been submitted by the firm. And the firm has submitted justification from their manufacturer wherein it has been mentioned that non-clinical & clinical studies are not applicable for the said product as per following justification. *"Albumin is a normal component of human plasma acts like physiological albumin, Albumin products derived from human plasma have been used as medicinal products for many years and therefore known as "preparations with well-established use".* ***Non-clinical studies*** *In the EMA (European) guideline on the core SPC for Human Albumin Solution (EMA/CHMP/BPWP/494462/2011/Rev.3), the following is stated regarding preclinical safety data (part 5.3):* *"Human albumin is a normal constituent of human plasma and acts like physiological albumin.*

		In animals, single dose toxicity testing is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models. *To date, human albumin has not been reported to be associated with embryo-foetal toxicity, oncogenic or mutagenic potential.* *No signs of acute toxicity have been described in animal models."* *Therefore,* **Clinical studies:** *Albumin has been clinically used for restoring colloidal osmotic pressure for more than 50 years. Therefore, the classical clinical development program has not been* *conducted with Albumin products. Data from literature studies indicate that albumin is safe and effective in the intended indication. Therefore, clinical data presented in* *Module 5 section of our registration dossier are within the scope of Literature references which is accepted in EU and Turkey authorities.*
Decision: Keeping in view legalized CoPP indicating product availability in country of origin and approval of Netherlands (Reference Regulatory Authority); Registration Board approved the products subject to compliance of current Import Policy for finished drugs.		
6.	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/ Product License Holder (abroad)	M/s Centurion Ilac. San . Ve Tic AS Gayretteple MAH. Hossohbet Sok. No:6 Besiktas/Istanbul
	Name, address of manufacturer(s)	M/s Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	Name of exporting country	Turkey
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** • Firm has submitted original, legalized CoPP (No.2021/2771) dated 17-09-2021 valid upto 23-03-2022 issued by Turkish Medicines and Medical Devices Agency, Ministry of Health, Republic of Turkey. 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) **GMP:** • The firm has also submitted EudraGMP No. NL/H 18/2008748 inspection of this manufacturer was conducted on 2018-11-09 by the competent authority of Netherlands for Biological medicinal products (list of product types) i.e. Blood products. The EudraGMP has also been verified online on 11-12-2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Member of Board of M/s Centurion, Besiktas/Istanbul According to the letter, the firm M/s Centurion, Besiktas/Istanbul certify that "M/s Himmel Pharmaceuticals (Pvt.) Ltd," with address "793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan" is their

		exclusive agent to register and market blood bloods including Cofact, 250IU/10ml & 500IU/20ml in the territory of Pakistan. The letter was issued on 27-02-2020. Firm has also submitted letter from Account Manager CDMO of the manufacturer M/s M/s Sanquin Plasma Products B.V., Netherland wherein the product license holder i.e. M/s Centurion, Besiktas/Istanbul has been authorized as exclusive and authorized distributor for export activities to Pakistan for the said products.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is I 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 25906 Dated 02-10-2020, Dy. No 14835 Dated 31-05-2021, Dy. No 15854 Dated 08-06-2021 & Dy. No 28710 Dated 20-10-2021
	Details of fee submitted	Rs. 50,000/- Dated 11-09-2020
	The proposed proprietary name / brand name	**Cofact** 250 IU, powder and solvent for solution for injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dose contains: Coagulation factor II …… 14 – 35 IU Coagulation factor VII…. 7 – 20 IU Coagulation factor IX…… 25 IU Coagulation factor X…. 14 – 35 IU *Protein C…….11– 39 IU *Protein S…….1 – 8 IU (* Anti-coagulation Proteins part of anticoagulant complex) **Solvent**: Water for Injection (10ml)
	Dosage form of applied drug	Cofact is supplied as a bluish, sterile and pyrogen-free lyophilised powder (250 IU) in vial and is supplied with a vial of water for injections.
	Pharmacotherapeutic Group of (API)	Antihemorrhagics, blood coagulation factors IX, II, VII and X
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	Pack Size: 1's (Cofact Powder for Solution for Injection 250IU/10ml in glass vial)
	Proposed unit price	Retail price as per SRO
	Shelf Life	36 months
	Storage Conditions	2°C-8°C
	The status in reference regulatory authorities	The product itself approved by The *Medicines* Evaluation *Board (MEB) The Netherlands* (https://english.cbg-meb.nl/)

		The product itself also approved by Finnish Medicine Agency, Finland https://www.fimea.fi/web/en/databases_and_registers/fimeaweb
	For generic drugs (me-too status)	Not registered
	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 Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	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 three stability studies for drug substance wherein data have been provided for Five batches for 18 months, three batches for 24 months and one batch for 24 months at Storage temperatures of - 25 °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.
	Analytical method validation/verification of product	The Cofact specifications are primarily based on Ph. Eur. Monograph 0554 Human Prothrombin Complex, supplemented with tests on AT, clarity (after reconstitution), colour (after reconstitution), stability (after reconstitution 3 hours at room temperature), sodium, citrate, TNBP, Tween 80, Protein C and Protein S. The methods which are described in detail in the Ph. Eur., i.e. the test for osmolality; solubility; total protein content; colour after reconstitution; clarity after reconstitution; endotoxins; pH; sodium and sterility, are not included in the dossier. The non-pharmacopoeial methods are provided in the dossier along with the potency assays, although described in the Ph. Eur, are also provided in the dossier. Validation of Analytical procedures are provided except for those test methods for which detailed description are published in Ph. Eur.
	Container closure system of the drug product	Cofact is supplied in hydrolytic glass vials with a bromobutyl rubber stopper, an aluminium cap and a flip-off seal. The primary container consists of colourless and transparent vials of type I glass (20 ml container for 10 ml of product) or Type II glass (50 ml container for 20 ml of product). These materials are routinely used for pharmaceutical products and are known to be inert. Bromobutyl rubber stoppers are widely used for parenteral products. The containers are packaged in secondary packaging material which protects the product from the influence of light. This is a standard

		precaution for this type of product. Cofact is not sensitive to light degradation. Cofact is supplied together with a vial of solvent, and a CE marked injection needle in a carton outer package.
	Stability study data of drug product	Firm has submitted stability study data of 3 batches. The real time stability study data is conducted at 2°C – 8 °C for 42 months. The accelerated stability study data is conducted at 30 °C for 24 months.
	Module-IV	In module 4 the firm has submitted that that "Prothrombin complex concentrates have been used for decades to restore deficient levels to normal values. This clinical practice has led to substantial proof of efficacy and safety of such products in treating patients with deficiencies. It is therefore not appropriate to investigate primary of secondary pharmacological effects of this plasma product in animal models." • Two thrombogenicity studies (one in rabbits and one in guinea pigs) were performed in order to investigate a possible change in thrombogenic potential of Cofact as compared to Prothrombin complex-SD. Furthermore, it has been submitted by the firm that "Standard toxicological investigations in animals have not been conducted, as they cannot be expected to contribute to the risk-benefit assessment of these naturally occurring plasma proteins. Naturally occurring humans proteins are not associated with mutagenic, carcinogenic or teratogenic effects in humans and there is no need to test such products in animal models." • Anaphylactic potential was studied in an in vivo rat model comparing the effect of Prothrombin complex-SD (the non-nanofiltered predecessor of Cofact) with pasteurised prothrombin complex (the heat-treated predecessor of Prothrombin complex-SD) on blood pressure. No hypotensive effects could be detected. However, it must be noted that this test was performed as part of quality control testing of a number of batches. The tests were not set up under GLP and were not reported in a study report. Therefore, the data should be considered as indicative only.
	Module-V	In module 5 the firm has submitted that the following studies; **Safety / PK study (Phase III study):** i. Open, not randomised, uncontrolled, Clinical tolerance, in vivo yield and PK "Evaluation of 'Prothrombin complex-SD' in haemophilia B" (No. subjects: 12) ii. Open, not randomised, uncontrolled, Clinical tolerance, in vivo yield and PK "Limited clinical evaluation of SD-treated (virus-inactivated) prothrombin complex with addition of a low concentration of AT (0.2 unit/ml)" (No. subjects: 3) **The above two studies were performed in patients with factor IX deficiency, haemophilia B.** Clinical pharmacology data on factor IX are available, but the other three coagulation factors, factor II, VII and X, cannot be studied in haemophilia patients. Therefore, the results of below mentioned study (comparing 2 Cofact dosing regimens) were used to describe the in vivo response and in vivo recovery data for factor II, VII, IX and X in patients on oral anticoagulants in an Addendum to the final report. **Efficacy /Safety (Phase IV study):** Open, randomised, comparative dose controlled- In vivo response and recovery of factor II, VII, IX and X "Reversal of oral anticoagulant therapy with Cofact, an open, randomised, single centre study with 93 patients treated with Cofact to

		reverse oral anticoagulant therapy" (No. subjects: 93) **Dose-finding Efficacy and safety (Phase IV study) :** Open, randomised, comparative dose controlled Compare efficacy of 2 dosage regimens (No. subjects: 28) **Efficacy /Safety(Phase IV study):** Open, randomised, comparative dose controlled-Compare efficacy of 2 dosage regimens "Reversal of oral anticoagulant therapy with Cofact, an open, randomised, single centre study with 93 patients treated with Cofact to reverse oral anticoagulant therapy" (No. subjects: 93) The firm has also submitted Periodic Safety Update Reports.
Decision: Keeping in view legalized CoPP indicating product availability in country of origin and approval of Netherlands (Reference Regulatory Authority); Registration Board approved the products subject to compliance of current Import Policy for finished drugs.		
7.	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/ Product License Holder (abroad)	M/s Centurion Ilac. San. Ve Tic AS Gayretteple MAH. Hossohbet Sok. No:6 Besiktas/Istanbul
	Name, address of manufacturer(s)	M/s Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	Name of exporting country	Turkey
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: • Firm has submitted original, legalized CoPP (No.2020/917) dated 23-03-2020 valid upto 23-03-2022 issued by Turkish Medicines and Medical Devices Agency, Ministry of Health, Republic of Turkey. 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) GMP: • The firm has also submitted EudraGMP No. NL/H 18/2008748 inspection of this manufacturer was conducted on 2018-11-09 by the competent authority of Netherlands for Biological medicinal products (list of product types) i.e. Blood products. The EudraGMP has also been verified online on 05-07-2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted letter of product specific authorization from Member of Board of M/s Centurion, Besiktas/Istanbul According to the letter, the firm M/s Centurion, Besiktas/Istanbul certify that "M/s Himmel Pharmaceuticals (Pvt.) Ltd," with address "793-D, Block 'C', Faisal Town, Lahore-54000, Pakistan" is their exclusive agent to register and market blood bloods including Cofact, 250IU/10ml & 500IU/20ml in the territory of Pakistan. The letter was issued on 27-02-2020. Firm has also submitted letter from Account Manager CDMO of the manufacturer M/s M/s Sanquin Plasma Products B.V., Netherland wherein the product license holder i.e. M/s Centurion, Besiktas/Istanbul has been authorized as exclusive and authorized distributor for export activities to Pakistan for the said products.

	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 25905 Dated 02-10-2020 ,Dy. No 14837 Dated 31-05-2021& Dy. No 2779 Dated 20-10-2021
	Details of fee submitted	Rs. 50,000/- Dated 11-09-2020
	The proposed proprietary name / brand name	Cofact 500 IU, powder and solvent for solution for injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Coagulation factor II …… 14 – 35 IU Coagulation factor VII….. 7 – 20 IU Coagulation factor IX…… 25 IU Coagulation factor X….. 14 – 35 IU *Protein C……..11– 39 IU *Protein S…….1 – 8 IU (* Anti-coagulation Proteins; parts of anticoagulant complex) **Solvent:** Water for Injection (20ml)
	Dosage form of applied drug	Cofact is supplied as a bluish, sterile and pyrogen-free lyophilised powder (500 IU) in vial and is supplied with a vial of water for injections.
	Pharmacotherapeutic Group of (API)	Antihemorrhagics, blood coagulation factors IX, II, VII and X
	Reference to Finished product specifications	Ph. Eur. Specifications
	Proposed Pack size	Pack Size: 1's (Cofact Powder for Solution for Injection 500IU/20ml in glass vial)
	Proposed unit price	Retail price as per SRO
	Shelf Life	36 months
	Storage Conditions	2°C-8°C
	The status in reference regulatory authorities	The product itself approved by The *Medicines* Evaluation *Board (MEB) The Netherlands* (https://english.cbg-meb.nl/) The product itself approved by Finnish Medicine Agency, Finland https://www.fimea.fi/web/en/databases_and_registers/fimeaweb
	For generic drugs (me-too status)	Not Registered
	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 Sanquin Plasma Products B.V., Plesmanlaan 125 1066 CX Amsterdam, Netherlands
	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 three stability studies for drug substance wherein data have been provided for Five batches for 18 months, three batches for 24 months and one batch for 24 months at Storage temperatures of - 25 °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.
	Analytical method validation/verification of product	The Cofact specifications are primarily based on Ph. Eur. Monograph 0554 Human Prothrombin Complex, supplemented with tests on AT, clarity (after reconstitution), colour (after reconstitution), stability (after reconstitution 3 hours at room temperature), sodium, citrate, TNBP, Tween 80, Protein C and Protein S. The methods which are described in detail in the Ph. Eur., i.e. the test for osmolality; solubility; total protein content; colour after reconstitution; clarity after reconstitution; endotoxins; pH; sodium and sterility, are not included in the dossier. The non-pharmacopoeial methods are provided in the dossier along with the potency assays, although described in the Ph. Eur, are also provided in the dossier. Validation of Analytical procedures are provided except for those test methods for which detailed description are published in Ph. Eur.
	Container closure system of the drug product	Cofact is supplied in hydrolytic glass vials with a bromobutyl rubber stopper, an aluminium cap and a flip-off seal. The primary container consists of colourless and transparent vials of type I glass, 50 ml container for 20 ml (500IU) of product. These materials are routinely used for pharmaceutical products and are known to be inert. Bromobutyl rubber stoppers are widely used for parenteral products. The containers are packaged in secondary packaging material which protects the product from the influence of light. This is a standard precaution for this type of product. Cofact is not sensitive to light degradation. Cofact is supplied together with a vial of solvent, and a CE marked injection needle in a carton outer package.
	Stability study data of drug product	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 30 °C for 24 months. The real time stability study data is conducted at 2°C – 8 °C for 42 months.
	Module-IV	In module 4 the firm has submitted that that "Prothrombin complex concentrates have been used for decades to restore deficient levels to normal values. This clinical practice has led to substantial proof of efficacy and safety of such products in treating patients with

		deficiencies. It is therefore not appropriate to investigate primary of secondary pharmacological effects of this plasma product in animal models." • **Two thrombogenicity studies (one in rabbits and one in guinea pigs) were performed in order to investigate a possible change in thrombogenic potential of Cofact as compared to Prothrombin complex-SD.** Furthermore, it has been submitted by the firm that "Standard toxicological investigations in animals have not been conducted, as they cannot be expected to contribute to the risk-benefit assessment of these naturally occurring plasma proteins. Naturally occurring humans' proteins are not associated with mutagenic, carcinogenic or teratogenic effects in humans and there is no need to test such products in animal models." • Anaphylactic potential was studied in an in vivo rat model comparing the effect of Prothrombin complex-SD (the non-nanofiltered predecessor of Cofact) with pasteurized prothrombin complex (the heat-treated predecessor of Prothrombin complex-SD) on blood pressure. No hypotensive effects could be detected. However, it must be noted that this test was performed as part of quality control testing of a number of batches. The tests were not set up under GLP and were not reported in a study report. Therefore, the data should be considered as indicative only.
	Module-V	In module 5 the firm has submitted that the following studies; Safety / PK study (Phase III study): i. Open, not randomised, uncontrolled, Clinical tolerance, in vivo yield and PK "Evaluation of 'Prothrombin complex-SD' in haemophilia B" (No. subjects: 12) ii. Open, not randomised, uncontrolled, Clinical tolerance, in vivo yield and PK "Limited clinical evaluation of SD-treated (virus-inactivated) prothrombin complex with addition of a low concentration of AT (0.2 unit/ml)" (No. subjects: 3) The above two studies were performed in patients with factor IX deficiency, haemophilia B. Clinical pharmacology data on factor IX are available, but the other three coagulation factors, factor II, VII and X, cannot be studied in haemophilia patients. Therefore, the results of below mentioned study (comparing 2 Cofact dosing regimens) were used to describe the in vivo response and in vivo recovery data for factor II, VII, IX and X in patients on oral anticoagulants in an Addendum to the final report. Efficacy /Safety (Phase IV study): Open, randomised, comparative dose controlled- In vivo response and recovery of factor II, VII, IX and X "Reversal of oral anticoagulant therapy with Cofact, an open, randomised, single centre study with 93 patients treated with Cofact to reverse oral anticoagulant therapy" (No. subjects: 93) Dose-finding Efficacy and safety (Phase IV study) : Open, randomised, comparative dose controlled Compare efficacy of 2 dosage regimens (No. subjects: 28) Efficacy /Safety (Phase IV study): Open, randomised, comparative dose controlled-Compare efficacy of 2 dosage regimens "Reversal of oral anticoagulant therapy with Cofact, an open, randomised, single centre study with 93 patients treated with Cofact to reverse oral anticoagulant therapy" (No. subjects: 93) The firm has also submitted Periodic Safety Update Reports.

Decision: Keeping in view legalized CoPP indicating product availability in country of origin and approval of Netherlands (Reference Regulatory Authority); Registration Board approved the products subject to compliance of current Import Policy for finished drugs.

D: Imported Veterinary Biologicals from Non-Reference Countries

Sr.#	Name of Importer	M/s. Bromed Animal Health 246-A, West Wood Colony, Lahore.
1.	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 IB - H120
	Composition	(Live Vaccine) Each dose contains: Lyophilized Live attenuated, Infectious Bronchitis Virus (IBV-H120) ≥103.5 EID50 at release.
	Finished product specifications	Eurpeon Pharmacopoeia Specification
	Pharmacological Group	Biologicals
	Shelf life	24 months (2^0C-8^0C)
	International availability	Egypt
	Products already registered in Pakistan	Reg No. 107933 Avian Infectious Bronchitis Virus, live strain H120: 10^3.0 EID50 - 10^4.5 EID50
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 31087R&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 05-11-2019 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	*Applied formulation is also present in BP*.
	Decision: Keeping in view legalized GMP and FSC indicating product availability in country of origin; Registration Board approved the products subject to compliance of current Import Policy for finished drugs.	
2.	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 IB - H120

	Composition	(Live Vaccine) Each dose contains: Lyophilized Live attenuated, Infectious Bronchitis Virus (IBV-H120) ≥103.5 EID50 at release.
	Finished product specifications	Eurpeon Pharmacopoeia Specification
	Pharmacological Group	Biologicals
	Shelf life	24 months (2^0C-8^0C)
	International availability	Egypt
	Products already registered in Pakistan	Reg No. 107933 Avian Infectious Bronchitis Virus, live strain H120: 10^3.0 EID50 - 10^4.5 EID50
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 31084 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 05-11-2019 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	*Applied formulation is present in BP.*
	Decision: Keeping in view legalized GMP and FSC indicating product availability in country of origin; Registration Board approved the products subject to compliance of current Import Policy for finished drugs.	
3.	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,	Form-5A Dy. No. 31086 R&I Dated 23-11-2020 Rs. 100,000/- Dated 23-11-2020

	Fee submitted	
	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.**	
4.	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 17-3-2022. 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.**	

5.	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.**	
6.	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	<u>Inactivated Bivalent Virus Vaccine Against New Castle Disease</u> 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.**	
7.	Name of Applicant	M/s Better Traders International, 24-Z, Saifullah Shaheed Road, Madina Town, Faisalabad.
	DSL details	M/s Better Traders International, Address: M/s Better Traders International, 24-Z/E, Saifullah Shaheed Road, Madina Town, Faisalabad. Valid till: 15 February 2022.
	Name of Manufacturer	M/s AVAC Vietnam Co., Ltd. Address: Highway A, Ngoc Lick, Trung Tac Province, Hung Yen City Veitnam
	Brand Name +Dosage Form + Strength	AVAC IB- H120
	Composition	Infectious Bronchitis Vaccine, Live Each dose contains: - Attenuated IB Virus strain H120…….Not less than 10^2 EID_{50}
	Finished product specifications	Manufacturer's Specifications
	Country of origin	Vietnam
	Pharmacological Group	Biological
	Shelf life	18 months (2^0C-8^0C)
	International availability	Vietnam
	Alternate Products already registered in Pakistan	JOVAC IB H120 Vaccine (Live Infectious Bronchitis Virus, attenuated H120 strain: at least 10^3.0 EID50)
	Date of application / Fee status	R&I 17667, (20/7/20) 100,000 (20/7/20)
	Demanded Price / Pack size	Decontrolled/2000 doses
	General documentation:	**<u>Free sale Certificate (Original Legalized):</u>** On the Certificate of free sale it is mentioned that the product **<u>Avac</u>**

		IB-H120 (at least 10^2 EID_{50} IB Virus, Strain H120) is registered in Vietnam, Reg No. Avac -06, can be freely sold in Vietnam and overseas markets. Issued to: M/s AVAC Vietnam Company Limited. Issued by: Department of Animal Health , Ministry of agriculture and Rural Development Vietnam. Validity: This certificate is valid for two years. (dated 12/5/2021) **Sole Agency Agreement:** Firm has submitted original legalized sole agency agreement between M/s AVAC Vietnam Company Limited. Address: Highway 5A, Ngoc Lich Village, Trung Tac Commune, Van Lam district, Hung Yen Province, and M/s Better Traders International Address (Head office): 23-Z, Saifullah Shaheed Road, Madina Town, Faisalabad**.** **GMP certificate (Original Legalized):** Issued to: M/s AVAC Vietnam Company Limited. Issued by: Department of Animal Health, Ministry of agriculture and Rural Development Socialist Republic of Vietnam. Validity: Five years from the date of approval (signed on 28th March 2017).
	Remarks of Evaluator	Firm in response to this division's letter submitted that product is in combo pack with following diluent: **Composition:** Each 100ml of diluent: Na_2HPO_4… 0.26g NaH_2PO_4… 0.45g Nacl…0.8g Methylene Blue… 0.001g Distilled water is enough…100ml Information about storage, administration, is also provided.
	Decision: 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 combopack before issuance of registration letter. Chairman Registration Board is authorized for issuance of letter.	
8.	Name of Applicant	M/s Better Traders International, 24-Z, Saifullah Shaheed Road, Madina Town, Faisalabad.
	DSL details	M/s Better Traders International, Address: M/s Better Traders International, 24-Z/E, Saifullah Shaheed Road, Madina Town, Faisalabad. Valid till: 15 February 2022.
	Name of Manufacturer	M/s AVAC Vietnam Co., Ltd. Address: Highway A, Ngoc Lick, Trung Tac Province, Hung Yen City Veitnam
	Brand Name +Dosage Form + Strength	AVAC ND- Lasota
	Composition	Live vaccine Each dose contains: - Newcastle Virus strain Lasota…. Not less than 10^6 EID_{50}
	Finished product specifications	Manufacturer's Specifications
	Country of origin	Vietnam
	Pharmacological Group	Biological
	Shelf life	24 months (2^0C-8^0C)

	International availability	Vietnam
	Alternate Products already registered in Pakistan	Reg No. 107934 Avipharm ND (Lyophilisate for suspension for chicken) Newcastle disease virus, live strain LaSota: minimum 10^6.0 EID50 - maximum 10^7.0 EID50 (*50% embryo infective dose)
	Date of application / Fee status	R&I 17666, 20/7/20 100,000
	Demanded Price / Pack size	Decontrolled/2000 doses
	General documentation:	**Free sale Certificate (Original Legalized):** On the Certificate of free sale it is mentioned that the product Avac ND-Lasota (at least 10^6 EID_{50} Newcastle Virus , Strain Lasota) is registered in Vietnam, Reg No. Avac -01, can be freely sold in Vietnam and overseas markets. Issued to: M/s AVAC Vietnam Company Limited. Issued by: Department of Animal Health , Ministry of agriculture and Rural Development Socialist Republic of Vietnam. Validity: This certificate is valid for two years. (dated 12/5/2021) Product name & Composition: Avac ND-Lasota (at least 10^6 EID_{50} Newcastle Virus , Strain Lasota) **Sole Agency Agreement:** Firm has submitted original legalized sole agency agreement between M/s AVAC Vietnam Company Limited. Address: Highway 5A, Ngoc Lich Village, Trung Tac Commune, Van Lam district, Hung Yen Province, and M/s Better Traders International Address (Headoffice): 23-Z, Saifullah Shaheed Road, Madina Town, Faisalabad. **GMP certificate(Original Legalized):** Issued to: M/s AVAC Vietnam Company Limited. Issued by: Department of Animal Health , Ministry of agriculture and Rural Development Socialist Republic of Vietnam. Validity: Five years from the date of approval (signed on 28th March 2017).
	Remarks of Evaluator	Firm in response to this division's letter submitted that product is in combo pack with following diluent: **Composition:** Each 100ml of diluent: Na_2HPO_4… 0.26g NaH_2PO_4… 0.45g Nacl…0.8g Methylene Blue… 0.001g Distilled water is enough…100ml Information about storage, administration, is also provided.
	Decision: 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 combopack before issuance of registration letter. Chairman Registration Board is authorized for issuance of letter.	
9.	Name of Applicant	M/s Better Traders International, 24-Z, Saifullah Shaheed Road, Madina Town, Faisalabad.
	DSL details	M/s Better Traders International, Address: M/s Better Traders International, 24-Z/E, Saifullah Shaheed Road, Madina Town, Faisalabad. Valid till: 15 February 2022.

	Name of Manufacturer	M/s AVAC Vietnam Co., Ltd. Address: Highway A, Ngoc Lick, Trung Tac Province, Hung Yen City Veitnam
	Brand Name +Dosage Form + Strength	AVAC GUMBORO PLUS
	Composition	Each dose contains: Attenuated Infectious Bursal Disease (IBD) Virus strain intermediate Plus……..not less than 10^2 EID_{50}
	Finished product specifications	Manufacturer's Specifications
	Country of origin	Vietnam
	Pharmacological Group	Biological
	Shelf life	18 months (2^0C-8^0C)
	International availability	Vietnam
	Alternate Products already registered in Pakistan	Not found strain intermediate Plus
	Date of application / Fee status	R&I 17668, (20/7/20) 100,000 (20/7/20)
	Demanded Price / Pack size	Decontrolled/2000 doses
	General documentation: **Free sale Certificate (Original Legalized):** On the Certificate of free sale, it is mentioned that the product **Avac Gumboro Plus (at least 10^2 EID_{50} Gumboro virus, Strain intermediate plus)** is registered in Vietnam, Reg No. Avac -07, can be freely sold in Vietnam and overseas markets. Issued to: M/s AVAC Vietnam Company Limited. Issued by: Department of Animal Health, Ministry of agriculture and Rural Development Vietnam. Validity: This certificate is valid for two years. (dated 12/5/2021) **Sole Agency Agreement:** Firm has submitted original legalized sole agency agreement between M/s AVAC Vietnam Company Limited. Address: Highway 5A, Ngoc Lich Village, Trung Tac Commune, Van Lam district, Hung Yen Province, and M/s Better Traders International Address (Head office): 23-Z, Saifullah Shaheed Road, Madina Town, Faisalabad. **GMP certificate(Original Legalized)::** Issued to: M/s AVAC Vietnam Company Limited. Issued by: Department of Animal Health, Ministry of agriculture and Rural Development Socialist Republic of Vietnam. Validity: Five years from the date of approval (signed on 28th March 2017).	
	Remarks of Evaluator	Firm in response to this division's letter submitted that product is in combo pack with following diluent: **Composition:** Each 100ml of diluent: Na_2HPO_4… 0.26g NaH_2PO_4… 0.45g Nacl…0.8g Methylene Blue… 0.001g Distilled water is enough…100ml Information about storage, administration, is also provided.
	Decision: **Registration Board deferred the case for submission of following by the firm:** **i. Valid legalized FSC indicating diluent in combopack** **ii. Clarification/ details of Intermediate Plus strain of Infectious Bursal Disease.**	

10	Name of Importer	Hilton Pharma (Pvt.) Ltd. Plot 13 & 14, Sector 15, Korangi Industrial Area Karachi.
	DSL details	License to sell drug as distributor valid till 19-jun-2022
	Name of Manufacturer	M/s PT. Medion Farma Jay Address: Office : 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 Gumboro A vaccine Freeze dried live vaccine
	Composition	Each dose of vaccine contains: Infectious bursal disease live vaccine,Cheville (1/68) strain .....> $10^{2.0}$ EID_{50}
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Freeze dried live vaccine against infectious bursal disease/ Gumboro disease in poultry
	Shelf life	Months (2-8°C) 24
	Products already registered in Pakistan	IBA Vac of M/s Forward Solutions.
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5-A Dy No. 26809 Dated: 12-10-2020, Dy No. 29865 dated 12-11-2021 Fee Submitted: Rs. 50000/- & Rs. 50000/- dated 5-10-2020, 12-11-2021.
	Demanded Price / Pack size	1000 dose
	General Documentation	• Legalized Certificate of Pharmaceutical Product (CoPP) No 18023/PI.500/F/10/2019 dated October 18,2018 issued by: Ministry of Agriculture Directorate General of livestock and animal health services Indonesia.
	Decision: Registration Board deferred the product for submission of Scientific literature confirming Immunological relevance of applied strain with circulating strain of Pakistan.	

E: Locally Manufactured Veterinary Vaccines

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	
	Decision: Registration Board deferred the product for submission/ confirmation of following: **i. Method of administration of vaccine** **ii. Container Closure System of diluent.**	

	iii.	**Confimation of faciltiy for manufacturing of diluent.**

F: Miscellaneous/ Deferred Cases

1. Imported Human Biological deferred in 308th meeting of Reg. Board applied by M/s ASTO Life Sciences Private Limited, Lahore.

Following biological drug has been deferred in 308th meeting of Reg. Board as per following details;

2.	Name and address of Importer	M/s ASTO Life Sciences Private Limited. Plaza No. 1, Block Orchard No.1 Paragon City, Barki Road, Dist. Lahore.
	Detail of DSL	Drug Sale License as a distributor No. 05-352-0068-045428D valid upto 21-09-2021
	Name and address of Manufacturer	Product License Holder & Manufacturer: M/s Adimmune corporation, No. 3 Section 1, Tanxing Road, Tanzi District, Taichung city 42743 Taiwan.
	Brand Name +Dosage Form + Strength	AdimFlu-S (QIV) Quadrivalent Influenza Vaccine
	Diary No. Date of R& I & fee	Dy. No. 31262 Dated 24-11-2020 (Rs. 100,000/- Dated 24-11-2020)
	Composition	Each 0.5ml PFS contains: Hemagglutinin of Influenza A Virus (H1N1) …...15µg HA Hemagglutinin of Influenza A Virus (H3N2) …...15µg HA Hemagglutinin of Influenza B Virus (Yamagata lineage) …...15µg HA Hemagglutinin of Influenza B Virus (Victoria lineage) …...15µg HA
	Pharmacological Group	Human Influenza Vaccine
	Type of Form	Form-5F
	Finished Product Specification	EUR. Ph. JP and CP
	Shelf Life	24 months (2^0C-8^0C)
	Document Details	i.CoPP No. 080558 dated 13-10-2020 (Notarized but not legalized) ii.GMP valid till 5-9-2021(Notarized but not legalized) iii.Copy of Sole Agency Agreement
	Pack size/ Price	1's PFS/ As per SRO.
	International Availability	Vaxigrip Tetra of M/s Sanofi Pastures France
	Products already registered in Pakistan	Vaxigrip Tetra of M/s Sanofi Aventis Pakistan Ltd.
	Initial Remarks of Evaluator (Khurram Khalid)	i. Notarized copy of Sole Agency/ Market Authorization certificate. ii. CoPP and GMP certificates are not legalized. iii. In stability data, following tests have not been performed in long term stability data; a. Fractionation test b. Test for freedom from Ether c. Test for freedom from abnormal toxicity d. Identity test e. Overall albumin content test. While accelerated studies of only one batch has been provided. iv. Clinical Trial Data a. Phase II: A Phase II, One arm, Single dose, Open label, Single center study, in 120 subjects b. Phase III: As Phase III, Single Dose, Randomized Double blind, Multiple-center Study. in 710 subjects. c. Phase III: Open label, Multiple-center Study, 174 subjects.

The case was deferred in 308th meeting of Registration Board as per following details:

"Registration Board deferred the products for submission of following by the firm:

a. Tabulated comparison of finished product specifications with pharmacopoeia monograph.

b. Accelerated stability data of three batches for 06 months."

The firm has submitted the following:

a. Tabulated comparison of finished product specifications with pharmacopoeia monograph indicating that the product complies with Ph. Eur. Specifications.
b. The firm has submitted accelerated stability data of 3 months for 1 batch and 02 months for 02 batches and informed that they don't have 6 months data.

Decision: Registration Board deffered the case for following:

i. **Confirmation from Ministry of Commerce regarding Trade with Taiwan.**
ii. **Submission of valid CoPP legalized from Embassy of Pakistan by the firm.**
iii. **Submission of 6 months accelerated stability data of 03 batches by the firm.**

1. Registration of imported products from M/s AA Pharma to M/s AJ Mirza Pharma deferred in deferred in 291st meeting of registration Board.

M/s A.J. Mirza Pharma (Pvt) Ltd., Karachi applied for the registration of following human biologicals in their name from M/s AA Pharma, Karachi as per following details:

Sr. No.	Name and address of Importer	M/s A.J. Mirza Pharma (Pvt) Ltd., 1st Floor, Shafi Court, Civil Lines, Merewether Road, Karachi
1.	Detail of DSL	License No. 0838 dated 08-01-2019 valid till 23-12-2020
	Reg. No.	047578
	Name and address of Manufacturer	Product License Holder & Manufacturer: M/s Shenyang Sunshine Pharmaceutical Co. Ltd., No. 3 A1, Road 10, Econ & Tech Development Zone, Shenyang 110027, China.
	Brand Name +Dosage Form + Strength	EPIAO 2000IU Injection
	Diary No. Date of R& I & fee	Dy. No. 182, 42989, 3656, 5036 & 10162 Dated: 03-02-2017, 17-12-2018, 28-1-2019, 04-2-2019 & 01-7-2019 Rs. 100000/- Dated: 01-02-2017
	Composition	Each 1ml vial contains: Recombinant Human Erythropoietin…….2000IU
	Pharmacological Group	rDNA Therapeutic Protein
	Type of Form	Form-5A
	Finished Product Specification	Not Provided
	Shelf Life	03 years (2^0C-8^0C)
	Document Details	Legalized CoPP No. 2017.79 dated 26-12-2017.
	Pack size/ Demanded Price	1's Vial/ Rs. 1029.60/-
	International Availability	Epogen 2000IU of M/s Amgen Inc., USA
	Products already registered in Pakistan	Gerepo 2000IU of M/s Titlis Pharma, Lahore.
2.	**Name and address of Importer**	M/s A.J. Mirza Pharma (Pvt) Ltd., 1st Floor, Shafi Court, Civil Lines, Merewether Road, Karachi
	Detail of DSL	License No. 0838 dated 08-01-2019 valid till 23-12-2020
	Reg. No.	047579
	Name and address of Manufacturer	**Product License Holder &Manufacturer:** M/s Shenyang Sunshine Pharmaceutical Co. Ltd., No. 3 A1, Road 10, Econ & Tech Development Zone, Shenyang 110027, China.
	Brand Name +Dosage Form + Strength	EPIAO 4000IU Injection
	Diary No. Date of R& I & fee	Dy. No. 182, 42989, 3656, 5036 & 10162 Dated: 03-2-2017, 17-12-2018, 28-1-2019, 04-2-2019 & 01-7-2019 Rs. 100000/- Dated: 01-02-2017
	Composition	Each 1ml vial contains: Recombinant Human Erythropoietin…….4000IU
	Pharmacological Group	rDNA Therapeutic Protein
	Type of Form	Form-5A
	Finished Product Specification	Not Provided
	Shelf Life	03 years (2^0C-8^0C)

	Document Details	Legalized CoPP No. 2017.79 dated 26-12-2017.
	Pack size/ Demanded Price	1's Vial/ Rs. 1144/-
	International Availability	Epogen 4000IU of M/s Amgen Inc., USA
	Products already registered in Pakistan	Gerepo 4000IU of M/s Titlis Pharma, Lahore.
3.	**Name and address of Importer**	M/s A.J. Mirza Pharma (Pvt) Ltd., 1st Floor, Shafi Court, Civil Lines, Merewether Road, Karachi
	Detail of DSL	License No. 0838 dated 08-01-2019 valid till 23-12-2020
	Reg. No.	047580
	Name and address of Manufacturer	**Product License Holder &Manufacturer:** M/s Shenyang Sunshine Pharmaceutical Co. Ltd., No. 3 A1, Road 10, Econ & Tech Development Zone, Shenyang 110027, China.
	Brand Name +Dosage Form + Strength	EPIAO 10000IU Injection
	Diary No. Date of R& I & fee	Dy. No. 182, 42989, 3656, 5036 & 10162 Dated: 03-2-2017, 17-12-2018, 28-1-2019, 04-2-2019 & 01-7-2019 Rs. 100000/- Dated: 01-02-2017
	Composition	Each 1ml vial contains: Recombinant Human Erythropoietin…….10000IU
	Pharmacological Group	rDNA Therapeutic Protein
	Type of Form	Form-5A
	Finished Product Specification	Not Provided
	Shelf Life	03 years (2^0C-8^0C)
	Document Details	Legalized CoPP No. 2017.79 dated 26-12-2017.
	Pack size/ Demanded Price	1's Vial/ Not Provided.
	International Availability	Epogen 10000IU of M/s Amgen Inc., USA
	Products already registered in Pakistan	Epocan 10000IU of M/s Macter International, Karachi.

The firm has provided the following documents for each product:

a. Application of Form-5A
b. Fee Challan of Rs. 100000/-
c. Copy of initial registration letter dated 15-02-2008.
d. Copy of last renewal submission dated 28-07-2015 with Rs. 40000/- fee.
e. Original termination letter in name of M/s AA Pharma, Karachi.
f. Original legalized letter of authorization in name of M/s AJ Mirza Pharma Private Limited, Karachi dated 17-12-2018.
g. Copy of NOC dated 10-08-2021 from M/s AA Pharma, Karachi.
h. Legalized CoPP No. 2017.79 dated 26-12-2017 issued by Liaoning Provincial Food and Drug Administration, China.
i. An undertaking that the given information is true and correct to best of their knowledge.
j. The firm has submitted the biosimilarity data as per following details:

WHO Biosimilarity Guidelines	**Data Submitted by the firm**
Quality Comparison 1. Physicochemical Characterization	Primary Structure i. Amino acid Sequence by LTQ (Thermo) and MALDI-TOFmass spectrograph (Non-comparative) ii. Sequence coverage Analysis by LC-MS (Comparative) iii. Amino acid constitution by HPLC (Non-comparative) iv. N-terminal Analysis (Non-comparative) v. C-terminal Analysis (Non-comparative) vi. Peptide Mapping by HPLC (Comparative) vii. Molecular Weight by MALDI-TOF MS (Non- Comparative) High order Structure i. Circular Dichroism (CD) (Comparative) ii. Disulphide-bond Analysis (Non- Comparative) Heterogenicity

	i. Capillary Zone Electrophoresis (Comparative) ii. Isoelectric focusing (Comparative) Glycosylation i. Sialic Acid Content (Comparative) ii. Native Carbohydrate Chain Analysis (Comparative) iii. Neutral Carbohydrate Chain Analysis (Comparative) iv. N-glycosylation sites identification and sites occupancy analysis (Comparative) v. O-glycosylation sites identification and sites occupancy analysis (Comparative) vi. N-glycan qualitative analysis (Comparative)
Biological Activity	In-Vitro Cell Proliferation Assay (Comparative)
Immunochemical properties	SDS-Page and Immunoblotting
Impurities	Dimers and related substances of higher molecular mass (Comparative) Host Cell and Vector derived DNA (Comparative) Host Cell derived proteins (Comparative) Bacterial Endotoxin
Stability Studies	Stability study is provided.
Non-clinical Comparison i. In-vitro Studies ii. In-vivo Studies a. Biological/ Pharmacodynamic activity b. Non- clinical toxicity as determined in one repeat dose toxicity study	i. In-vitro Studies a. Cell proliferation assay (Comparative) ii. In-vivo Studies a. Pharmocokinetic method The relationship of invivo effect and time under same administration in BalBc inbred strain mice (Comparative) The relationship of invivo effect and dosage under same sampling time in BalBc inbred strain mice (Comparative) b. Bioassay in normocythaemic mice The relationship of invivo effect and time under same administration in BalBc mice (Comparative) Toxicology The comparison of toxicological profile between EPIAO and Eprex in rats after subcutaneous injection for 28 days.
Clinical Comparison	A prospective, randomized, double-blind, parallel group study to establish the therapeutic equivalence of EPIAO with the standard treatment Eprex in subjects with Chronic Kidney Disease (CKD) related Anaemia not yet on dialysis **(Only Protocol)**.

The case was deferred in 291st meeting of registration Board as per following details:

"Registration Board deferred the case for submission of following by the firm:

a. Valid legalized approval of demanded shelf life from regulatory body of country of origin.

b. Complete clinical trial data under biosimilarity studies."

The firm has submitted the following:

i. Copy of approval letter of 02 years shelf life No. F. 1-12/2004-Reg-I dated 24-12-2009.

ii. A prospective, Randomized, Double blind, parallel Group Study to evaluate 1:1 Dose Conversion from Eprex to Epiao in term of clinical Efficacy and Safety in subjects with End-Stage Renal Disease on Haemodialysis.

Decision: 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. 047579) & Epiao 4000IU (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.

3. Imported Veterinary Biological applied by M/s Uranus Biotech (Private) Limited, Islamabad deferred in 293rd meeting of Registration Board.

Following product of M/s Uranus Biotech (Private) Limited, Islamabad was deferred in 293rd meeting of Registration Board as per following details:

Name of Importer	M/s Uranus Biotech (Private) Limited, Office No. 112, First Floor, Arooj Arcade, Sector F-10 Markaz, Islamabad
DSL details	License No. DSL-839-ICT/2013 dated 26-02-2018 valid till 25-02-2018
Name of Manufacturer	M/s Chongqing Auleon Biologicals Co. Ltd., The Fourth Branche Road, Banqiao Industrial Park, Rongchang District, Chongqing, P.R. China.
Brand Name +Dosage Form + Strength	Echinococcosis Recombinant Subunit Vaccine (Sheep & goats)
Composition	Each dose contains: Eg95 antigen……50µg
Finished product specifications	Innovator Specifications
Pharmacological Group	Veterinary Vaccine
Shelf life	12 months (2^0C-8^0C)
International availability	China
Products already registered in Pakistan	Not Available
Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No. 10322, 29965, 7518& 3293 Dated: 20-03-2018, 06-09-2018, 20-02-2019&11-04-2019 Rs. 100000/- dated 14-03-2018
Demanded Price / Pack size	1's Vial (40 doses)/ De-controlled.
General documentation	Valid legalized GMP certificate No. (2016) GMP 23013 dated 21-12-2016 valid till 20-12-2021 Legalized Free Sale Certificate dated 23-11-2017 valid till 22-11-2018.
Decision of RB in 291st meeting	*Registration Board deferred the case for submission of evidence of availability of above formulation in reference regulatory authorities.*

The firm has now submitted that the product is only registered in Kyrgyzstan and not in any reference regulatory authority. Moreover, the firm has submitted article regarding prevalence of Echinococcosis in Pakistan instead of availability of formulation in reference countries.

Decision: Registration Board referred the case to Animal Husbandry Commissioner for comments regarding the need of vaccine, prevalence of discease (Echinococcosis) and Immunological relevance of Eg95 antigen/strain in Pakistan.

4. Imported veterinary biological applied by M/s Vet Line International, Lahore deferred in 297th meeting of Registration Board.

Following product of M/s Vet Line International, Lahore was deferred in 297th meeting of Registration Board as per following details:

Name and address of Importer	M/s Vet Line International, Plot No. 939-A,Block-J, Phase-I,LDA Avenue,Lahore
Detail of DSL	No. 05-352-0066-040712D dated 09-02-2019 renewed upto09-02-2021
Name and address of Manufacturer	**Product License Holder:** M/s Laprovet Hungary Veterinary Pharmaceuticals Ltd., 1107 Budapest Horog u. 32-34. Hungary (the wholly owned subsidiary of Laprovet S.A.S. 7 rue du Tertreau, Arched'Oe 2,37390, Notre Dame D' Oe, France. **Contract Manufacturer:** M/s Ceva-Phylaxia Veterinary Biologicals Co. Ltd., 1107 Budapest, Szallass u.5. Hungary.
Brand Name +Dosage Form + Strength	ITA New Flu H9
Diary No. Date of R& I & fee	Dy. No. 23585(R&I) dated 09-07-2018 Rs. 100000/- dated 09-07-2018

Composition	Each dose (0.2ml) of vaccine contains: Inactivated Avian Influenza virus, type A, sub-type H9N2…. min. 8log2 HI Inactivated Newcastle disease virus, LaSota strain…. min. 5log2 HI
Pharmacological Group	Veterinary Vaccine
Type of Form	Form-5A
Finished Product Specification	As per Innovator.
Shelf Life	24 months (2^0C-8^0C)
Document Details	i. Valid Legalized GMP certificate of M/s Ceva-Phylaxia Veterinary Biologicals Co. Ltd., Hungary No. 02.2/3807-2/2017 dated 17-07-2017 issued by Directorate of Veterinary Medicinal Products, Hungary ii. Valid Legalized FSC No. 02.2/2397-2/2018 dated 20-04-2018 issued by Directorate of Veterinary Medicinal Products, Hungary iii. Contract manufacturing certificate No. 02.2/3281-2/2018 dated 13-06-2018 issued by Directorate of Veterinary Medicinal Products, Hungary
Pack size	500ml(2000 doses)
International Availability	UEMOA (West African community including 8 countrie)
Products already registered in Pakistan	AI-OLVAC of M/s Forward Solutions.
Decision of RB in 297th meeting	*Registration Board deferred the product for evidence of availability of said product in any of the regulatory authorities or any three stringent regulatory bodies of former erstwhile Eastern Europe. The decision of the board in the 293rd meeting regarding above product is deleted.*

The firm has now submitted that the product is not registered in any of the stringent regulatory authorities as disease is not prevalent in Europe. Moreover, the firm has submitted that following vaccines manufactured in reference countries for export are registered and marketed in Pakistan e.g. Gallimune 208 Flu H9 M.E, Ai-Olvac, Nobilis Influenza H9N2+ND etc.

Decision: Registration Board deferred the case for confirmation of Influenza disease status in country of origin and reference regulatory authorities.

5. Name of Importer: M/s Vet Line International,
55/S, 1st Floor Main Shadman Market, Lahore.

Sterile Diluent of Avipox Vaccine

Case background**:**

Registration Board in its 288th meeting considered the case for the subject product and decided as under:

"Registration Board deferred the case for submission of clarification regarding not importing diluent in combo pack by the firm".

The firm in response to decision of Registration Board in its 288th meeting submitted that the applied product is imported product and their manufacturer has same packing and it is difficult for them regarding its costing to import in combo pack, so it becomes too costly. They import this applied product in limited quantity and it's not possible that their manufacturer provides them the customized packing.

After considering the clarification of the firm Board in its 291st decided as under:

"Keeping in view the valid legalized GMP and Free Sale Certificates indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs".

Now the M/s. Vet Line International vide their letter dated 09th September 2021 and 22nd September 2021 has requested for issuance of Registration letter of sterile diluent in combo pack with their registered Avipox Vaccine (Reg. No. 085010). Firm has submitted following documents with the application:

i. Fee challan of Rupee 7500/- (Slip No. 18745537536).
ii. Copy of English translation of marketing authorization of AVIPOX issued by Hungarian Authority could be verified at https://atiportal.nebih.gov.hu/moengallatgykesz.html.
iii. Copy of fee challan (slip No.1920696) dated 23rd of August 2019 for change in address of importer.
iv. Copy of Eudra GMDP of Ceva-Phylaxia Veterinary Biologicals Co., limited.

Name of Importer	M/s Vet Line International, 55/S, 1st Floor Main Shadman Market, Lahore.
DSL details	No. 60-A/DGBT/11/2015 dated 12-02-2015 valid till 11-02-2019

	Name of Manufacturer	**Product License Holder:** M/s Laprovet Hungary Veterinary Pharmaceuticals Ltd., 1107 Budapest Horog u. 32-34. Hungary (the wholly owned subsidiary of Laprovet S.A.S. 7 rue du Tertreau, Arched'Oe 2,37390, Notre Dame D' Oe, France. **Contract Manufacturer:** M/s Ceva-Phylaxia Veterinary Biologicals Co. Ltd., 1107 Budapest, Szallass u.5. Minutes of 291st of Meeting of Registration Board, DRAP (2-4th September, 2019) 1309 Hungary.
	Brand Name +Dosage Form + Strength	Sterile Diluent of Avipox Vaccine
	Composition	Each vial of 10ml contains: Glycerol…….1.5ml Water, highly purified……..ad10ml
	Finished product specifications	As per Innovator.
	Pharmacological Group	Diluent for veterinary vaccine
	Shelf life	60 months (20C-80C)
	International availability	Egypt, Bangladesh
	Products already registered in Pakistan	Sterile Diluent to be used with already registered vaccine AviPox (Reg. No. 085010)
	Type of Form Dy No & Date of application, Fee submitted	Form-5A Dy. No.033700(R&I) dated 11-10-2018 Rs. 100000/- 11-10-2018
	Demanded Price / Pack size	20 Vials x 10ml
	General documentation	i. Legalized GMP certificate of M/s Ceva-Phylaxia Veterinary Biologicals Co. Ltd., Hungary No. 02.2/3807-2/2017 dated 17-08-2017 issued by Directorate of Veterinary Medicinal Products, Hungary. ii. Contract manufacturing certificate No. 02.2/3281-2/2018 dated 13-06-2018 for Avipox Vaccine issued by Directorate of Veterinary Medicinal Products, Hungary. iii. Legalized FSC No. 02.2/3917-2/2018 dated 13-07-2018 issued by Directorate of Veterinary Medicinal Products, Hungary.
	Decision of RB in 288th Meeting.	*Registration Board deferred the case for submission of clarification regarding not importing diluent in combo pack by the firm.*
	Decision of RB in 291st Meeting.	*Keeping in view the valid legalized GMP and Free Sale Certificates indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs.*
	Decision: Keeping in view market authorization of Avipox vaccine issued by Hungary and legalized GMP & Free Sale Certificate; Registration Board approved the diluent as combo pack.	

6.	**Name of Indenter/ Manufacturer**	**Manufacturer**	**Name of Drug (s)/ Composition & Therapeutic**	**Date of application / Fee status**	**Documentary Details**	**Remarks**	**Decision of RB(M-254)**
	Vet. Pharma Trading Company, New Steel Market, Near Regent	KBNP, Inc. Dugok-ri, Sinam, Yesan, Chungnam. Korea.	Himmvac Fowl Pox Vaccine Each dose contains: Fowl Pox virus 2775 strain…30%	16-Apr-11 Deposited fee 15000 Balance Fee 85000	CoPP No. 6-268 dated 2nd July, 2010	Me too. Document are not valid and out dated. May be deferred for Fee	Deferred for clarification regarding strain details with local compatibility, completion of documents,

	Cinema, G.T. Road, Gujranwala - Pakistan. /		(at least 102.0 EID50) (Biological Product Vaccine). **(For Veterinary Use).**			confirmation and completion of documents.	balance fee and me too status.

Evaluation by BE&R:

Now the firm has submitted following documents:

Free sale certificate; Scanned copy of Free sale certificate certified by Animal and Plant quarantine agency of the Ministry for Agriculture and Rural Affairs of the Republic of Korea on 28-01-2021.

Name of Product	**Composition**
Himmvac Fowl Pox vaccine	Each one dose Contains: Fowl Pox Virus, 2775 strain at least $10^{2.0}$ EID_{50} *(different from composition on form 5A)

Fee challan; of Rupee 135000/- Slip No. 54865209286.

Strain details; (Virus name, Origin History, Specific Coding of Master Seed and Working Seed)

Documents still not submitted by the firm are as under:

i. Evidence of locally registered product.
ii. Local compatibility of strain.
iii. Valid legalized GMP certificate of manufacturer.
iv. Sole agency agreement was from February 2012-February 2014 (it is expired Now)

Information which was not part of previous agenda pattern added here from Form 5A:

Proposed Shelf Life: 24 months

Storage Temperature: 2-4 ^{0}C

FPP Specifications; Not Mentioned

Pack Size; 1000 doses

Unit Price of Drug; Decontrolled.

Decision: Registration Board deferred the product for submission of following by the firm:

i. Valid legalized GMP certificate
ii. Valid legalized Free Sale certificate
iii. Evidence of local availability of formulation
iv. Scientific literature confirming Immunological relevance of applied strain with circulating strain of Pakistan
v. Original or notarized copy of valid Sole Agency Agreement.

7.	**Name of Indenter/ Manufacturer**	**Manufacturer**	**Name of Drug (s)/ Composition & Therapeutic**	**Date of application / Fee status**	**Documentary Details**	**Remarks**	**Decision of RB(M-254)**
	Vet. Pharma Trading Company, New Steel Market, Near Regent Cinema, G.T. Road, Gujranwala - Pakistan. /	KBNP, Inc. Dugok-ri, Sinam, Yesan, Chungnam. Korea.	Himmvac Dalguban SG9R Live Vaccine Each dose contains: Salmonella gallinarum 9R strain……..at least 2x107 CFU/dose (Poultry Vaccine for fowl typhoid).	Date of application 19-Jul-12 Deposited fee 15000 Balance Fee 85000	Legalized/ notarized CoPP, Prod. Reg No.6-136 dated 3-12-1986 CoPP No 100906 dated 18-10-2010	Documents are outdated May be Deferred.	Deferred for confirmation of remaining fee, me too status and legalized authentic documents

Evaluation by BE&R:

Now the firm has submitted following documents:

Free sale certificate; Scanned copy of Free sale certificate certified by Animal and Plant quarantine agency of the Ministry for Agriculture and Rural Affairs of the Republic of Korea on 28-01-2021.

Name of Product	Composition
Himmvac Dalguban SG9R Live Vaccine	Each one dose Contains: Salmonella gallinarum 9R strain……..at least 2x107 CFU

Fee challan; of Rupee 135000/- Slip No. 0762501058.

Documents still not submitted by the firm are as under:

i. Evidence of Me Too.
ii. Valid legalized GMP certificate of manufacturer.
iii. Sole agency agreement was from February 2012-February 2014 (it is expired Now)

Information which was not part of previous agenda pattern is added here from Form 5A:

Proposed Shelf Life: 24 months

Storage Temperature: 2-8 ^{0}C

FPP Specifications; Not Mentioned

Pack Size; 1000 doses

Unit Price of Drug; Decontrolled.

Decision:

Registration Board deferred the product for submission of following by the firm:

i. Valid legalized GMP certificate
ii. Valid legalized Free Sale certificate
iii. Evidence of local availability of formulation
iv. Original or notarized copy of valid Sole Agency Agreement.

8.	Name of Indenter/ Manufacturer	Manufacturer	Name of Drug (s)/ Composition & Therapeutic	Date of application / Fee status	Documentary Details	Remarks	Decision of RB(M-256)
	Vet. Pharma Trading Company, New Steel Market, Near Regent Cinema, G.T. Road, Gujranwala - Pakistan. /	KBNP, INC, Dugok-ri, Sinam, Yesan, Chungnam, Korea Indication: For the active immunization of dogs against Canine distemper, Infectious Canine hepatitis, Parvovirus infection, Parainfluenza-2 virus infection and Leptospirosis.	Himmvac DHPPL vaccine, Canine vaccine Active ingredients and amounts per unit gram. For complete qualitative composition including recipients. **Freeze-dried fraction:** DHPP Live vaccine per dose Active ingredients Freeze dried, Modified Live Canine distemper virus Qty 25% (at least 103.5 EID 50/Dose) Infectious	Date of application 11-7-2012 Fee deposited 15000 dated 19-7-2012 + 85000 dated 15.5.2014 vide Challan no. 0133450 Balance fee Nil The Product Is available in the Country of origin Packing: 1 doses, 5 doses Shelf life	CoPP No. 113686 dated 23-2-2012 Prod Lic No. 6-148 dated 29-3-1988 Free Sale Certificate Yes	Sole Agent Authorization agreement shall be in effect from Dec.15,2015 to Dec. 14, 2017	Deferred for expert opinion of following regarding confirmation of need vis-à-vis compatibility with local immunogenic requirement, safety profile: a. Dr. Qurban Ali, Animal Husbandry Commissioner, Ministry Food & National Security, Islamabad. b. Prof. Khushi Muhammad, UVAS, Lahore c. Prof. Akram Munir, Ripha

			Canine Hepatitis virus Qty 10% (at least 103.0 TCID 50/Dose) Canine Parvovirus Qty 25% (at least 105.0 TCID 50/Dose) Canine Parainfluenza type 2 virus Qty 30% (at least 104.0 TCID50/Dose) **Liquid fraction (LCI): Leptospira Bacterin per dose** Active ingredients Inactivated Leptospira icterohaemorrhagiae Qty (at least 108.0/ml) Leptospira canicola Qty (at least 108.0/ml)	12 months after manufacturing date			University, Lahore.

Decision (M-263): Registration Board deferred product for confirmation of already registered similar product / me too status and approval status by reference regulatory authorities. The Board also advised to incorporate data for application, fee deposited, CoPP and other related details.

Evaluation by BE&R:

Now the firm has submitted following documents:

Free sale certificate; Scanned copy of Free sale certificate certified by Animal and Plant quarantine agency of the Ministry for Agriculture and Rural Affairs of the Republic of Korea on 28-01-2021.

Name of Product	Composition
Himmvac DHPPL Vaccine	Each one dose Contains: **Freeze Dried, Modified live DHPP Vaccine** Canine distemper Virus….at least $10^{3.5}EID_{50}$ Infectious canine Hepatitis Virus …. At least $10^{3.0}TCID_{50}$ Canine Parvovirus …. At least $10^{5.0}TCID_{50}$ Canine Parainfluenza type 2 virus …. At least $10^{4.0}TCID_{50}$ **Leptospira Bacterin, Inactivated Vaccine** Leptospira Canicola …. at least 10^{8}/ml Leptospira icterohaemorhagiae …. at least 10^{8}/ml

A web page showing evidence of availability of applied formulation in Indonesia.

Documents still not submitted by the firm are as under:

i. Evidence of Me Too.
ii. Valid legalized GMP certificate of manufacturer.
iii. Sole agency agreement was from 15 December 2015 to 14 December 2017 (it is expired Now)

	Information which was not part of previous agenda pattern is added here from Form 5A: Storage Temperature: 2-8 ^{0}C FPP Specifications; Not Mentioned Unit Price of Drug; Decontrolled.					
	Decision: Registration Board deferred the product for submission of following by the firm: **i. Valid legalized GMP certificate** **ii. Valid legalized Free Sale certificate** **iii. Evidence of local availability of formulation** **iv. Original or notarized copy of valid Sole Agency Agreement.**					
9.	**Name of Importer & Manufacturer**	**Brand Name & Composition**	**Type of Form Dy No & Date of application Fee submitted Pack size/ Demanded Price**	**Document details (CoPP) Me too status/New molecule**	**Remarks**	**Decision(M-266)**
	M/s Agriprom Pakistan (Pvt) Ltd. 66 west wood colony, thokar niaz baig, Lahore. M/s Laboratorios VencoFarma Do Brasil Ltda. 237 Travessa Dalva de Oliveira, Parque das Industrias Leve, Londrina-PR	Vencomax 12 Each dose (1 ml) contains: Lyophilized part: Distemper Virus (Rockborn strain)….. at least $10^{2,5}$ $TCID_{50}$-/dose Canine adenovirus CAV 2……. at least $10^{2,5}$ $TCID_{50}$/dose Parvovirus Cornell 916…… at least $10^{2,5}$ $TCID_{50}$/dose Parainfluenza virus AMV…….. at least $10^{2,5}$ $TCID_{50}$/dose Gentammicin….. maximum 30 µg/ml Amphotericin B…….. Maximum 2.5 µg/ml. Liquid Part: Leptospira canicola bacterin……. 1,5 x 10^6 germs/dose Leptospira icterohaemorrhageni Bacterin……. Leptospira copenhageni bacterin ……. 1,5 x 10^6 germs/dose Leptospira Pomona bacterin …..1,5 x 10^6 germs/dose Leptospira grippotyphosora bacterin ….1,5 x 10^6 germs/dose Leptospira pyrogenes bacterin ….1,5 x 10^6	Form 5-A 08-ADC(BD) 04-01-2017 312(R&I) 04-01-2017 Rs. 100000/- 03-01-2017 1 dose vial (lyophilized) 20's 1 dose vial (liquid) 20's	Valid legalize GMP Certificate N^0 159/2016 Legalize FSC N^0 940/2016	Separate fee for the registration of liquid part is required. The firm submitted diluent is part of formulation and can not be used separately. Stability data is not submitted. The firm was asked to submit data however it was not provided. One of the indications in the vaccine is treatment of hepatitis. The firm was asked to provide clarification regarding which antigen/ viral strain is involved in the prophylaxis against Hepatitis. The firm submitted that CAV2 virus is involved in prophylaxis against hepatitis. However the available literature indicates that	Deferred for evaluation of product by Dr. Qurban Ali and submission/ clarification of following by the firm: 1. Separate fee for the registration of liquid part. 2. Stability data. 3. One of the indications in the vaccine is treatment of hepatitis while firm has submitted that CAV2 virus is involved in prophylaxis against hepatitis. However the available literature indicates that CAV-1 vaccines provide immunity against Hepatitis. This requires supporting evidence from published literature/ reference regulatory agencies

		germs/dose Leptospira hardjo bacterin …..1,5 x 10^6 germs/dose (Vaccine against Canine Distemper, Parvovirus, Coronavirus, Parainfluenza, Hepatitis, Adenoviruses and Leptospirosis) Shelf Life: 24months			CAV-1 vaccines provide immunity against Hepatitis. This requires clarification.	

Evaluation by BE&R:

Now the firm in their reply dated 13th September, 2021 submitted following:

i. Valid legalized GMP
ii. Valid legalized free sale certificate
iii. **Evaluation of product by Dr. Qurban Ali; dated 6th jan 2021**

Conclusion of Evaluation: Product at serial No. 1-4(Vancomax12, Paraven RC2, Ronvac, Raive Cannis) are recommended for registration. Product at serial No. 1,3,4 are for pets namely dogs and cats and are required in veterinary medical practice. Product at serial No. 2 is for calves and is required to prevent early age mortality, which could be curtailed through this vaccine.

"M/s. Agriprom Pakistan (Pvt) Ltd" has also applied on 21st September 2021 for pre -registration variation- Change of title / name of manufacturer of their product (vaccines), Paraven R2C, from **Laboratories Vencofarma Do Brasil Ltda** to **Dechra Brasil Produtos Veterinarios Ltda.,** having the manufacturing site same i.e. Travessa Dalva de Oliveira 237 CEP 86030-370 Londrina, Parana, Brazil. Firm has also mentioned that there is no change in product formulation, API source, Pack Size, Specifications, manufacturing process, and shelf life, this is only administrative change and has submitted following:

i. Fee challan of rupee 150,000/- (Deposit slip No.2234137994).
ii. Copy of Drug Sale License (of M/s. Agriprom Pakistan Pvt. Ltd.)
iii. Copy of site master file Dechra Brasil Produtos Vetrinarios Ltda. (Legalized and Notarized).
iv. Copy of revised Power of Attorny (Sole agency agreement) with English translation, between Agriprom Pakistan Pvt. Ltd. and Dechra Brasil Produtos Veterinarios Ltda. (Legalized and Notarized).
v. Copy of Good Manufacturing Certificate (GMP) with English translation of dechra Brasil Produtos Veterinarios Ltda.
vi. Copy of company Registration Certificate, with English translation of Dechra Brasil Produtos Veterinarios Ltda.
vii. Copy of Free Sale Certificate with English translation of Paraven R2C.
viii. Undertaking by the firm that formulation, API source & specifications, manufacturing process, release and shelf life specifications have not changed.
ix. Undertaking that the provided documents are true.

Free sale Certificate (original legalized): On the certificate following is mentioned:

This is to certify that the product for veterinary use denominated Vancomax is legally registered at the Brazilian Ministry of Agriculture, Livestock and Food Supply(MAPA) under number 9.091/99, valid until 09/20/2029 for trade and export by the company Dechra Brasil Produtos Veterinaries Ltda, which is duly registered at MAPA under number PR 000007-8

Sole Agency Agreement:

Firm has submitted product specific sole agency agreement between

M/s. Dechra Brasil Produtos Veterinarios Ltda

Address: Travessa Dalva de Oliveira 237 Londrina- PR.

and **M/s. Agriprom Pakistan Pvt Ltd.**

Address: Plot No. 19B, off Abdul Sattar Edhi Road Near Qazalbash Chowk, District Lahore.

GMP certificate :

It is mentioned on the certificate that the company Dechra Brasil Produtos Veterinarios Ltda located at : Travessa Dalva de Oliveira 237, industrias Leves, ZIP code 86030-370 Londrina/PR. Is duly registered at Ministry of Agriculture, Livestock and Food supply, under number PR-000007-8 and operates in compliance with normative

instruction no. 13, of October 3, 2013 which endorses the rules of Good Manufacturing Practices for products for veterinary use. (electronically signed on dated 13-10-2020.)
Validity: Not mentioned.

Remarks of Evaluator:

i. From the free sale certificate, it is not clear that the product is in market of country of origin.

Decision: Registration Board deferred the product for submission of following:

i. Valid legalized Free Sale certificate confirming registration and availability status in country of origin.
ii. Separate fee for the registration of liquid part.
iii. Stability data for applied formulation.
iv. One of the indications in the vaccine is treatment of hepatitis while firm has submitted that CAV2 virus is involved in prophylaxis against hepatitis. However, the available literature indicates that CAV-1 vaccines provide immunity against Hepatitis. This requires supporting evidence from published literature/ reference regulatory agencies.
v. Evidence of local availability of formulation

10.	**Name of Importer & Manufacturer**	**Brand Name & Composition**	**Type of Form Dy No & Date of application Fee submitted Pack size/ Demanded Price**	**Document details (CoPP) Me too status/New molecule**	**Remarks**	**Decision(M-266)**
	M/s Agriprom Pakistan (Pvt) Ltd. 66 west wood colony, thokar niaz baig, Lahore. M/s Laboratorios VencoFarma Do Brasil Ltda. 237 Travessa Dalva de Oliveira, Parque das Industrias Leve, Londrina-PR	Paraven R2C. Each dose (5ml) contains: Bovine Coronavirus ……..$10^{4.5}TCID_{50}$ Rotavirus G6 ……$10^{4.5}TCID_{50}$ Rotavirus G10 ……$10^{4.5}TCID_{50}$ Escherichia coli O26 bacterin….10^5 germs Escherichia coli K99/F41 bacterin sample S30 ...….10^5 germs Escherichia coli 0111 bacterin…..10^5 germs Clostridium perfringens C toxoid, β toxin …….atleast 10UI/dose Clostridium perfringens D toxoid, ἐ toxin …….atleast 10UI/dose (vaccine against Bovine Rotavirus, coronavirus, Colibacillosis and Enteroxaemia) Shelf Life: 24months	Form 5-A 08-ADC(BD) 04-01-2017 312(R&I) 04-01-2017 Rs. 100000/- 03-01-2017 Pack size 50ml	Valid legalize GMP Certificate N^0 159/2016 Legalize FSC N^0 940/2016	New formulation Stability data is not submitted. The firm was asked to submit data however it was not provided	Deferred for evaluation of product by Dr. Qurban Ali and submission/ clarification of following by the firm: Stability data.
	Evaluation by BE&R: Now the firm in their reply dated 13th September, 2021 submitted following: i. **Stability Studies** ii. Clinical data iii. Valid legalized GMP iv. Valid legalized free sale certificate v. Specifications					

vi. **Evaluation of product by Dr. Qurban Ali; dated 6th jan 2021**

Conclusion of Evaluation: Product at serial No. 1-4(Vancomax12, Paraven RC2, Ronvac, Raive Cannis) are recommended for registration. Product at serial No. 1,3,4 are for pets namely dogs and cats and are required in veterinary medical practice. Product at serial No. 2 is for calves and is required to prevent early age mortality, which could be curtailed through this vaccine.

And "M/s. Agriprom Pakistan (Pvt) Ltd" has also applied on 21st September 2021 for pre -registration variation- Change of title / name of manufacturer of their product (vaccines), Paraven R2C, from **Laboratories Vencofarma Do Brasil Ltda** to **Dechra Brasil Produtos Veterinarios Ltda.,** having the manufacturing site same i.e. Travessa Dalva de Oliveira 237 CEP 86030-370 Londrina, Parana, Brazil. Firm has also mentioned that there is no change in product formulation, API source, Pack Size, Specifications, manufacturing process, and shelf life, this is only administrative change and has submitted following:

i. Fee challan of rupee 150,000/- (Deposit slip No.2234137994)
ii. Copy of Drug Sale License (of M/s. Agriprom Pakistan Pvt. Ltd.)
iii. Copy of site master file Dechra Brasil Produtos Vetrinarios Ltda. (Legalized and Notarized).
iv. Copy of revised Power of Attorny (Sole agency agreement) with English translation, between Agriprom Pakistan Pvt. Ltd. and Dechra Brasil Produtos Veterinarios Ltda. (Legalized and Notarized).
v. Copy of Good Manufacturing Certificate (GMP) with English translation of dechra Brasil Produtos Veterinarios Ltda.
vi. Copy of company Registration Certificate, with English translation of Dechra Brasil Produtos Veterinarios Ltda.
vii. Copy of Free Sale Certificate with English translation of Paraven R2C.
viii. Undertaking by the firm that formulation, API source & specifications, manufacturing process, release and shelf life specifications have not changed.
ix. Undertaking that the provided documents are true.

Finished product specifications	As per Innovator's Specifications

General documentation:

Free sale Certificate (original legalized): On the certificate following is mentioned:

This is to certify that the product for veterinary use denominated Paraven R2/C Inactivated Vaccine against Bovine Rotavirus, Coronavirus, Colibacillosis and Enterotoxemia is legally registered at the Ministry of Agriculture, Livestock and Food Supply(MAPA) under number 9.558/2010, valid until 01/21/2030 for trade and export by the company Dechra Brasil Produtos Veterinaries Ltda, which is duly registered at MAPA under number PR 000007-8.

Qualitative and Quantitative Formula:

Each dose of 5ml of the product contains:

Bovine corona virus	Minimum $10^{4.5}$ $TCID_{50}$
Rotavirus G6	Minimum $10^{4.5}$ $TCID_{50}$
Rotavirus G10	Minimum $10^{4.5}$ $TCID_{50}$
Escherichia coli O26 bacterin	Minimum 10^5 UFC
Escherichia coli K99/F41 bacterin Sample S30	Minimum 10^5 UFC
Escherichia coli 0111 bacterin	Minimum 10^5 UFC
Clostridium Perfringens C toxoid, B toxin	Minimum 10UI
Clostridium Perfringens D toxoid, E toxin	Minimum 10UI
Methyl paraben	Maximum 0.0125ml
Aluminium Hydroxide Gel	Maximum 25mg
Buffered Saline Q.S.	5ml

Sole Agency Agreement:

Firm has submitted product specific sole agency agreement between

M/s. Dechra Brasil Produtos Veterinarios Ltda

Address: Travessa Dalva de Oliveira 237 Londrina- PR.

and **M/s. Agriprom Pakistan Pvt Ltd.**

Address: Plot No. 19B, off Abdul Sattar Edhi Road Near Qazalbash Chowk, District Lahore.

GMP certificate:

It is mentioned on the certificate that the company Dechra Brasil Produtos Veterinarios Ltda located at : Travessa Dalva de Oliveira 237, industrias Leves, ZIP code 86030-370 Londrina/PR. Is duly registered at Ministry of Agriculture, Livestock and Food supply, under number PR-000007-8 and operates in

compliance with normative instruction no. 13, of October 3, 2013 which endorses the rules of Good Manufacturing Practices for products for veterinary use. (electronically signed on dated 13-10-2020.) Validity: Not mentioned.		
Remarks of Evaluator	i. From the free sale certificate, it is not clear that the product is in market of country of origin. ii. Composition of product on Form 5A is different from Free sale certificate.	
Decision: Registration Board deferred the product for submission of following by the firm: **i. Valid legalized Free Sale Certificate confirming registration and availability status in country of origin.** **ii. Clarification regarding difference of compositon in Form-5A & Free Sale Certificate.**		

11.	Name of Importer & Manufacturer	Brand Name & Composition	Type of Form Dy No & Date of application Fee submitted Pack size/ Demanded Price	Document details (CoPP) Me too status/New molecule	Remarks	Decision (M-266)
	M/s Agriprom Pakistan (Pvt) Ltd. 66 west wood colony, thokar niaz baig, Lahore. M/s Laboratorios VencoFarma Do Brasil Ltda. 237 Travessa Dalva de Oliveira, Parque das Industrias Leve, Londrina-PR	Ronvac Each dose contains: Inactivated virus Feline Rhinotracheitis…… minimum $10^{-4}TCID_{50}$ Inactivated virus Calicivirosis ..minimum $10^{-4}TCID_{50}$ Inactivated virus Feline Panleukopenia ..... minimum $10^{-4}TCID_{50}$ (Vaccine against Feline Panleukopenia, Calicivirus and Rhinotracheitis Shelf Life: 24months	Form 5-A 08-ADC(BD) 04-01-2017 312(R&I) 04-01-2017 Rs. 100000/- 03-01-2017 1 dose vial 40's	Valid legalize GMP Certificate N^0 159/2016 Legalize FSC N^0 940/2016	Stability data is not submitted. The firm was asked to submit data however it was not provided.	Deferred for review of product by Dr. Qurban Ali and submission/ clarification of following by the firm: a. Stability data.

Evaluation by BE&R:

Evaluation by BE&R:

Now the firm in their reply dated 13th September, 2021 submitted following:

i. Valid legalized GMP
ii. Valid legalized free sale certificate
iii. **Evaluation of product by Dr. Qurban Ali; dated 6th jan 2021**

Conclusion of Evaluation: Product at serial No. 1-4 (Vancomax12, Paraven RC2, Ronvac, Raive Cannis) are recommended for registration. Product at serial No. 1,3,4 are for pets namely dogs and cats and are required in veterinary medical practice. Product at serial No. 2 is for calves and is required to prevent early age mortality, which could be curtailed through this vaccine.

"M/s. Agriprom Pakistan (Pvt) Ltd" has also applied on 21st September 2021 for pre -registration variation- Change of title / name of manufacturer of their product (vaccines), Paraven R2C, from **Laboratories Vencofarma Do Brasil Ltda** to **Dechra Brasil Produtos Veterinarios Ltda.,** having the manufacturing site same i.e. Travessa Dalva de Oliveira 237 CEP 86030-370 Londrina, Parana, Brazil. Firm has also mentioned that there is no change in product formulation, API source, Pack Size, Specifications, manufacturing process, and shelf life, this is only administrative change and has submitted following:

i. Fee challan of rupee 150,000/- (Deposit slip No.2234137994)
ii. Copy of Drug Sale License (of M/s. Agriprom Pakistan Pvt. Ltd.)
iii. Copy of site master file Dechra Brasil Produtos Vetrinarios Ltda. (Legalized and Notarized).
iv. Copy of revised Power of Attorny (Sole agency agreement) with English translation, between Agriprom Pakistan Pvt. Ltd. and Dechra Brasil Produtos Veterinarios Ltda. (Legalized and Notarized).
v. Copy of Good Manufacturing Certificate (GMP) with English translation of dechra Brasil Produtos Veterinarios Ltda.
vi. Copy of company Registration Certificate, with English translation of Dechra Brasil Produtos Veterinarios

Ltda.

vii. Copy of Free Sale Certificate with English translation of Paraven R2C.

viii. Undertaking by the firm that formulation, API source & specifications, manufacturing process, release and shelf life specifications have not changed.

ix. Undertaking that the provided documents are true.

Free sale Certificate (original legalized): On the certificate following is mentioned:

This is to certify that the product for veterinary use denominated Ronvac is legally registered at the Brazilian Ministry of Agriculture, Livestock and Food Supply(MAPA) under number 6.830/1999, valid until 03/22/2029 for trade and export by the company Dechra Brasil Produtos Veterinaries Ltda, which is duly registered at MAPA under number PR 000007-8

Sole Agency Agreement:

Firm has submitted product specific sole agency agreement between

M/s. Dechra Brasil Produtos Veterinarios Ltda

Address: Travessa Dalva de Oliveira 237 Londrina- PR.

and **M/s. Agriprom Pakistan Pvt Ltd.**

Address: Plot No. 19B, off Abdul Sattar Edhi Road Near Qazalbash Chowk, District Lahore.

GMP certificate:

It is mentioned on the certificate that the company Dechra Brasil Produtos Veterinarios Ltda located at : Travessa Dalva de Oliveira 237, industrias Leves, ZIP code 86030-370 Londrina/PR. Is duly registered at Ministry of Agriculture, Livestock and Food supply, under number PR-000007-8 and operates in compliance with normative instruction no. 13, of October 3, 2013 which endorses the rules of Good Manufacturing Practices for products for veterinary use. (electronically signed on dated 13-10-2020.)

Validity: Not mentioned.

Remarks of Evaluator:

i. From the free sale certificate, it is not clear that the product is in market of country of origin.

Decision: Registration Board deferred the product for submission of following:

i. Valid legalized Free Sale certificate confirming registration and availability status in country of origin.

ii. Stability data for applied formulation.

12. Deferred case of M/s Hipra Pakistan (Private) Limited, Lahore.

The following products of M/s Hipra Pakistan (Private) Limited, Lahore were deferred in 291st meeting of Registration Board as per following details.

1.	Name of Importer	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
	DSL details	License to sell drug as distributor No. 0011000 0004579 valid till 19-Feb-2022
	Name of Manufacturer	**Product License Holder & Manufacturer**: M/S Laboratorios Hipra, S.A.de La Selva, 135, 17170 Amer (Girona) Spain (for batch release in the EU, quality control and secondary packaging. Also responsible for manufacturing of solvent/diluent) **Manufacturer:** M/s Laboratorios Hipra, S.A. Carretera C-63, Km 48,300, poligono Industrial El Rieral, 17170 Amer (Gerona) Spain (Also responsible for primary packaging)
	Brand Name +Dosage Form + Strength	**Gumbohatch** lyophilisate and solvent for suspension for injection,
	Composition	Each dose contains:- Live attenuated infectious bursal disease virus (IBDV), strain 1052……$10^{1.48}$- $10^{2.63}$ PU (Potency Units) **Solvent:** Disodium phosphate dodecahydrate. Potassium dihydrogen phosphate. Sodium chloride Potassium chloride

		Water for injection
	Finished product specifications	BP Specification
	Pharmacological Group	Oily Emulsion Veterinary Viral Vaccine
	Shelf life	24 months(2^0C-8^0C)
	Products already registered in Pakistan	Transmune IBD (Ceva France) Bursaplex (Zoetis US)
	Type of Form Dy. No & Date of application, Fee submitted	Form-5A Dy. No. 37705 (R&I) Dated 14-11-2018, Dy. No. 30870 (R&I) Dated 19-11-2020. Rs. 100,000/- Dated 14th November 2018
	Demanded Price / Pack size	Decontrolled/ 5,000 Doses (500mL Vial) & 1000ml Solvent
	General documentation	CoPP No.10/20/150458 issued by EMA dated 19-10-2020
	Registration Board deferred in 291st meeting the case for submission of following by the firm: a. Evidence of availability of product in reference regulatory authorities. **b.** Clarification regarding the difference in address of manufacturer on CoPP from Form-5A & Letter of Authorization. **The firm's response:** i. The firm has submitted new CoPP issued by EMA wherein the product is freely available. ii. In the new CoPP the address is correctly mentioned.	
	Remarks of Evaluator	
	Decision: Keeping in view legalized CoPP indicating product availability in country of origin and approval of EMA (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs.	
2.	Name of Importer	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
	DSL details	License to sell drug as distributor No. 0011000 0004579 valid till 19-Feb-2022
	Name of Manufacturer	M/S LABORATORIOS HIPRA, S.A. Avda. La Selva,135, Amer,17170 (Gerona) Spain
	Brand Name +Dosage Form + Strength	**Evant 1000dose** Suspension and Solvent for oral spray
	Composition	Each dose of vaccine contains: Eimeria acervulina, strain 003……332-450 Eimeria maxima, strain 013…….196-265 Eimeria mitis, strain 006…….293-397 Eimeria praecox, strain 007…….293-397 Eimeria tenella, strain 004……..276-374 **Composition of Solvent (Hipramune T):** Montanide IMS (**Adjuvant)** Blue coloring Agent Red coloring Agent Vanillin
	Finished product specifications	BP's Specification
	Pharmacological Group	Veterinary vaccine
	Shelf life	10 months at 2-8°C
	International availability	Spain
	Products already registered in Pakistan	
	Type of Form Dy No & Date of application, Fee submitted	Form 5-A Dy.No. 1819 (R&I) Date:26-03-2019, Rs.100,000/- Date: 26-03-2019,
	Demanded Price / Pack size	Decontrolled/ 1000 Doses vaccine & 50ml diluent
	General documentation	Legalized COPP No. 05/20/150457 dated 19-10-2020 Issued by EMA

	Registration Board deferred in 291st meeting the case for submission of following by the firm: a. Valid legalized approval of product in country of origin. b. Evidence of availability of product in combopack in country of origin. **The firm's response:** The firm has submitted new CoPP issued by EMA wherein the product is freely available in combo pack.	
	Remarks of Evaluator	
	Decision: Keeping in view legalized CoPP indicating product availability in country of origin and approval of EMA (Reference Regulatory Authority); Registration Board approved the product subject to compliance of current Import Policy for finished drugs.	

13. Deferred case of M/s Hi-Tech Pharmaceuticals (Pvt) Ltd, Lahore.

The following products of M/s Hi-Tech Pharmaceuticals (Pvt) Ltd, Lahore were deferred in 312th meeting of Registration Board as per following details.

1.	**Name of Importer &** Address	**M/s Hi-Tech Pharmaceuticals (Pvt) Ltd** 1-C, Shadman Chowk, Jail Road, Lahore
	DSL Details	License to Sell Drugs as Distributor No: 05-352-0063-066935D valid till 3 Mar 2023
	Name of Manufacturer & Address	**Zoetis Inc.** 601 West Cornhusker Highway Lincoln, NE 68521-3577, USA
	Brand Name/Dosage Form	**Scour Guard 4KC**10dose vial
	Composition	Each 2ml dose contains: Bovine Rotavirus (Strain Lincoln Isolate)…..≥1.93 RP^1 at release&≥1.31 RP^1 at expiration Bovine Rotavirus (Strain B223)…….≥1.70 RP^1 at release&≥1.00 RP^1 at expiration Bovine Coronavirus (Strain Hansen Isolate)…≥2.40 RP^1 at release&≥1.20 RP^1 at expiration Escherichia coli (K99 pilus antigen) Strain NL-1005….≥1.40 RP^1 at release&≥1.00 RP^1 at expiration Clostridium perfringens Type C (Strain NL-1003) producing beta toxin…≥30 IAU^2/ml at release&≥10 IAU^2/mlatexpiration [1]RP Relative Potency [2] IAU International Antitoxin Units
	Finished Product Specifications	Ph. Eur.'s Specifications
	Pharmacological Group	Veterinary vaccine (Killed)
	Shelf Life & Storage	18 Months ($2^oC – 7^o$ C)
	International Availability	United States of America (USA)
	Products already Registered in Pakistan	No alternate is registered as per available record.
	Type of Form,Dy. No & Date of Application Fee Submitted	Form – 5A Dy. No 7606 Dated09-03-2021 Rs. 100,000.00 dated 09-03-2021
	Demanded Price&Pack Size	Decontrolled 10 dose Vial x 10
	General Documentation	Legalized Certificate of Licensing and Inspection (CLI) No. 20-01996, dated 11 Aug 2020issued by Center for veterinary Biologicals USA.
	Registration Board deferred the case by decided as under: Registration Board deferred the product for submission of stability data of the product including all parameters as mentioned in finished product specifications. The firm has submitted stability study data for 22 batches for 24 months for above mentioned product in 10 dose vial (Pack size) **but only potency test has been performed.**	
	Remarks:	In stability study data only potency test has been performed.
	Decision: Registration Board deferred the case for submission of stability data of the product including all parameters as mentioned in finished product specifications.	

2.	Name of Importer & Address	M/s Hi-Tech Pharmaceuticals (Pvt) Ltd 1-C, Shadman Chowk, Jail Road, Lahore
	DSL Details	License to Sell Drugs as Distributor No: 05-352-0063-066935D valid till 3 Mar 2023
	Name of Manufacturer & Address	**Zoetis Inc.** 601 West Cornhusker Highway Lincoln, NE 68521-3577, USA
	Brand Name/Dosage Form	**Calf-Guard one** dose vial
	Composition	Each 3ml dose contains: Bovine Rotavirus (Strain Lincoln Isolate) ….$\geq 10^{5.1}$ $TCID_{50}$[1] at release&$\geq 10^{4.6}$ $TCID_{50}$[1] at expiration Bovine Coronavirus (Strain Hansen Isolate)…$\geq 10^{4.2}$ $TCID_{50}$[1] at release&$\geq 10^{3.7}$ $TCID_{50}$[1] at expiration [1]TCID Tissue Culture Infectious Dose
	Finished Product Specifications	Ph. Eur.'s Specifications
	Pharmacological Group	Veterinary vaccine (Bovin Rotavirus-Coronavirus, Modified Live virus)
	Shelf Life & Storage	18 Months ($2^oC – 7^o$ C)
	International Availability	United States of America (USA)
	Products already Registered in Pakistan	No alternate is registered as per available record.
	Type of Form, Dy. No & Date of Application Fee Submitted	Form – 5A Dy. No 7603 Dated 09-03-2021 Rs. 100,000.00 dated 09-03-2021
	Demanded Price&Pack Size	Decontrolled one dose Vial x 25
	General Documentation	Legalized Certificate of Licensing and Inspection (CLI) No. 20-02034, dated 14th Aug 2020issued by Center for veterinary Biologicals USA.
	Registration Board deferred the case by decided as under: Registration Board deferred the product for submission of following by the firm: a. Stability data of the product including all parameters as mentioned in finished product specifications. b. Safety and Efficacy Data of the product. The firm has submitted stability study data for 6 batches for 21 months for above mentioned product in one dose vial (Pack size) with 0,3,6,9,12,18 & 21 months' time interval **but only potency test has been performed.** And Safety, Efficacy data has also been submitted.	
	Remarks:	In stability study data only potency test has been performed.
	Decision: Registration Board deferred the case for submission of stability data of the product including all parameters as mentioned in finished product specifications.	
3.	**Name of Importer &** Address	**M/s Hi-Tech Pharmaceuticals (Pvt) Ltd** 1-C, Shadman Chowk, Jail Road, Lahore
	DSL Details	License to Sell Drugs as Distributor No: 05-352-0063-066935D valid till 3 Mar 2023
	Name of Manufacturer & Address	**Zoetis Inc.** 601 West Cornhusker Highway Lincoln, NE 68521-3577, USA
	Brand Name/Dosage Form	**One Shot Ultra 7** 10dose vial
	Composition	**Lyophilized Component:** Each dose contains; Mannheimiahaemolytica (Type A1, Strain NL 1009)…> 1.3 RP[1]Leukotoxoid&$\geq$ 1.6 RP[1] CapsularAntigen **Liquid Component:** Each dose contains; Clostridium chauvoei (Strain F) ….> 2.28 opacity units &a minimumflagellarcontent of 0.6 RU/dose Clostridium septicum (Strain A (IRP-111)}…> 32 L+ units[2] Clostridium novyi (Strain 8296)…..> 6,000MLD[3]

		Clostridium sordellii (Strain 5918) ≥ 20 L+ units[2] Clostridium perfringens Type C (Strain PC8)…≥ 300 L+ units[2] Clostridium perfringens Type D (Strain 317)…≥ 100 L+ units[2] [1]RP Relative Potency [2]Unit of toxin,pre-inactivation [3]MLD-Mouse Lethal Dose,pre-inactivation
	Finished Product Specifications	Ph. Eur.'s Specifications
	Pharmacological Group	Veterinary vaccine (Killed)
	Shelf Life & Storage	24 Months (2°C – 7° C)
	International Availability	United States of America (USA)
	Products already Registered in Pakistan	No alternate is registered as per available record.
	Type of Form,Dy. No & Date of Application Fee Submitted	Form – 5A Dy. No 7605 Dated09-03-2021 Rs. 100,000.00 dated 09-03-2021
	Demanded Price&Pack Size	Decontrolled/ 10 dose Vial (1's)
	General Documentation	Legalized Certificate of Licensing and Inspection (CLI) No. 20-02030 dated 14th Aug 2020issued by Center for veterinary Biologicals USA.
	Remarks:	Stability study for liquid part has not been submitted. Initially the firm submitted application on DSL with importer name M/s Hi-Tech Pharmaceuticals. Later on the firm new DSL along with revised Form 5A wherein the importer name has been changed to Hi-Tech Pharmaceuticals Pvt. Ltd. With the application the firm also submitted revised distribution agreement(addendum) with the new name, copy of DSL and approval of new name by SECP.
	Registration Board deferred the case by decided as under: Registration Board deferred the product for submission of stability data of liquid component of the product including all parameters as mentioned in finished product specifications. The firm has submitted stability study data of liquid component of the product (10 dose vial) for 3 batches for 27 months with 0,3,7,12,18, 21 & 24 months' time interval **but only potency test has been performed.**	
	Remarks:	In stability study data only potency test has been performed.
	Decision: Registration Board deferred the case for submission of stability data of the product including all parameters as mentioned in finished product specifications.	
4.	**Name of Importer &** Address	**M/s Hi-Tech Pharmaceuticals (Pvt) Ltd** 1-C, Shadman Chowk, Jail Road, Lahore
	DSL Details	License to Sell Drugs as Distributor No: 05-352-0063-066935D valid till 3 Mar 2023
	Name of Manufacturer & Address	**Zoetis Inc.** 601 West Cornhusker Highway Lincoln, NE 68521-3577, USA
	Brand Name/Dosage Form	**Bovi Shield Gold FP 5 L5** 50 dose vial
	Composition	**Lyophilized Component:** Each dose contains: Bovine Rhinotracheitis Virus (Strain passage C-13)….≥ $10^{4.9}$ TCID $_{50}$[1] Bovine Virus Diarrhea Virus Type 1 (Strain NADL)..≥ $10^{4.5}$ TCID $_{50}$[1] Bovine Virus Diarrhea Virus Type 2 (Strain 53637)…≥ $10^{5.3}$ TCID $_{50}$[1] Parainfluenza Virus (Strain AL-IM)…..≥ $10^{7.3}$ TCID $_{50}$[1] Bovie Respiratory Syncytial Virus (Strain BRSV/375)..≥ $10^{4.6}$ TCID $_{50}$[1] [1]TCID Tissue Culture Infectious Dose **Liquid Component:** Each dose contains: Leptospira canicola (Strain C-51)….≥ 1200 NU[1] Leptospira grippotyphosa (Strain MAL 1540)…..≥ 1200 NU[1] Leptospira hadjo (Strain WHO)…..≥ 1200 NU[1] Leptospira icterohaemorrhagiae (Strain NADL (11403)}….≥ 1200 NU[1]

		Leptospira pomona (Strain T262)…≥ 1200 NU[1] [1]NU Nephelometric units, pre-inactivation
	Finished Product specifications	Innovator's Specifications
	Pharmacological Group	Veterinary vaccine (Viral Modified Live vaccine with diluent comprised of bacterin fluid)
	Shelf Life & Storage	18 Months ($2^oC – 7^o$ C)
	International Availability	United States of America (USA)
	Products already Registered in Pakistan	No alternate is registered as per available record.
	Type of Form, Dy. No & Date of Application Fee Submitted	Form – 5A Dy. No 7602 Dated 09-03-2021 Rs. 100,000.00 dated 09-03-2021
	Demanded Price&Pack Size	Decontrolled 50 dose Vial Plus 2ml vial
	General Documentation	Legalized Certificate of Licensing and Inspection (CLI) No. 20-02031, dated 14th Aug 2020issued by Center for veterinary Biologicals USA.
	Remarks of the Evaluator	In stability study data for Lyophilized part, the pack size has not been mentioned, only potency test has been performed & the test has been performed on 0,18 or 19 months which is not as per ICH guidelines. Stability study for liquid part has not been submitted. Initially the firm submitted application on DSL with importer name M/s Hi-Tech Pharmaceuticals. Later on the firm new DSL along with revised Form 5A wherein the importer name has been changed to Hi-Tech Pharmaceuticals Pvt. Ltd. With the application the firm also submitted revised distribution agreement(addendum) with the new name, copy of DSL and approval of new name by SECP.
	Registration Board deferred the case by decided as under: Registration Board deferred the product for submission of following by the firm: Stability data of the Lyophilized and Liquid parts of the product including all parameters as mentioned in finished product specifications at 0, 3, 6, 9, 12, 18 months interval. The firm has submitted stability study data of liquid component of the product (2ml) for 6 batches for 33 months with 0,3,6,9,12,18, 24,30 & 33 months' time interval **but only potency test has been performed.** The firm has submitted stability study data for 3 batches for 19 months for **Lyophilized** part of the product in 50 dose vial (Pack size) with 0,3,6,9,12 & 19 months' time interval **but only potency test has been performed.**	
	Remarks:	In stability study data only potency test has been performed.
	Decision: Registration Board deferred the case for submission of stability data of the product including all parameters as mentioned in finished product specifications.	

14. Transfer of registration of imported veterinary vaccine from m/s eros pharmaceuticals, pvt ltd. Karachi to m/s Jovac Global Pak lahore

Sr. No	Manufacturer	Name & Composition	Documents details
1	Jovac "Jordan Bio Industries Center" Yajouz, near the Agriculture nursery, Amman-Jordan	**Jova Zeit 1** vaccine (Inactivated Newcastle Disease Virus.) Injectable water in oil emulsion. Each 0.3 ml vaccine contains; Inactivated Newcastle Disease Virus Strain Lasota.....atleast $10^{9.0}$ EID_{50}	Transfer letter with Reg No. 039937 dated 31-05-2010 Renewal application submission date 18-05-2020
2		**Jova Zeit 7** vaccine Each 0.2 ml vaccine contains; Inactivated Avian influenza Subtype H9N2.....at least $10^{8.2}$ EID_{50}	Copy of registration letter with Reg No. 091375 dated 12-09-2018

3		**Jova Zeit 1,7** vaccine Each 0.2 ml vaccine contains; Inactivated Avian influenza Subtype H9N2.....at least $10^{8.2}$ EID_{50} Inactivated Newcastle Disease Virus.....at least 10^{9} EID_{50}	Copy of registration letter with Reg No. 091371 dated 12-09-2018
4		**Jova Zeit 1,2,4** vaccine Each dose of vaccine contains; Inactivated Newcastle Disease Virus.....at least 10^{9} EID_{50} Inactivated infectious Bronchitis virus Strain .M4...Atleast $10^{6.8}$ Inactivated Egg Drop Syndrome Virus Strain Atleast 1000 HA...76	Transfer letter with Reg No. 039937 dated 31-05-2010 Renewal application submission date 18-05-2020

The application was evaluated as per SOPs approved in 283rd meeting revised in 292nd meeting of Registration Board. Details are as under;

1. Jova Zeit 1

Requirement as per SOP	**Document submitted**	**Remarks**
Application on Form 5A with required fee as per relevant SRO.	Fee of 150,000/- has been submitted & Along with application on Form 5-A	
Copy of registration letter and last renewal status	Transfer letter with Reg No. 039937 dated 31-05-2010. Renewal application submission date 18-05-2020	
Termination letter (original) from manufacturer for previous importer.	Termination of Agency agreement letter has been submitted	
Authority letter/sole agent letter (original) from manufacturer.	Notarized copy of distribution agreement with the manufacturer wherein the firm has been authorized for its products.	
Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.	NOC from the previous importer i.e. M/s Eros Pharmaceuticals Karachi dated 20-05-2021	
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 CoPP No. 5/5/10/003280 dated 18-03-2021 issued by Veterinary & Animal Health Directorate, Mo Agriculture the Hashemite Kingdom of Jordan	
Undertaking that the provided information/ documents are true/ correct.	Provided	

	Name of Importer	**M/s <u>Jovac Global Pak</u>** Address: Plot No 17, Block-D EME DHA,Phase 12 Lahore Pakistan
	DSL details	License to sell drug as distributor No.05-352-0066-072607D Valid till 15-June-2023
	Name of Manufacturer	Jovac "Jordan Bio Industries Center" Yajouz, near the Agriculture nursery, Amman-Jordan
	Brand Name + Dosage Form + Strength	Jova Zeit 1 vaccine (Inactivated Newcastle Disease Virus.) Injectable water in oil emulsion.
	Composition	Each 0.3 ml vaccine contains; Inactivated Newcastle Disease Virus Strain Lasota.....atleast $10^{9.0}$ EID_{50}
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Biologicals /Vaccine
	Shelf life	24 Months (Store at 2^0C to 8^0C)
	Products already registered in Pakistan	Already registered. Now applied for transfer of registration
	Type of Form	Form 5-A

	Dy. No. Date of Application, Fee submitted	Dated:8-June-2021. Dy No:15847. Fee Submitted: Rs. 150030/- Dated 7-June-2021
	Demanded Price/ Pack size	Pack Size: 300 ml
	General Documentation	• Legalized Certificate of Pharmaceutical Product (COPP) No.5/5/10/003280 issued by Ministry of Agriculture Veterinary and Animal Health Directorate Jordan. Dated:18-March-2021
	Remarks	
	Decision	

2. Jova Zeit 7

Requirement as per SOP	Document submitted	Remarks
Application on Form 5A with required fee as per relevant SRO.	Fee of 150,000/- has been submitted & Along with application on Form 5-A	
Copy of registration letter and last renewal status	Copy of registration letter with Reg No. 091375 dated 12-09-2018	
Termination letter (original) from manufacturer for previous importer.	Termination of Agency agreement letter has been submitted	
Authority letter/sole agent letter (original) from manufacturer.	Notarized copy of distribution agreement with the manufacturer wherein the firm has been authorized for its products.	
Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.	NOC from the previous importer i.e. M/s Eros Pharmaceuticals Karachi dated 20-05-2021	
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 CoPP No. 010330 dated 28-10-2020 issued by Veterinary & Animal Health Directorate, Mo Agriculture the Hashemite Kingdom of Jordan	

	Name of Importer	**M/s Jovac Global Pak** Address: Plot No 17, Block-D EME DHA,Phase 12 Lahore Pakistan
	DSL details	License to sell drug as distributor No.05-352-0066-072607D Valid till 15-June-2023
	Name of Manufacturer	Jovac "Jordan Bio Industries Center" Yajouz, near the Agriculture nursery, Amman-Jordan
	Brand Name + Dosage Form + Strength	Jova Zeit 7 vaccine Injectable water in oil emulsion.
	Composition	Each 0.2 ml vaccine contains; Inactivated Avian influenza Subtype H9N2.....at least $10^{8.2}$ EID_{50}
	Finished product specifications	As per innovator
	Pharmacological Group	Biologicals /Vaccine
	Shelf life	24 Months (Store at 2^0C to 8^0C)
	Products already registered in Pakistan	Already registered. Now applied for transfer of registration
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5-A Dated:8-June-2021. Dy No:15846. Fee Submitted: Rs. 150030/- Dated 7-June-2021
	Demanded Price/Pack size	Pack Size: 300 ml Bottle
	General Documentation	• Legalized Certificate of Pharmaceutical Product (COPP) No.5/5/10/010330 issued by Ministry of Agriculture Veterinary and Animal Health Directorate Jordan. Dated:28-10-2020
	Remarks	
	Decision	

3. Jova Zeit 1,7

Requirement as per SOP	Document submitted	Remarks
Application on Form 5A with required fee as per relevant SRO.	Fee of 150,000/- has been submitted & Along with application on Form 5-A	
Copy of registration letter and last renewal status	Copy of registration letter with Reg No. 091371 dated 12-09-2018	
Termination letter (original) from manufacturer for previous importer.	Termination of Agency agreement letter has been submitted	
Authority letter/sole agent letter (original) from manufacturer.	Notarized copy of distribution agreement with the manufacturer wherein the firm has been authorized for its products.	
Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.	NOC from the previous importer i.e. M/s Eros Pharmaceuticals Karachi dated 20-05-2021	
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 CoPP No. 003478 dated 18-03-2021 issued by Veterinary & Animal Health Directorate, Mo Agriculture the Hashemite Kingdom of Jordan	

	Name of Importer	**M/s <u>Jovac Global Pak</u>** Address: Plot No 17, Block-D EME DHA,Phase 12 Lahore Pakistan
	DSL details	License to sell drug as distributor No.05-352-0066-072607D Valid till 15-June-2023
	Name of Manufacturer	Jovac "Jordan Bio Industries Center" Yajouz, near the Agriculture nursery, Amman-Jordan
	Brand Name + Dosage Form + Strength	Jova Zeit 1,7 vaccine Injectable water in oil emulsion.
	Composition	Each 0.2 ml vaccine contains; Inactivated Avian influenza Subtype H9N2.....at least $10^{8.2}$ EID_{50} Inactivated Newcastle Disease Virus.....at least 10^{9} EID_{50}
	Finished product specifications	As per innovator
	Pharmacological Group	Biologicals /Vaccine
	Shelf life	24 Months (Store at 2^0C to 8^0C)
	Products already registered in Pakistan	Already registered. Now applied for transfer of registration
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5-A Dated:8-June-2021. Dy No:15845. Fee Submitted: Rs. 150030/- Dated 7-June 2021
	Demanded Price/ Pack size	Pack Size: 300 ml Bottle
	General Documentation	• Legalized Certificate of Pharmaceutical Product (COPP) No.<u>5/5/10/003278 </u>issued by Ministry of Agriculture Veterinary and Animal Health Directorate Jordan. Dated:18-03-2021
	Remarks	
	Decision	

4. Jova Zeit 1,2,4

Requirement as per SOP	Document submitted	Remarks
Application on Form 5A with required fee as per relevant SRO.	Fee of 150,000/- has been submitted & Along with application on Form 5-A	
Copy of registration letter and last renewal status	Transfer letter with Reg No. 039937 dated 31-05-2010. Renewal application submission date 18-05-2020	

Termination letter (original) from manufacturer for previous importer.	Termination of Agency agreement letter has been submitted	
Authority letter/sole agent letter (original) from manufacturer.	Notarized copy of distribution agreement with the manufacturer wherein the firm has been authorized for its products.	
Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.	NOC from the previous importer i.e. M/s Eros Pharmaceuticals Karachi dated 20-05-2021	
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 CoPP No. 003489 dated 18-03-2021 issued by Veterinary & Animal Health Directorate, Mo Agriculture the Hashemite Kingdom of Jordan	

	Name of Importer	**M/s <u>Jovac Global Pak</u>** Address: Plot No 17, Block-D EME DHA,Phase 12 Lahore Pakistan
	DSL details	License to sell drug as distributor No.05-352-0066-072607D Valid till 15-June-2023
	Name of Manufacturer	Jovac "Jordan Bio Industries Center" Yajouz, near the Agriculture nursery, Amman-Jordan
	Brand Name + Dosage Form + Strength	Jova Zeit 1,2,4 vaccine Injectable water in oil emulsion.
	Composition	Each dose of vaccine contains; Inactivated Newcastle Disease Virus.....at least 10^{9} EID_{50} Inactivated .infectious Bronchitis virus Strain M4...Atleast $10^{6.8}$ Inactivated Egg Drop Syndrome Virus Strain 76...Atleast 1000 HA
	Finished product specifications	Ph. Eur.
	Pharmacological Group	Biologicals /Vaccine
	Shelf life	24 Months (Store at 2^{0}C to 8^{0}C)
	Products already registered in Pakistan	Already registered. Now applied for transfer of registration
	Type of Form Dy. No. Date of Application, Fee submitted	Form 5-A Dated:8-June-2021. Dy No:15844. Fee Submitted: Rs. 150030/- Dated 7-June 2021
	Demanded Price/ Pack size	Pack Size: 300 ml Bottle
	General Documentation	• Legalized Certificate of Pharmaceutical Product (COPP) No.<u>5/5/10/003279 </u>issued by Ministry of Agriculture Veterinary and Animal Health Directorate Jordan. Dated:18-03-2021
	Remarks	

Decision: Keeping in view legalized CoPPs indicating products availability in country of origin and NOC submitted by M/s Eros Pharmaceuticals, Karachi; Registration Board cancelled the registration of Jova Zeit 1 (Reg No. 039937), Jova Zeit 7 (Reg No. 091375) & Jova Zeit 1, 7 (Reg No. 091371) from M/s Eros Pharmaceuticals, Karachi and granted in name of M/s Jovac Global Park, Plot No. 17, Block-D EME DHA, Phase 12, Lahore subject to the compliance of current Import Policy for Finished Drugs and verification of cold storage facility.

Item No. V Any other item with the permission of Chair (Additional Agenda Minutes)

Pharmaceutical Evaluation Cell

Item No. 1: Agenda of Evaluator PEC-I:

Case NO. I: Registration application submitted on Form 5F for local manufacturing:
New Section:

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.
The firm has not applied for registration of any product is this section.

1.	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. 24355 dated 03/09/2021
	Details of fee submitted	PKR 30,000/-: dated 14/07/2021
	The proposed proprietary name / brand name	Aqua J 5ml 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	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 5ml glass ampoule by M/s Pfizer, MHRA Approved.
	For generic drugs (me-too status)	Water for injection 5ml by M/s GSK, Reg. No. 088255
	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 & 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 5ml injection by M/s Shaigan Pharmaceuticals by performing all the quality tests.
	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.	KW-01	KW-02	KW-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)	No previous approval of any product with stability.
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 from 28/03/2021 to

Remarks OF Evaluator:

Observations	**Response**
The submitted stability study data is submitted till 3rd month time point, therefore you are required to submit stability studies till 6th month time point along with the record of digital data logger for monitoring of humidity and temperature for real time and accelerated stability.	The firm has submitted the stability data at 6th month time point for accelerated as well as for real time stability testing along with the record of digital data logger for monitoring of humidity and temperature for real time and accelerated stability.
Submit details including Batch number, manufacturing and expiry date of the comparator product against which pharmaceutical equivalence were conducted.	Mfg: M/s Shaigan Pharmaceutical (pvt) Ltd. Batch No. 206 Mfg date: 14/12/2020 Expiry date: 13/12/2022

Decision: Approved.

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

Case no. II: Registration applications of Form 5F

2.	Name, address of Applicant / Marketing Authorization Holder	M/s Herbion Pakistan Pvt Ltd. Industrial Triangle , Kahuta Road, Islamabad
	Name, address of Manufacturing site.	M/s Herbion Pakistan Pvt Ltd. 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	The firm has submitted copy of GMP certificate dated 17-07-2019. The certificate is valid till 20-05-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of grant of revised / relocated section letter dated 09-04-2020 in which Tablet (general) section is specified.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24969: 25-11-2019
	Details of fee submitted	PKR 50,000/-: 25-11-2019

	The proposed proprietary name / brand name	**VOCAB 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	Oblong shaped beige yellow color film coated tablet plain on both sides
	Pharmacotherapeutic Group of (API)	Proton pump inhibitor
	Reference to Finished product specification	In house specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	**(PMDA Japan** Approved)
	For generic drugs (me-too status)	Not Applicable
	Name and address of API manufacturer.	Jiangxi Synergy Pharmaceutical Co. Ltd. Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi 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 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 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.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Takecab Tablet of Takeda Pharma. Firm has submitted results of CDP for their product against Takecab Tablet of Takeda Pharma.
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and analytical method validation of the drug product.
STABILITY STUDY DATA		

Manufacturer of API	Jiangxi Synergy Pharmaceutical Co. Ltd. Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province China.		
API Lot No.	20201201BD		
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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Vc (10)ST-001	Vc (10)ST-002	Vc (10)ST-003
Batch Size	700 Tablet	700 Tablet	700 Tablet
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	28-04-2021	28-04-2021	28-04-2021
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)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of written confirmation for active substances exported to EU (No. JX200001) issued by Jiangxi Food and Drug Administration dated 20-11-2020. The drug manufacturing license of the firm is verified from SFDA official website. The SFDA official website specifies Jiangxi Tonghe Pharmaceutical Co., Ltd. As the name of Pharmaceutical manufacturing company (Number Gan20160125) having the same address as that of Jiangxi Synergy
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of license to import drugs for clinical trials, examination, test or analysis dated 25-02-2021 for import of 0.1Kg vonoprazan fumarate from Jiangxi Synergy. Firm has also submitted copy of commercial invoice specifying import of 0.1Kg vonoprazan fumarate. The invoice is cleared by AD (I&E) DRAP dated 25-02-2021.
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 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	Firm has submitted HPLC audit trail reports and 21 CFR compliance certificate
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 submitted real time and accelerated stability study data of 3 batches till 6 months.

3.	Name, address of Applicant / Marketing Authorization Holder	M/s Herbion Pakistan Pvt Ltd. Industrial Triangle , Kahuta Road, Islamabad
	Name, address of Manufacturing site.	M/s Herbion Pakistan Pvt Ltd. 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	The firm has submitted copy of GMP certificate dated 17-07-2019. The certificate is valid till 20-05-2022.
	Evidence of approval of manufacturing facility	Firm has submitted copy of grant of revised / relocated section letter dated 09-04-2020 in which Tablet (general) section is specified.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24974: 25-11-2019
	Details of fee submitted	PKR 50,000/-: 25-11-2019
	proposed proprietary name / brand name	VOCAB 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	Oblong shaped biplanar bisect line on both sides, pink color film coated tablet
	Pharmacotherapeutic Group of (API)	Proton pump inhibitor
	Reference to Finished product specification	In house specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	(PMDA Japan Approved)
	For generic drugs (me-too status)	Not Applicable
	Name and address of API manufacturer.	Jiangxi Synergy Pharmaceutical Co. Ltd. Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi 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 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 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.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Takecab 20mg Tablet of Takeda Pharma. Firm has submitted results of CDP for their product against Takecab Tablet of Takeda Pharma.20mg
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and analytical method validation of the drug product.

STABILITY STUDY DATA

Manufacturer of API	Jiangxi Synergy Pharmaceutical Co. Ltd. Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province China.		
API Lot No.	20201201BD		
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, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Vc (20)ST-001	Vc (20)ST-002	Vc (20)ST-003
Batch Size	700 Tablet	700 Tablet	700 Tablet
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	28-04-2021	28-04-2021	28-04-2021
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)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of written confirmation for active substances exported to EU (No. JX200001) issued by Jiangxi Food and Drug Administration dated 20-11-2020. The drug manufacturing license of the firm is verified from SFDA official website. The SFDA official website specifies Jiangxi Tonghe Pharmaceutical Co., Ltd. As the name of Pharmaceutical manufacturing company (Number Gan20160125) having the same address as that of Jiangxi Synergy
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of license to import drugs for clinical trials, examination, test or analysis dated 25-02-2021 for import of 0.1Kg vonoprazan fumarate from Jiangxi Synergy. Firm has also submitted copy of commercial invoice specifying import of 0.1Kg vonoprazan fumarate. The

		invoice is cleared by AD (I&E) DRAP dated 25-02-2021.
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 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	Firm has submitted HPLC audit trail reports and 21 CFR compliance certificate
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 submitted real time and accelerated stability study data of 3 batches till 6 months.
- Chairman Registration Board constituted a panel for product specific inspection for verification of authenticity of submitted stability study data vide letter No.

Name of Manufacturer	M/s Herbion Pakistan (Pvt.) Ltd. Industrial triangle, Kahuta road, Humak, Islamabad.
Date of Inspection	15-11-2021
Purpose of Inspection	Verification of authenticity of stability data for purpose of registration of drugs with reference DRAP's letter no. F.1-2/2020-PEC (AD PEC-III) dated 04-11-2021.
Name of Inspector	01 Mr. Abdullah Additional Director PE&R. 02 Mr. Farooq Aslam AD PEC DRAP, Islamabad.

Focus of Inspection:

The inspection was focused on a thorough evaluation for establishing the genuineness of submitted data for stability studies of following products namely:

Sr. No.	**Name / Composition of Drugs**
01	Vocab Tablet 10 mg Each film coated tablet contains: Vonoprazan Fumarate ……10 mg
02	Vocab Tablet 20 mg Each film coated tablet contains: Vonoprazan Fumarate ……20 mg

Q. No.	**Content**	**Remarks**
1.	Do you have documents confirming the import of API including approval from DRAP?	The firm has imported Vonoprazan Fumarate raw material vide invoice no. JXS210157 dated 28-01-2021 manufactured by M/s Jiangxi Synergy Pharmaceutical import & export co., Ltd. China and got DRAP clearance vide no. 687/2021/DRAP dated: 25-02-2021.
2.	Do you have any rationale behind selecting the particular manufacturer of API?	Remote audit based on the documentation including drug manufacturing license.
3.	Do you have documents confirming the import of API reference standard and impurity standards?	The firm had presented a statement letter from the manufacturer of drug substance mentioning that 100mg WS for analysis of drug substance was dispatched along with the 0.1KG of Drug substance Vonoprazan Fumarate without mentioning on invoice. The firm did not have the documents confirming the import of impurity standards.
4.	Do you have certificate of Analysis of the API, reference standards and impurity standards?	The COAs of reference standard for drug substance and impurity analysis.

5.	Do you have any approval of API, or GMP certificate of API manufacturer issued by regulatory authority of county of origin?	The firm had valid GMP Certificate of M/s Jiangxi Synergy Pharmaceutical import & export co., Ltd. China issued by Jiangxi Provincial Drug Administration, valid till 19-11-2022.
6.	Do you use API manufacturer method of testing?	The firm used API manufacturer's method of testing.
7.	Do you have stability studies reports on API?	The firm had stability studies reports on API of API manufacturers. Accelerated (40˚C ± 2˚C / RH 75% ± 5%) – 6 months Real time (30˚C ± 2˚C / RH 65% ± 5%) – 18 months Batches: 20190801BD, 20190802BD, 20190803BD
8.	If Yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	The firm has referred to specificity parameter of analytical method verification studies wherein impurity spiking was done, to establish their method as SIM.
9.	Do you have method for quantifying the impurities in the API?	Yes, the firm had the validated methods for quantifying the impurities.
10.	Do you have some remaining quantities of the API, its reference standard and Impurities standards?	The firm had some quantity of API and working standard but no remaining quantities of impurities standards at the time of inspection.
11.	Have you used pharmaceutical grade excipients?	The firm had used pharmaceutical grade excipients.
12.	Do you have documents confirming the import of the used excipients?	N/A. Excipients were purchased locally.
13.	Do you have test reports and other records on the excipients used?	The firm had certificates of analysis of the excipients used.
14.	Do you have written and authorized protocols for the development of tablets?	The firm had written protocols for the development of Vocab 10 mg tablets and Vocab 20 mg tablets.
15.	Have you performed Drug-excipients compatibility studies?	No, the firm used innovator formulation.
16.	Have you performed comparative dissolution studies?	The firm had performed comparative dissolution studies for Vocab 10 mg tablets and Vocab 20 mg tablets with Takecab tablets 10 mg and Takecab tablets 20 mg respectively manufactured by Takeda pharmaceuticals Japan.
17.	Do you have product development (R&D) section	The firm had product development (R&D) section.
18.	Do you have necessary equipment available in product development section for development of tablets?	Product development section had necessary equipment to develop Vocab 10 mg tablets and Vocab 20 mg tablets.
19.	Are the equipment in product development section qualified?	The available equipment in product development section were qualified.
20.	Do you have proper maintenance / calibration / re-qualification program for the equipment used in PD section?	The firm had proper maintenance / calibration / re-qualification program for the equipment used in product development section.
21.	Do you have qualified staff in product development section with proper knowledge and training in product development?	Yes
22.	Have you manufactured three stability batches for the stability studies of tablets as required?	The firm had manufactured three initial stability batches for the stability studies of Vocab 10 mg tablets and Vocab 20 mg tablets. The accelerated studies were done in Climatic test chamber (Votschtecnik, France) and long-term studies were done in Climatic test chamber (

<table>
<tr><td></td><td></td><td>Votschtecnik, France).</td></tr>
<tr><td>23.</td><td>Do you have any criteria for fixing the batch size of stability batches?</td><td>There was no criteria for fixing the batch size except the machine capacity.</td></tr>
<tr><td>24.</td><td>Do you have complete record of production of stability batches?</td><td>The firm had record of production of stability batches
<table>
<tr><th>Batch No.</th><th>Mfg. Date</th></tr>
<tr><td colspan="2">Vocab Tablets 10 mg (batch Size 700 tablet)</td></tr>
<tr><td>VOC (10)-ST-001</td><td>04-2021</td></tr>
<tr><td>VOC (10)-ST-002</td><td>04-2021</td></tr>
<tr><td>VOC (10)-ST-003</td><td>04-2021</td></tr>
<tr><td colspan="2">Vocab Tablets 20 mg 9batch size 700 tablets)</td></tr>
<tr><td>VOC (20)-ST-001</td><td>04-2021</td></tr>
<tr><td>VOC (20)-ST-002</td><td>04-2021</td></tr>
<tr><td>VOC (20)-ST-003</td><td>04-2021</td></tr>
</table></td></tr>
<tr><td>25.</td><td>Do you have protocols for stability testing of stability batches?</td><td>The firm had protocol for stability testing of stability batches.</td></tr>
<tr><td>26.</td><td>Do you have developed and validated the method for testing of stability batches.</td><td>The firm had developed method of Vocab Tablet 10 mg and Vocab Tablet 20 mg for testing of stability batches of applied formulations.</td></tr>
<tr><td>27.</td><td>Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?</td><td>Not Applicable.</td></tr>
<tr><td>28.</td><td>Do you have documents confirming the qualification of equipment / instruments being used in the test and analysis of API and the finished drug?</td><td>The firm had proper documents confirming the qualification of equipment / instruments being used in the test and analysis of Vonoprazan Fumarate API and the finished drug.</td></tr>
<tr><td>29.</td><td>Do your method of analysis stability indicating?</td><td>Yes, the method used for analysis of finished product and drug substance was stability indicating.</td></tr>
<tr><td>30.</td><td>Do your HPLC software 21CFR compliant?</td><td>FPP testing had been conducted on HP-QCE-048 (shimadzu LC-2030) and HP-QCE-001 (shimadzu 2080), which were 21 CFR compliant.</td></tr>
<tr><td>31.</td><td>Can you show Audit Trial reports on Testing?</td><td>The audit trail report was reproduced at the time of inspection.</td></tr>
<tr><td>32.</td><td>Do you have some remaining quantities of degradation products and stability batches?</td><td>The firm had remaining quantities of stability batches kept on stability testing.
<table>
<tr><th>Batch No.</th><th>Tablets used for stability studies</th><th>Remaining quantities</th></tr>
<tr><td colspan="3">Vocab Tablets 10 mg</td></tr>
<tr><td>VOC (10)-ST-001</td><td>140</td><td>161</td></tr>
<tr><td>VOC (10)-ST-002</td><td>140</td><td>161</td></tr>
<tr><td>VOC (10)-ST-003</td><td>140</td><td>161</td></tr>
<tr><td colspan="3">Vocab Tablets 20 mg</td></tr>
<tr><td>VOC (20)-ST-001</td><td>140</td><td>161</td></tr>
<tr><td>VOC (20)-ST-002</td><td>140</td><td>161</td></tr>
<tr><td>VOC (20)-ST-003</td><td>140</td><td>161</td></tr>
</table></td></tr>
<tr><td>33.</td><td>Do you have commitment batches kept on stability testing?</td><td>The firm had stability batches kept on stability testing.</td></tr>
<tr><td>34.</td><td>Do you have valid calibration status for the equipment used in tablet production and analysis?</td><td>The firm had valid calibration status for the equipment used in Vocab Tablets production and analysis (by Delta Control Automation Co. Pvt. Ltd).</td></tr>
</table>

35.	Do proper and continuous monitoring and control are available for stability chamber?	Adequate monitoring and control were available for stability chamber.
36.	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Yes, the area was inspected and was found compliant with current goof manufacturing practices.

Conclusion:

The panel concluded that the authenticity of submitted stability data for Vocab 10mg tablet and Vocab 20mg tablet was verifiable from the available record to the satisfactory level at the time of inspection.

Panel of Inspector:

Mr. Abdullah (Additional Director, PE&R Division)

Mr. Farooq Aslam (Assistant Director PEC)

Decision: The Board decided to approve Vocab 10 mg tablets and Vocab 20 mg tablets with innovator's specifications. 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.

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

Item No. 2: Agenda of Evaluator PEC-IV

Case no. 01 Registration applications of newly granted DML or New section (Human)

a. New DML

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.

4.	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. 24873 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: dated 31/08/2021
	proposed proprietary name / brand name	Ensol- DS IV Infusion 500mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100mL contains: Glucose Anhydrous…….5gm%w/v Sodium Chloride…….....0.9%w/v
	Pharmaceutical form of applied drug	Intravenous Infusion
	Pharmacotherapeutic Group of (API)	Other IV Solution Additives Glucose ATC CODE: V06DC01 Sodium Chloride ATC CODE: A12CA01
	Reference to Finished product specification	BP

	Proposed Pack size	500mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose DS Intravenous Infusion BP of **Baxter Healthcare Ltd.** Caxton Way, Thetford Norfolk IP24 3SE United Kingdom **BAXTER 0.9% SODIUM CHLORIDE and 5% GLUCOSE AHB1064 1000mL injection BP of TGA approved** https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-01661-3&d=20211115172310101 Package size: 500 mL, 1000 mL 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL Any unused product or waste material should be disposed of in accordance with local requirements.
	For generic drugs (me-too status)	Sterifluid- DS (Intravenous Infusion BP) of Frontier Glucose Ltd. Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan (Reg # 050860)
	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.	**Sodium Chloride:** Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China **Glucose Anhydrous:** 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	Sodium Chloride: 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: (2871, 2872 and 2873) **Glucose Anhydrous:** 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	Sterisol -DS Infusion of Frontier Glucose Ltd Reg # 050860
	Analytical method validation/verification of product	Method verification studies has been submitted including accuracy, precision, specificity and robustness.

STABILITY STUDY DATA

Manufacturer of API	Sodium Chloride: Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China Glucose anhydrous: Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China.		
API Lot No.	Sodium Chloride: 20200204 Glucose Anhydrous: 20200427-2		
Description of Pack (Container closure system)	500mL 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	26-07-2020	26-07-2020	26-07-2020
Date of Initiation	27-07-2020	27-07-2020	27-07-2020
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.	**Sodium Chloride:** Copy of DML Certificate (Certificate No# Gan 20110113) for Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China issued by China Food and Drug Administration valid upto 03-12-2025 is submitted **Glucose Anhydrous:** 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).	**Glucose Anhydrous:** 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. **Sodium Chloride:** Firm has submitted copy invoice (invoice# HZA20CS88024) dated: 17-04-2020 from Hangzhou Zhongbao Imp & Exp. Corp.Ltd., China, cleared by DRAP Lahore office dated 08-06-2020
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	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.	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.	Health Products Regulatory Authority China and the link is attached
2.	3.2. S.4.3	• Submit in details performance of Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for Sodium chloride • 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.	• The detailed performance of Analytical Method Verification of sodium chloride is submitted. • The detailed performance of Analytical Method Verification of accuracy is submitted. • The detailed performance of Analytical Method Verification of Precision is submitted.
3.	3.2. S.4.4	• COA of drug substance Glucose anhydrous from drug substance manufacturer include Bacterial Endotoxin 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.	• Revised COA with all tests submitted. • The invoice & the brochure of the HPLC & RI Detector is attached below as per your requirements

4.	3.2. S.5	COA of reference standard of anhydrous glucose is submitted, 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.	The COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference Standard of Glucose Monohydrate. We regret the inconvenience caused in this regard and the COA of Glucose Monohydrate CRS is attached
5.	3.2.P.1	• In MHRA Glucose (as monohydrate) is used as starting material while in applied formulation Glucose anhydrous used. Clarification is required.	The Otsuka china is used glucose as starting material in formulation and the link is attached for your convenience.
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	Submitted.
8.	3.2. P.5.3	• Perform specificity parameter and provide results along with raw data sheets for both glucose anhydrous and Sodium chloride. • Submitted Analytical Method Verification report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter for both glucose anhydrous and Sodium chloride. • Describe sample preparation procedure for performance of precision parameter as for both glucose anhydrous and Sodium chloride. • As per relevant guidelines & structure of Form 5F Analytical test method validation/Verification has to be performed at the time of formulation development, while according to your submitted data, Analytical test method verification has been performed after commencement of stability studies 05-01-2021 while stability studies started on 27-07-2020. Justification shall be submitted in this	• The details of specificity parameter for glucose anhydrous & Sodium Chloride of drug product is submitted. (In place of standard they used Sterifluid- DS Standard) • The details of accuracy parameter for glucose Anhydrous & Sodium Chloride of drug product is submitted. • The details of precision parameter of drug product for Glucose Anhydrous & Sodium Chloride Anhydrous & Sodium Chloride is submitted. • According to CTD guidelines, the only guidance given is regarding the parameters of Validation/Verification of analytical method. There is no specified time frame given for Validation/Verification of analytical

		regard.	method in CTD guidelines which means it could had either be done during the stability or at the time of formulation development. The CTD guideline
9.	3.2. P.8.2	Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard	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.

Decision: Approved with BP specifications with Euro Caps.

- **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	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. 24874 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: dated 31/08/2021
	proposed proprietary name / brand name	Ensol- DS IV Infusion 1000mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100mL contains: Glucose Anhydrous…….5gm%w/v Sodium Chloride…….....0.9%w/v
	Pharmaceutical form of applied drug	Intravenous Injection
	Pharmacotherapeutic Group of (API)	Other IV Solution Additives Glucose ATC CODE: V06DC01 Sodium Chloride ATC CODE: A12CA01
	Reference to Finished product specification	BP
	Proposed Pack size	1000mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose DS Intravenous Infusion BP of **Baxter Healthcare Ltd.**Caxton Way, Thetford Norfolk IP24 3SE United Kingdom BAXTER 0.9% SODIUM CHLORIDE and 5% GLUCOSE AHB1064 1000mL injection BP of TGA approved
	For generic drugs (me-too status)	Macsol- DS (Intravenous Infusion BP) of **SEARLE IV**

		SOLUTIONS (PVT) LTD. 1.5 Km Manga Raiwind Road, Manga Mandi, Distt. Lahore - Pakistan (Reg # 041433)
	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.	**Sodium Chloride:** Copy of DML Certificate (Certificate No# Gan 20110113) for Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China issued by China Food and Drug Administration valid upto 03-12-2025 is submitted **Glucose Anhydrous:** 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.
	Module-II (Quality Overall Summary)	**Glucose Anhydrous:** 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. **Sodium Chloride:** Firm has submitted copy invoice (invoice# HZA20CS88024) dated: 17-04-2020 from Hangzhou Zhongbao Imp & Exp. Corp.Ltd., China, cleared by DRAP Lahore office dated 08-06-2020
	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	**Sodium Chloride:** 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: (2871, 2872 and 2873) **Glucose anhydrous:** 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	Macsol- DS (Intravenous Infusion BP) of **SEARLE IV SOLUTIONS (PVT) LTD.** (MAC AND RAINS PHARMACEUTICALS)
	Analytical method validation/verification of product	Method verification studies has been submitted including accuracy, precision, specificity and robustness.
STABILITY STUDY DATA		

Manufacturer of API	**Sodium Chloride**: Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China **Glucose anhydrous:** Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China.		
API Lot No.	Sodium Chloride: 20200204 Glucose: 20200427-2		
Description of Pack (Container closure system)	1000mL 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	26-07-2020	26-07-2020	26-07-2020
Date of Initiation	27-07-2020	27-07-2020	27-07-2020
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.	**Sodium Chloride:** Copy of DML Certificate (Certificate No. # 20160106) for Nanchang Baiyun Pharmaceutical Co., Ltd Address: Yangzizhou Forest Farm, Qingshanhu District, Nanchang city, Jiangxi province, China issued by China food & Drug Administration valid up to 03-12-2025 is submitted **Glucose anhydrous:** 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 & HZA20CS88024) dated: 28-04-2020 & 17-04-2020 from Hangzhou Zhongbao Imp & Exp. Corp. Ltd, China & Weifang Shengtai Medicine Co., Ltd. The East of Changda Road, Changle county, Weifang Shandong, China cleared by DRAP Lahore office dated 08-06-2020 & 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	NA

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

Remarks Of Evaluator:

Remarks Of Evaluator:

S.No	Section	Shortcomings Communicated	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.	Health Products Regulatory Authority China and the link is attached
2.	3.2. S.4.3	• Submit in details performance of Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for Sodium chloride • 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.	• The detailed performance of Analytical Method Verification of sodium chloride is submitted. • The detailed performance of Analytical Method Verification of accuracy is submitted. • The detailed performance of Analytical Method Verification of Precision is submitted.
3.	3.2. S.4.4	• COA of drug substance Glucose anhydrous from drug substance manufacturer include Bacterial Endotoxin 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.	• Revised COA with all tests submitted. • The invoice & the brochure of the HPLC & RI Detector is attached below as per your requirements
4.	3.2. S.5	COA of reference standard of anhydrous glucose is submitted, 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.	The COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference Standard of Glucose Monohydrate. We regret the inconvenience caused in this regard and the COA of Glucose Monohydrate CRS is attached
5.	3.2.P.1	• In MHRA Glucose (as monohydrate) is used as starting material while in applied formulation Glucose anhydrous used. Clarification is required.	The Otsuka china is used glucose as starting material in formulation and the link is attached for your convenience.

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	Submitted.
8.	3.2. P.5.3	• Perform specificity parameter and provide results along with raw data sheets for both glucose anhydrous and Sodium chloride. • Submitted Analytical Method Verification report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter for both glucose anhydrous and Sodium chloride. • Describe sample preparation procedure for performance of precision parameter as for both glucose anhydrous and Sodium chloride. • As per relevant guidelines & structure of Form 5F Analytical test method validation/Verification has to be performed at the time of formulation development, while according to your submitted data, Analytical test method verification has been performed after commencement of stability studies 05-01-2021 while stability studies started on 27-07-2020. Justification shall be submitted in this regard.	• The details of specificity parameter for glucose anhydrous & Sodium Chloride of drug product is submitted. (In place of standard they used Sterifluid- DS Standard) • The details of accuracy parameter for glucose Anhydrous & Sodium Chloride of drug product is submitted. • The details of precision parameter of drug product for Glucose Anhydrous & Sodium Chloride Anhydrous & Sodium Chloride is submitted. • According to CTD guidelines, the only guidance given is regarding the parameters of Validation/Verification of analytical method. There is no specified time frame given for Validation/Verification of analytical method in CTD guidelines which means it could had either be done during the stability or at the time of formulation development. The CTD guideline
9.	3.2. P.8.2	Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard	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

Decision: Approved with BP specifications with Euro Caps.

- **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 for local manufacturing of (veterinary) drugs

a. Deferred Cases

6.	Name and address of manufacturer / Applicant	MYLAB Pvt. Ltd, Khankah Shariff Bahawalpur.
	Brand Name +Dosage Form + Strength	I-ZVS Oral Solution
	Composition	Each 1000ml Contains: Zinc…800mg Vitamin E…150,000mg Selenium…1670mg
	Diary No. Date of R& I & fee	Dy.No 40629 dated 06-12-2018 Rs.20,000/- 04-12-2018
	Pharmacological Group	Vitamin & mineral
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	50ml, 100ml, 250ml, 500ml, 1liter, 5 liter: Decontrolled
	Me-too status (with strength and dosage form)	Not found
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator[IV].	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: Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. For salt form of Zinc and Selenium **(M-296)**
	Evaluation by PEC: Firm revised their formulation with submission of copy fee challan of Rs: 30000/- Deposit slip No# 2430041230, Dated:23-08-2021	
	Brand Name +Dosage Form + Strength	I-ZVS Oral Solution
	Composition	Each 1000ml Contains: Zinc…8000mg Vitamin E…150,000mg Selenium…1670mg
	Pack size & Demanded Price	50ml, 100ml, 250ml, 500ml, 1liter, 5 liter: Decontrolled
	Me-too status (with strength and dosage form)	I-ZVS ORAL SOLUTION of M/ s CHERISHED PHARMACEUTICALS (Reg# 069632)
	Decision: Approved with innovator's specification. Registration letter will be issued after submission of applicable fee	
7.	Name and address of manufacturer / Applicant	MYLAB Pvt. Ltd, Khankah Shariff Bahawalpur.
	Brand Name +Dosage Form + Strength	Streplin Injection
	Composition	Each ml Contains: Procaine Penicillin G…200mg Dihydrostreptomycin Sulphate Eq. to Dihydrostreptomycin…200mg
	Diary No. Date of R& I & fee	Dy.No 40604 dated 06-12-2018 Rs.20,000/- Dated 04-12-2018
	Pharmacological Group	Antibiotic
	Type of Form	Form 5

	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	50ml :Decontrolled
	Me-too status (with strength and dosage form)	Reg.No.083244 Streplin Inj of M/S Selmore Pharmaceuticals
	GMP status	Panel inspection conducted on 13-09-2018 to 14-09-2018 recommends renewal of DML and grant of additional sections.
	Previous remarks of the Evaluator[IV].	Alternate brand name: • Megapen
	Previous decision(s)	Deferred for following: Deferred for confirmation of required manufacturing facility "Liquid injectable Penicillin section" from licensing division**. (M-296)**
	Evaluation by PEC:	Firm submitted section letter for Liquid injectable Penicillin section" of Dated: 03-12-2018
	Decision: Approved with innovator's specification. Registration letter will be issued after submission of applicable fee	

Case no. 03 Registration applications of newly granted DML or New section (Veterinary)

b. Deferred Cases

8.	Name and address of manufacturer / Applicant	M/s Krypton Pharma (pvt) limited Plot No. 52,Phase-1,M-3 Industrial city Sahianwala Faisalabad Pakistan
	Brand Name +Dosage Form + Strength	KP-COLIDOX T (Oral Powder)
	Composition	Each 1000g contains: Tylosin Tartrate (E.P.)….. 100g Doxycycline (B.P.)….. 40g Colistin Sulphate (B.P)… …….300MIU
	Diary No. Date of R& I & fee	Dy.No. 1167 dated 08-01-2021 Rs 20,000 Dated 08-01-2021
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specifications	In house Specification
	Pack size & Demanded Price	50g, 100g, 250g, 500g, 450g, 1Kg, 2.5Kg, 5Kg, 10Kg, 15Kg, 20Kg, 25Kg in plastic cane
	Me-too status (with strength and dosage form)	N.A
	GMP status	TCD PLUS Oral Powder of M/s Leads Pharma Islamabad (Reg# 058853)
	Previous remarks of the Evaluator[IV].	New license yet not issued.
	Previous decision(s)	Deferred for following: Deferred for revision of formulation in terms of salt form of Doxycycline along with submission of requisite fee**. (M-297)**
	Evaluation by PEC:	Firm revised their formulation without submission of fee as follows: Each 1000g contains: Tylosin Tartrate (E.P.)….. 100g Doxycycline as HCl (B.P.)….. 40g Colistin Sulphate (B.P)… …….300MIU
	Decision: Approved with innovator's specification. Board further decided that Registration letter will be issued after submission of Rs: 30000/- fee for change for formulation.	
9.	Name and address of manufacturer / Applicant	M/s Krypton Pharma (Pvt) Ltd Plot No. 052, M-3 Industrial city Sahianwala, Faisalabad
	Brand Name +Dosage Form + Strength	KP-OXYN C (Oral Powder)
	Composition	Each Kg contains: Neomycin Sulphate (EP)..... 200g Colistin Sulphate (BP).....240MIU Oxytetracycline(USP) …...…….200g

	Diary No. Date of R& I & fee	Dy.No. 1211 dated 08-01-2021 Rs 20,000 Dated 08-01-2021
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specifications	In House specification
	Pack size & Demanded Price	50gm, 100gm, 250gm, 450gm, 500 gm, 1 Kg, 2.5 Kg, 5 Kg, 10Kg, 15Kg, 20Kg, 25Kg in plastic Jar/Bag
	Me-too status (with strength and dosage form)	N.A
	GMP status	OXCINOCOL W/S ORAL POWDER of M/s Attabak Pharmaceuticals , Islamabad (Reg # 034533)
	Previous remarks of the Evaluator[IV].	New license yet not issued.
	Previous decision(s)	Deferred for following: Deferred for revision of formulation in terms of salt form of Oxytetracycline along with submission of requisite fee**. (M-297)**
	Evaluation by PEC:	Firm revised their formulation without submission of fee as follows: Each Kg contains: Neomycin Sulphate (EP)..... 200g Colistin Sulphate (BP).....240MIU Oxytetracycline HCl(USP) …...…….200g
	Decision: Approved with innovator's specification. Board further decided that Registration letter will be issued after submission of Rs: 30000/- fee for change for formulation.	
10.	Name and address of manufacturer / Applicant	M/s Krypton Pharma (pvt) limited Plot No. 52,Phase-1,M-3 Industrial city Sahianwala Faisalabad Pakistan
	Brand Name +Dosage Form + Strength	KP-ONC (Oral Powder)
	Composition	Each Kg contains: Neomycin Sulphate (EP)….. 250g Colistin Sulphate (BP) …..500MIU Oxytetracycline (USP) ….300g
	Diary No. Date of R& I & fee	Dy.No. 1210 dated 08-01-2021 Rs 20,000 Dated 08-01-2021
	Pharmacological Group	Antibiotics, Antibacterial
	Type of Form	Form-5
	Finished product Specifications	In house Specification
	Pack size & Demanded Price	50gm, 100gm, 250gm, 450gm, 500 gm, 1 Kg, 2.5 Kg, 5 Kg, 10Kg, 15Kg, 20Kg, 25Kg in plastic Jar/Bag
	Me-too status (with strength and dosage form)	N.A
	GMP status	ST Neolistin Oral Powder of M/s Leads Pharma ISLAMABAD (Reg # 078242)
	Previous remarks of the Evaluator[IV].	New license yet not issued.
	Previous decision(s)	Deferred for following: Deferred for revision of formulation in terms of salt form of Oxytetracycline along with submission of requisite fee**. (M-297)**
	Evaluation by PEC:	Firm revised their formulation without submission of fee as follows: Each Kg contains: Neomycin Sulphate (EP)….. 250g Colistin Sulphate (BP) …..500MIU Oxytetracycline (USP) ….300g
	Decision: Approved with innovator's specification. Board further decided that Registration letter will be issued after submission of Rs: 30000/- fee for change for formulation.	

Case no. 04 Registration applications of drugs for which stability study data is submitted

a. Verification of stability study data

Deferred case:

11.	Name and address of manufacturer / Applicant	M/s Pearl Pharmaceuticals Plot # 204, street 1, 1-10/3 Islamabad.
	Brand Name +Dosage Form + Strength	Lazol-D 30mg capsule
	Composition	Each capsule contains: Dexlansoprazole 17% pellets……30mg
	Diary No. Date of R& I & fee	Dy. No. 26705, 03/08/2018, Rs: 20,000/- Dated:03/08/2018
	Pharmacological Group	Proton Pump inhibitor
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulator Authorities	Dexilant Delayed Release Capsule 30mg of USFDA approved
	Me-too status	Razodex 30mg Capsules of M/S Getz Pharma
	GMP status	The last inspection conducted on 08-02-2018 and report concludes that overall GMP compliance was found satisfactory.
	Remarks of the Evaluator[IV]	

STABILITY STUDY DATA			
Drug	Lazol-D 30mg capsule		
Name of Manufacturer	M/s Pearl Pharmaceuticals Plot # 204, street 1, 1-10/3 Islamabad.		
Manufacturer of API	M/S Vision Pharmaceuticals (Pvt)., Ltd is submitted.		
API Lot No.	DLP539		
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: : 0,1,2,3,4,6 (month) Real Time: 0,1,2,3,4,6 (month)		
Batch No.	Trial=01	Trial=02	Trial=03
Batch Size	500 Capsule	500 Capsule	500 Capsule
Manufacturing Date	11-2019	11-2019	11-2019
Date of Initiation	12-2019	12-2019	12-2019
No. of Batches	03		
Date of Submission	20-07-2020 (17559)		

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	Not valid

<table>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Copy of COA [Batch# DLP539 (17%)] from M/S Vision Pharmaceuticals (Pvt) Ltd is submitted.

Copy of COA (Batch# DLP539) from M/S Pearl Pharmaceuticals is submitted.</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Yes</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Yes</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>Certificate of Good manufacturing practice Based on inspection conducted on 11-02-2019</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Not valid</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Not applicable</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>Yes</td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study On their product with Razodex capsules The details are as follows:
<table><tr><th>Feature</th><th>Reference product</th><th>Product of Searl</th></tr><tr><td>Brand name</td><td>Razodex 30mg Capsules</td><td>Lazole D 30mg Capsules</td></tr><tr><td>Batch No.</td><td>023C47</td><td>Trial 3</td></tr></table>● Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 5.5 Acetate buffer
3. pH 7 Phosphate buffer</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>YEs</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>No</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>Yes</td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td colspan="2">Shortcomings communicated</td><td>Reply</td></tr>
</table>

<table>
<tr><td>Gelatin capsule shell used while innovator is using HPMC. Justify.</td><td>We have performed stability studies on our product and found stable with these hard gelatin shells during accelerated and real time conditions of stability studies.
No capsule shell manufacturer in Pakistan is manufacturing HPMC base capsule shells. So availability of these shells would be a problem.
However firm did not performed compatibility study with gelatin shell.</td></tr>
<tr><td>In Assay method one chromatogram provided. Clarify.</td><td>We are preparing only one sample that’s why one chromatogram is attached.</td></tr>
<tr><td>Dilution from 1st month and onward change in dissolution than initial, Method not followed in terms of dilutions from 1st month onward. Clarify</td><td>Dilution can be changed both in standard and sample but final concentrations should remain same and our standard and sample have the same concentrations.</td></tr>
<tr><td>Provide record of remaining quantities of stability batches and details of no of units used at each time point.</td><td>
<table>
<tr><th>Trial</th><th>Total capsule recieved</th><th>No of capsules used for single testing</th><th>No of capsules used for Accelerated stability</th><th>No of capsules used for real stability</th><th>Total capsules used</th><th>Remaining capsules quantity</th><th>Remaining qty in real time</th></tr>
<tr><td>Trial 1</td><td>364</td><td>26</td><td>130</td><td>130</td><td>130+130=260</td><td>364-260=104</td><td>104</td></tr>
<tr><td>Trial 2</td><td>364</td><td>26</td><td>130</td><td>130</td><td>130+130=260</td><td>364-260=104</td><td>104</td></tr>
<tr><td>Trial 3</td><td>371</td><td>26</td><td>130</td><td>130+06 capsules used in comparative dissolution.</td><td>130+130=260</td><td>364-260=104</td><td></td></tr>
</table>
</td></tr>
<tr><td>In dissolution testing calculations, weight of standard different than mentioned in analytical testing method. Justify.</td><td>We can vary the weight of standard it depends upon the final concentrations of the sample. The final concentrations of sample and standard should remain same</td></tr>
<tr><td>Potency of standard not mentioned in calculation of assay and dissolution. Clarify.</td><td>We take standard as 100% in assay and dissolution.</td></tr>
<tr><td>Comparative dissolution Studies should be 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. While performed comparative dissolution is not conducted in these pH and according to WHO guidelines</td><td>We have also done comparative stability studies on three different pH physiological ranges. Acid stage (pH 1.2) Buffer (pH 5.5) Buffer (pH 7.0) we followed the specification of our source (Vision pharmaceuticals) both in stability studies and in comparative dissolution</td></tr>
</table>

for comparative dissolution.		
The panel is requested to confirm & report the following: Remaining quantity of capsules for real time studies.		
12.	Name and address of manufacturer / Applicant	M/s Pearl Pharmaceuticals Plot # 204, street 1, 1-10/3 Islamabad.
	Brand Name +Dosage Form + Strength	Lazol-D 60mg capsule
	Composition	Each capsule contains: Dexlansoprazole 22.5% pellets……60mg
	Diary No. Date of R& I & fee	Dy. No. 26706, 03/08/2018, Rs: 20,000/- Dated:03/08/2018 (Duplicate)
	Pharmacological Group	Proton Pump inhibitor
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulator Authorities	Dexilant Delayed Release Capsule 60mg of USFDA approved
	Me-too status	Razodex 60mg Capsules of Getz pharma
	GMP status	The last inspection conducted on 08-02-2018 and report concludes that overall GMP compliance was found satisfactory.
	Remarks of the Evaluator[IV]	

STABILITY STUDY DATA

Drug	Lazol-D 60mg capsule		
Name of Manufacturer	M/s Pearl Pharmaceuticals Plot # 204, street 1, 1-10/3 Islamabad.		
Manufacturer of API	M/S Vision Pharmaceuticals (Pvt)., Ltd is submitted.		
API Lot No.	DLP467		
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: : 0,1,2,3,4,6 (month) Real Time: 0,1,2,3,4,6 (month)		
Batch No.	Trial=01	Trial=02	Trial=03
Batch Size	500 Capsule	500 Capsule	500 Capsule
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	11-2019	11-2019	11-2019
No. of Batches	03		
Date of Submission	16-06-2020 (13769)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	**Documents To Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm	Not valid

<table>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Copy of COA [Batch# DLP467 (22.5%)] from M/S Vision Pharmaceuticals (Pvt)., Ltd is submitted.
Copy of COA (Batch# DLP467) from M/S Pearl Pharmaceuticals is submitted.</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Yes</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Yes</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>Certificate of Good manufacturing practice Based on inspection conducted on 11-02-2019</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Not valid</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Not applicable</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>Yes</td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study On their product with Razodex capsules The details are as follows:
<table><tr><th>Feature</th><th>Reference product</th><th>Product of Searl</th></tr><tr><td>Brand name</td><td>Razodex 60mg Capsules</td><td>Lazole D 30mg Capsules</td></tr><tr><td>Batch No.</td><td>025C48</td><td>Trial 3</td></tr></table>● Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 5.5 Acetate buffer
3. pH 7 Phosphate buffer</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>Yes</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Not submitted.</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>Yes</td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td colspan="2">Shortcomings communicated</td><td>Reply</td></tr>
<tr><td colspan="2">Gelatin capsule shell used while</td><td>We have performed stability studies on our product and found stable</td></tr>
</table>

<table>
<tr><td>innovator is using HPMC. Justify.</td><td>with these hard gelatin shells during accelerated and real time conditions of stability studies.
No capsule shell manufacturer in Pakistan is manufacturing HPMC base capsule shells. So availability of these shells would be a problem
However firm did not performed compatibility study with gelatin shell.</td></tr>
<tr><td>In Assay method one chromatogram provided. Clarify.</td><td>We are preparing only one sample that’s why one chromatogram is attached.</td></tr>
<tr><td>Dilution from 1st month and onward change in dissolution than initial, Method not followed in terms of dilutions from 1st month onward. Clarify</td><td>Dilution can be changed both in standard and sample but final concentrations should remain same and our standard and sample have the same concentrations.</td></tr>
<tr><td>Provide record of remaining quantities of stability batches and details of no of units used at each time point.</td><td>
<table>
<tr><td>Trial</td><td>Total capsule recieved</td><td>No of capsules used for single testing</td><td>No of capsules used for Accelerated stability</td><td>No of capsules used for real stability</td><td>Total capsules used</td><td>Remaining capsules quantity</td><td>Remaining qty in real time</td></tr>
<tr><td>Trial 1</td><td>364</td><td>26</td><td>130</td><td>130</td><td>130+130=260</td><td>364-260=104</td><td>104</td></tr>
<tr><td>Trial 2</td><td>364</td><td>26</td><td>130</td><td>130</td><td>130+130=260</td><td>364-260=104</td><td>104</td></tr>
<tr><td>Trial 3</td><td>371</td><td>26</td><td>130</td><td>130+06 capsules used in comparative dissolution.</td><td>130+130=260</td><td>364-260=104</td><td>105</td></tr>
</table>
</td></tr>
<tr><td>In dissolution testing calculations, weight of standard different than mentioned in analytical testing method. Justify.</td><td>We can vary the weight of standard it depends upon the final concentrations of the sample. The final concentrations of sample and standard should remain same</td></tr>
<tr><td>Potency of standard not mentioned in calculation of assay and dissolution. Clarify.</td><td>We take standard as 100% in assay and dissolution.</td></tr>
<tr><td>Comparative dissolution Studies should be 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. While performed comparative dissolution is not conducted in these pH and according to WHO guidelines for comparartive dissolution.</td><td>We have also done comparative stability studies on three different pH physiological ranges. Acid stage (pH 1.2) Buffer (pH 5.5) Buffer (pH 7.0) we followed the specification of our source (Vision pharmaceuticals) both in stability studies and in comparative dissolution</td></tr>
<tr><td colspan="2">The panel is requested to confirm & report the following:
Remaining quantity of capsules for real time studies.</td></tr>
</table>

Report on investigation of authenticity / genuineness of data submitted for registration of Lazol-D (Dexlansoprazole) 30mg & 60mg Capsule by M/s. Pearl Pharmaceuticals, Plot # 204 Street 1, I-10/3, Islamabad

Background:

Chairman Registration Board constituted the following panel for onsite investigation to confirm genuineness / authenticity of stability data and associated documents, import of API, quality, specification, test analysis and facilities etc. of M/s. Pearl Pharmaceuticals, Plot # 204 Street 1, I-10/3, Islamabad for registration of Lazol-D (Dexlansoprazole) 30mg & 60mg Capsule

Composition of Panel:

1. Mr. Akhtar Abbas Khan, Additional Director (QA&LT), DRAP, Islamabad.
2. Hafiz M. Ali Tayyab, Assistant Director Registration-II, PE&R Division, DRAP, Islamabad.

The inspection report is being submitted for your kind perusal.

<table>
<tr><th>Sr. No.</th><th>Question</th><th>Observation by panel</th></tr>
<tr><td>1.</td><td>Do you have documents confirming the import of API including approval from DRAP?</td><td>Firm has purchased Dexlansoprazole Pellets locally from M/s. Vision Pharmaceuticals, Islamabad.</td></tr>
<tr><td>2.</td><td>What was the rationale behind selecting the particular manufacturer of API?</td><td>API manufacturer is selected being local manufacturer.</td></tr>
<tr><td>3.</td><td>Do you have documents confirming the import reference standard and impurity standards?</td><td>Firm has received working standard from M/s. Vision Pharmaceuticals, Islamabad. No Impurity standard received.</td></tr>
<tr><td>4.</td><td>Do you have certificate of Analysis of the API, reference standards and impurity standards?</td><td>Firm has COA of API. COA of Impurity Standard not available.</td></tr>
<tr><td>5.</td><td>Do you have any approval of API or GMP certificate of API manufacturer issued by regulatory authority of country of origin?</td><td>GMP certificate of M/s. Vision Pharmaceuticals, Islamabad is available.</td></tr>
<tr><td>6.</td><td>Do you use API manufacturer method of testing?</td><td>The firm has used API manufacturer method of testing.</td></tr>
<tr><td>7.</td><td>Do you have stability studies reports on API?</td><td>The firm has API stabilities reports conducted by API manufacturer.</td></tr>
<tr><td>8.</td><td>If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?</td><td>Degradation products have not been quantified.</td></tr>
<tr><td>9.</td><td>Do you have method for quantifying the impurities in the API?</td><td>Firm has not performed any impurity testing.</td></tr>
<tr><td>10.</td><td>Do you have some remaining quantities of the API, its reference standard and impurities standards?</td><td>Firm has remaining quantity of API as follows.
<table>
<tr><th>API</th><th>Batch No.</th><th>Remaining Quantity</th></tr>
<tr><td>Dexlansoprazole 30mg (17%)</td><td>DLP539</td><td>740gm</td></tr>
<tr><td>Dexlansoprazole 60mg (22.5%)</td><td>DLP467</td><td>600gm</td></tr>
</table>
Small quantity of working standard is present.
Impurity standards not received.</td></tr>
<tr><td>11.</td><td>Have you used pharmaceutical grade excipients?</td><td>Not Applicable.</td></tr>
<tr><td>12.</td><td>Do you have documents confirming the import of the used excipients?</td><td>Not Applicable.</td></tr>
<tr><td>13.</td><td>Do you have test reports and other records on the excipients used?</td><td>Not Applicable.</td></tr>
<tr><td>14.</td><td>Do you have written and authorized protocols for the development ?</td><td>Not Applicable.</td></tr>
</table>

<table>
<tr><td>15.</td><td>Have you performed Drug-excipients compatibility studies?</td><td>Not Applicable.</td></tr>
<tr><td>16.</td><td>Have you performed comparative dissolution studies?</td><td>Comparative dissolution studies have been performed against Razodex Capsule of M/s. Getz Pharma.
<table>
<tr><td>Detail</td><td>Test product</td><td>Reference product</td></tr>
<tr><td>Brand</td><td>Lazol-D 30mg Capsule</td><td>Razodex 30mg Capsule</td></tr>
<tr><td>Medium</td><td colspan="2">pH 1.2 HCl, pH 5.5 Acetate buffer, pH 7 Phosphate buffer</td></tr>
</table>
<table>
<tr><td>Detail</td><td>Test product</td><td>Reference product</td></tr>
<tr><td>Brand</td><td>Lazol-D 60mg Capsule</td><td>Razodex 60mg Capsule</td></tr>
<tr><td>Medium</td><td colspan="2">pH 1.2 HCl, pH 5.5 Acetate buffer, pH 7 Phosphate buffer</td></tr>
</table></td></tr>
<tr><td>17.</td><td>Do you have product development (R&D) section</td><td>No separate product development (R&D) section.</td></tr>
<tr><td>18.</td><td>Do you have necessary equipment's available in product development section for development of new product?</td><td>No separate product development (R&D) section. However, manufacturing of stability batches was carried out in commercial manufacturing area.</td></tr>
<tr><td>19.</td><td>Are the equipments in product development section qualified?</td><td>No separate product development (R&D) section</td></tr>
<tr><td>20.</td><td>Do you have proper maintenance / calibration / re-qualification program for the equipment used in PD section?</td><td>No separate product development (R&D) section. However, firm has proper maintenance / re-qualification program for the equipment used</td></tr>
<tr><td>21.</td><td>Do you have qualified staff in product development section with proper knowledge and training in product development?</td><td>Firm has technical and qualified staff in the concerned commercial manufacturing area.</td></tr>
<tr><td>22.</td><td>Have you manufactured three stability batches for the stability studies of new product as required?</td><td>Firm has manufactured 03 stability batches (Trial-1, Trial -2, Trial -3) for Lazol-D 30mg capsule and (Trial-1, Trial -2, Trial -3) for Lazol-D 60mg capsule having batch size of 500 Capsules each.</td></tr>
<tr><td>23.</td><td>Do you have any criteria for fixing the batch size of stability batches?</td><td>Criteria for fixing batch size is number of tests required and testing frequency.</td></tr>
<tr><td>24.</td><td>Do you have complete record of production of stability batches?</td><td>Complete record of production of stability batches for Lazol-D 30mg & 60mg Capsule available.</td></tr>
<tr><td>25.</td><td>Do you have protocols for stability testing of stability batches?</td><td>Product testing protocol available for Lazol-D 30mg & 60mg Capsule.</td></tr>
<tr><td>26.</td><td>Do you have developed and validated the method for testing of stability batches?</td><td>Firm has not performed any steps of validation.</td></tr>
<tr><td>27.</td><td>Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?</td><td>Not Applicable.</td></tr>
<tr><td>28.</td><td>Do you have documents confirming the qualification of equipments / instruments being used in the test and analysis of API and the finished drug?</td><td>Equipment used in testing are qualified.</td></tr>
<tr><td>29.</td><td>Do your method of analysis stability indicating?</td><td>Degradation products have not been quantified.</td></tr>
<tr><td>30.</td><td>Do your HPLC software is 21CFR compliant?</td><td>HPLC is 21CFR compliant.</td></tr>
<tr><td>31.</td><td>Can you show Audit Trail reports on New product testing?</td><td>Audit trail reports for Testing of Lazol-D 30mg & 60mg Capsule are available.</td></tr>
</table>

32.	Do you have some remaining quantities of degradation products and stability batches?	Firm has 52 Capsules of each of only stability batches kept in stability chamber for Real time stability.
33.	Do you have stability batches kept on stability testing?	Stability batches are kept in stability chamber for Real time stability testing. Up to 12-month Real time stability completed.
34.	Do you have valid calibration status for the equipments used for production and analysis of new product?	Firm has valid calibration status for equipment used in analysis of products. Manufacturing equipments are not calibrated.
35.	Do proper and continuous monitoring and control are available for stability chamber?	Proper and continuous monitoring record for stability chamber is available along with backup generator.
36.	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Related manufacturing area, equipment, personnel and utilities be rated as GMP compliant. GMP fair compliant report dated 23-07-2018.

Observations;

1. Firm has exact quantity of 52 Capsules of each of stability batches for onward stability testing of 18th & 24th month as 26 capsules are used in single test.
2. Firm has not performed any analytical method validation.
3. Degradation testing not performed.
4. Impurity test not performed.

Previous Decision: Registration Board decided to deferred the Lazol-D 30mg capsule and Lazol-D 60mg capsule for performance of analytical method validation by finished product manufacturer **(M-307)**

- Firm submitted Analytical method validation protocol and report dated:31-08-2021.
- In Specificity they are not using placebo (inert pellet/ excipients) and submit an undertaking that they will now perform specificity with inert pellets before commercial batch production.
- And 24th month time point stability data of dated 01-11-2021 submitted.

Decision: Registration Board decided to approve registration of Lazol-D 30mg capsule and Lazol-D 60mg capsule (Dexlansoprazole) with Innovator's specifications by M/s Pearl Pharmaceuticals. 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.
Registration letter will be issued after submission of applicable fee.

Item No. 3: Agenda of Evaluator PEC-V
Case No. I: Deferred Cases (Veterinary) Local Manufacturing

13.	Name and address of manufacturer / Applicant	"M/s Selmore Pharmaceuticals Pvt Ltd. 36-Km, Multan Road Lahore."
	Brand Name +Dosage Form + Strength	Actibol Injection 100ml
	Composition	"Each 100ml contains: Cynocobalamin Vit B12…50mg Sodium selenite…100mg Adenosine triphospate tetra sodium dihydrate salt…100mg Potassium asparate semihydrate…1g Magnesium aspartate tetrahydrate…1.5g"
	Diary No. Date of R& I & fee	Dy.No 8788 dated 27-02-2019 Rs.20,000/- 26-02-2019
	Pharmacological Group	Vitamins with minerals
	Type of Form	Form 5
	Finished product Specification	
	Pack size & Demanded Price	100ml Glass vial
	Me-too status	021212 Biodyl Injectable Solution 5x10 ml, 50ml
	GMP status	05-03-2018,17-08-2018 & 16-10-2018 Conclusion: 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 Aerosal 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-V	• Reference for specs has not been provided. • Evidence of me too with 100 ml pack size is required.
	Decision of 297th Meeting: Deferred for the following: a) Submission of reference of specification for finished pharmaceutical product. b) Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	a) Submission of reference of specification for finished pharmaceutical product. Selmore Specification. b) Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. 052320 Biosal Injection By Zakfas Pharmaceuticals (Pvt) Ltd. Multan	
	Decision of 307 Meeting: Deferred for the submission of rationale for use of adenosine in the applied formulation.	
	Firms Reply: It is stated that *adenosine triphosphate*, a complex molecule that contains the nucleoside *adenosine* and a tail consisting of three phosphates. As far as known, all organisms from the simplest bacteria to humans use ATP as their primary energy currency. The energy level it carries is just the right amount for most biological reactions. Nutrients contain energy in low-energy covalent bonds which are not very useful to do most kinds of work in the cells.The ATP is used for many cell functions including *transport work* moving substances across cell membranes. It is also used for *mechanical work*, supplying the energy needed for muscle contraction. It supplies energy not only to the heart muscle (for blood circulation) and skeletal muscle (such as for gross body movement) but also to the chromosomes and flagella to enable them to carry out their many function.A major role of ATP is in *chemical work*, supplying the needed energy to synthesize the multi-thousands of types of macromolecules that the cell needs to exist.So, adenosine is intended to be used for exhausted and weak animals to boost up their bodies.	
	Decision of 313th meeting: Approved with Innovator's specifications	
14.	Name and address of manufacturer / Applicant	"M/s Selmore Pharmaceuticals Pvt Ltd. 36-Km, Multan Road Lahore."
	Brand Name +Dosage Form + Strength	Amino Vita Injection 250ml
	Composition	"Each ml contains: L-Arginine HCL...1.42mg L-Cysteine HCL...0.02mg Monosodium Glutamate...0.08mg L-Histidine HCL...0.02mg L-Isoleucine HCL...0.525mg L-Leucine...0.6mg L-Lysine HCL...0.525mg DL-Methionine...0.525mg L-Threonine...0.35mg L-Tryptophan...0.175mg L-Phenylaline...0.35mg L-Valine...0.525mg Thiamine HCL...0.1mg

		Riboflavin...0.05mg Pyridoxine HCL...0.1mg Nicotinamide ...3mg Dextrose...50mg Calcium Chloride...2mg Potassium Chloride...2mg Magnesium sulphate...2mg Sodium acetate...7.5mg D-Pantothenol...0.1mg"
	Diary No. Date of R& I & fee	Dy.No 8789 dated 27-02-2019 Rs.20,000/- 26-02-2019
	Pharmacological Group	Vitamins,Aminoacid, Mineral Supplement
	Type of Form	Form 5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	250ml glass vial. As per SRO.
	Me-too status	Me too 020083 AMINOVITAL HIGH INJECTION
	GMP status	05-03-2018,17-08-2018 & 16-10-2018 Conclusion: 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 Aerosal 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-V	Evidence of Me Too is required.
	Decision of 297th Meeting: Deferred for the 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-V: Firm has submitted following Me too 020083 AMINOVITAL HIGH INJECTION and their applied formulation is as per ME too but there was typographical error in agenda, that has been verified from dossier.	
	Strength mentioned in previous Agenda: L-Tryptophan...0.165mg, L-Phenylaline...0.45mg, Riboflavin...3mg Applied formulation: L-Tryptophan...0.175mg, L-Phenylaline...0.35mg, Riboflavin...0.05mg	
	Decision of M-307: Deferred for the evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	
	Firms Reply Firm has submitted following Me too 020083 AMINOVITAL HIGH INJECTION	
	Decision: The Board deferred the case for revision of strength of L-Arginine in the formulation as per me-too reference (i.e from 1.425mg to 1.42mg) along with the submission of applicable fee for revision of formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
15.	Name and address of manufacturer / Applicant	"M/s Fahmir Pharma Pvt Ltd.26 km, Lahore Jaranwala Road, Main Stop Mandianwala, Sharaqpur, Distt. Sheikhupura"
	Brand Name+Dosage Form+Strength	Dona 50mg Capsule
	Composition	"Each Capsule Contains: Diclofenac potassium pellets…50mg"

	Diary No. Date of R& I & fee	Dy.No 7033 dated 19-02-2019 Rs.20,000/- Dated 15-02-2019
	Pharmacological Group	NSAID
	Type of Form	Form 5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	2x10's,Rs.3.5/Capsule, Rs.70/20 capsule
	Approval status of product in Reference Regulatory Authorities.	Could not be confirmed.
	Me-too status	068238 "Naveflam Capsules 50mg. M/s Navegal Laboratories, Hattar."
	GMP status	Central Licensing Board in its 259th meeting held on 29-30th March 2018 has considered and approved the grant of drug manufacturing license by way of formulation with Tablet (General) Section.
	Remarks of the Evaluator	Source of pellets, along with stability studies data, GMP certificate of supplier and differential fee in case of import of pellets shall be submitted.
	Previous Decision of 295th: Deferred for COA, GMP of pellets manufacturer and stability studies of three batches of pellets conducted in accordance with zone IV-A conditions.	
	Firms Reply: **Source of pellets:** Vision Pharmaceuticals.	
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.		

Item No. 4: Agenda of Evaluator PEC-VII

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 / 03 Products

16.	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,6 7/2,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. 23210 dated 30-aug-2021
	Details of fee submitted	PKR 30,000/-: (4134931450) dated 19/07/2021
	proposed proprietary name / brand name	Zolnex 0.25 mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Alprazolam…….0.25 mg
	Pharmaceutical form of applied drug	White, Round shaped, bisect oral tablet
	Pharmacotherapeutic Group of (API)	Benzodiazepine
	Reference to Finished product specification	USP

	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Xanax 0.25 mg tablet by M/s Upjohn, USFDA Approved.
	For generic drugs (me-too status)	Zolam 0.25 mg Tablet by M/s Saydon,
	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 Alprazolam 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 substances (2-Amino-5-Chlorobenzophenone), 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 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (541921),(551318), (560670)
	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 Xanax 0.25 mg tablet by Pfizer by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the innovator brand that is Xanax 0.25 mg tablet by Pfizer 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 uniformity of contents missing

STABILITY STUDY DATA

Manufacturer of API	M/s Cambrex Profarmaco Milano S.R.L Via Curiel,34-20067 Paullo-Milano,Italy.
API Lot No.	801012
Description of Pack	Alu-PVC blister packed in unit carton (3×10's)

(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.	Trial-01	Trial-02	
Batch Size	5000 tab	5000 tab	
Manufacturing Date	02-2021	02-2021	
Date of Initiation	09-02-2021	23-02-2021	
No. of Batches	02		

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 No. II-API/44/H/2019 issued by Italian Medicine Agency.
3.	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
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 #.	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 use of "Magnesium stearate" in 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

3.	3.2.P.5	In assay the injection volume prescribed inn USP is 25 ul but firm used 100 ul. justification is needed	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)
4.	3.2.P.5	The USP monograph for this dosage form includes content uniformity test. Justify the exemption of these tests.	In the content uniformity test internal standard TRIAZOLAM is used (Reference USP 43) which was not received with the shipment. We used alternate method for uniformity of dosage units by way of weight variation.
5.		• 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.	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

Strength	**Formulation development analysis finished date**	**CDP end date**
0.5 mg	01/03/2021	03/03/2021
0.25 mg	17/03/2021	19/03/2021
1 mg	24/03/2021	25/03/2021

Decision: Approved.

- **Firm will submit content uniformity test data as per USP monograph before issuance of letter.**
- **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 of drugs for which stability study data is submitted

a. Verification of stability study data

Report of Inspection: Verification of authenticity of stability data of Empozin-M Tablet in reference to DRAP PEC Letter No. F.11-95/2014-Wnsfeild-DRAP (P) 4349

Name of Manufacturer	M/S Wnsfeild Pharmaceuticals,
Physical Address	Plot # 122, Block- A Phase-V, Industrial Estate, Hattar, Kpk
Date of Inspection	12-11-2021
Purpose of inspection	Verification of authenticity of stability data of Empozin-M 5/500, 12.5/500 and 12.5/1000 in reference to DRAP PEC Letter No. F.1-2/2020-PEC VII dated 15-11-2021.
Name of inspector	Dr. Qurban Ali, Member Registration Board Faisal Shahzad Federal Inspector of Drugs, DRAP, Peshawar.

17.	Name and address of manufacturer / Applicant	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar,Kpk

	Brand Name+Dosage Form + Strength	**Empozin-M 5/500 mg Tablet**
	Composition	Each film coated tablet contains: Empagliflozin……..5mg Metformin hydrochloride……500mg
	Diary No. Date of R& I & fee	1454.., dated 07/3/2019, Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Antihyperglycemic
	Type of Form	Form-5D
	Finished product Specification	Innovator specifications
	Pack size & Demanded Price	As per brand leader
	Approval status of product in Reference Regulatory Authorities	Synjardy Tablets 5/500MG of Boehringer Ingelheim (USFDA Approved)
	Me-too status	EmpaMet 5/500 mg by Hilton Pharma
	GMP status	Last GMP inspection was conducted on 18-01-2018 unanimously recommends the renewal of DML no. 000610 by way of formulation.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Empozin-M 5/500 mg Tablet		
Name of Manufacturer	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate Hattar, Kpk		
Manufacturer of API	**Empagliflozin:** M/s Zhejiang Hongyuan Pharmaceutical Co., Ltd., Zhejiang, China. **Metformin hydrochloride:** M/s Shouguang Fukang Pharmaceutical Co., Ltd, Shangdong Province, China		
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin hydrochloride:** 4250/1203/18/A-0184PM		
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: 0,1,2,3,4,6 months Real Time: 0,3,6 months		
Batch No.	T-028	T-029	T-030
Batch Size	1200	1200	1200
Manufacturing Date	January-2020	January-2020	January-2020
Date of Initiation	29-01-2020	29-01-2020	29-01-2020
No. of Batches	03		
Date of Submission	2-11-2020 (Dy. No.28943)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not Available

2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA of API (Batch # EPG20190101) from M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted. **Metformin hydrochloride:** Copy of COA of API (Batch# 4250/1203/18/A-0184PM) from M/s IOL Chemicals and Pharmaceutical Co., Ltd, India has been submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Provided
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The firm has submitted accelerated & real time stability studies for 3 batches by Zheijang Hongyuan China **Metformin hydrochloride:** The firm has submitted accelerated & real time stability studies for 3 batches by IOL chemicals and Pharmaceuticals Ltd. India
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** The firm has submitted copy of GMP certificate # ZJ20180032 of Zhejiang Hongyiaan pharma issued by China Food and Drug Administration valid upto 14-03-2023. **Metformin hydrochloride:** The firm has submitted copy of GMP certificate Pb.2018/ 1895 of API manufacturer issued by Food and Drug Administration Punjab, valid up to 31-12-2021.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** The firm has submitted copy of invoice for the purchase of Empagliflozin (450 gm) attested by Assistant Director (I & E) DRAP, dated 20-03-2019. **Metformin hydrochloride:** The firm has submitted copy of commercial invoice for the purchase of metformin hydrochloride (2225 Kg) attested by Assistant Director DRAP, Karachi dated 22-11-2018
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes
9.	Drug-excipients compatibility studies (where applicable)	No, as firm claims to use same excipients as innovator
10.	Complete batch manufacturing record of three stability batches.	Yes
11.	Record of comparative dissolution data (where applicable)	Provided
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	HPLC software is 21 CFR compliant and it can be inspected at the time of inspection.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Stability chambers temperature and humidity is recorded by inbuild data logger and record is also monitored manually in log book.

Remarks of evaluator:

S No	Deficiency	Response
1.	GMP certificate(s) of API manufacturers issued by regulatory authority of the country of origin is required.	Valid GMP copy of M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted.
2.	COA and import documents of impurity standards are required	Not available
3.	Provide complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods.	The complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods were provided
4.	Certificate of analysis of API from API manufacturer and finished product manufacturer is needed.	Provided
5.	Documents for the procurement of API with approval from DRAP for both empagliflozin and metformin	Commercial Invoice of both API empagliflozin and Metformin hydrochloride along with Form 6 was provided
6.	Record of comparative dissolution data	Provided
7.	It was mentioned that the method to quantifying the impurities in the API is not available how you will justify this	Firm claim that the method to quantifying the impurities in the API is available from API manufacturer
8.	Dissolution is not according to USFDA method justification is needed	Dissolution is performed as per innovators specification (Synjardy)at the time of submission of files its method of dissolution was not included in USFDA

18.	Name and address of manufacturer / Applicant	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar,Kpk
	Brand Name +Dosage Form + Strength	Empozin-M 12.5/500 mg Tablet
	Composition	Each film coated tablet contains: Empagliflozin……..12.5mg Metformin hydrochloride……500mg
	Diary No. Date of R& I & fee	14543, dated 07/3/2019, Rs.20,000/- dated 05-03-2019 (1900583)
	Pharmacological Group	Antihyperglycemic
	Type of Form	Form-5D
	Finished product Specification	Innovator specifications
	Pack size & Demanded Price	As per brand leader
	Approval status of product in Reference Regulatory Authorities	Synjardy Tablets 12.5/500MG of Boehringer Ingelheim (USFDA Approved)
	Me-too status	EmpaMet 12.5/500 mg by Hilton Pharma
	GMP status	Last GMP inspection was conducted on 18-01-2018 unanimously recommends the renewal of DML no. 000610 by way of formulation.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Empozin-M 12.5/500 mg Tablet
Name of Manufacturer	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate Hattar, Kpk

Manufacturer of API	**Empagliflozin:** M/s Zhejiang Hongyuan Pharmaceutical Co., Ltd., Zhejiang, China. **Metformin hydrochloride:** M/s Shouguang Fukang Pharmaceutical Co., Ltd, Shangdong Province, China		
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin hydrochloride:** 4250/1203/18/A-0184PM		
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: 0,1,2,3,4,6 months Real Time: 0,3,6 months		
Batch No.	T-031	T-032	T-033
Batch Size	1200	1200	1200
Manufacturing Date	January-2020	January-2020	January-2020
Date of Initiation	29-01-2020	29-01-2020	29-01-2020
No. of Batches	03		
Date of Submission	2-11-2020 (Dy. No.28943)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not Available
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA of API (Batch # EPG20190101) from M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted. **Metformin hydrochloride:** Copy of COA of API (Batch# 4250/1203/18/A-0184PM) from M/s IOL Chemicals and Pharmaceutical Co., Ltd, India has been submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Provided
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The firm has submitted accelerated & real time stability studies for 3 batches by Zheijang Hongyuan China **Metformin hydrochloride:** The firm has submitted accelerated & real time stability studies for 3 batches by IOL chemicals and Pharmaceuticals Ltd. India
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** The firm has submitted copy of GMP certificate # ZJ20180032 of Zhejiang Hongyiaan pharma issued by China Food and Drug Administration valid upto 14-03-2023. **Metformin hydrochloride:** The firm has submitted copy of GMP certificate Pb.2018/ 1895 of API manufacturer issued by Food and Drug Administration Punjab, valid up to 31-12-2021.
6.	Documents for the procurement of API	**Empagliflozin:** The firm has submitted copy of invoice for

	with approval from DRAP (in case of import).	the purchase of Empagliflozin (450 gm) attested by Assistant Director (I & E) DRAP, dated 20-03-2019. **Metformin hydrochloride:** The firm has submitted copy of commercial invoice for the purchase of metformin hydrochloride (2225 Kg) attested by Assistant Director DRAP, Karachi dated 22-11-2018
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes
9.	Drug-excipients compatibility studies (where applicable)	No, as firm claims to use same excipients as innovator
10.	Complete batch manufacturing record of three stability batches.	Yes
11.	Record of comparative dissolution data (where applicable)	Provided
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	HPLC software is 21 CFR compliant and it can be inspected at the time of inspection.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Stability chambers temperature and humidity is recorded by inbuild data logger and record is also monitored manually in log book.

REMARKS OF EVALUATOR

S No	Deficiency	Response
1.	GMP certificate(s) of API manufacturers issued by regulatory authority of the country of origin is required.	Valid GMP copy of M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted.
2.	COA and import documents of impurity standards are required	Not available
3.	Provide complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods.	The complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods were provided
4.	Certificate of analysis of API from API manufacturer and finished product manufacturer is needed.	Provided
5.	Documents for the procurement of API with approval from DRAP for both empagliflozin and metformin	Commercial Invoice of both API empagliflozin and Metformin hydrochloride along with Form 6 was provided
6.	Record of comparative dissolution data	Provided
7.	It was mentioned that the method to quantifying the impurities in the API is not available how you will justify this	Firm claim that the method to quantifying the impurities in the API is available from API manufacturer
8.	Dissolution is not according to USFDA method justification is needed	Dissolution is performed as per innovators specification (Synjardy)at the time of submission of files its method of dissolution was not included in USFDA

19.	Name and address of manufacturer / Applicant	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar,Kpk
	Brand Name +Dosage Form + Strength	Empozin-M 12.5/1000 mg Tablet
	Composition	Each film coated tablet contains: Empagliflozin……..12.5mg Metformin hydrochloride……1000mg
	Diary No. Date of R& I & fee	14544, dated 07/3/2019, Rs.20,000/- 05-03-2019 (1900584)
	Pharmacological Group	Antihyperglycemic
	Type of Form	Form-5D
	Finished product Specification	Innovator specifications
	Pack size & Demanded Price	As per brand leader
	Approval status of product in Reference Regulatory Authorities	Synjardy Tablets 12.5/1000MG of Boehringer Ingelheim (USFDA Approved)
	Me-too status	EmpaMet 12.5/1000 mg by Hilton Pharma
	GMP status	Last GMP inspection was conducted on 18-01-2018 unanimously recommends the renewal of DML no. 000610 by way of formulation.
	Remarks of the Evaluator	Assay is by HPLC

STABILITY STUDY DATA

Drug	Empozin-M 12.5/1000 mg Tablet		
Name of Manufacturer	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate Hattar, Kpk		
Manufacturer of API	**Empagliflozin:** M/s Zhejiang Hongyuan Pharmaceutical Co., Ltd., Zhejiang, China. **Metformin hydrochloride:** M/s IOL chemical and pharmaceuticals Ltd. Village Fatehgarh Channa Tehsil Barnala District Barnala India		
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin hydrochloride:** 4250/1203/18/A-0184PM		
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: 0,1,2,3,4,6 months Real Time: 0,3,6 months		
Batch No.	T-016	T-017	T-018
Batch Size	1200	1200	1200
Manufacturing Date	January-2020	January-2020	January-2020
Date of Initiation	29-01-2020	29-01-2020	29-01-2020
No. of Batches	03		
Date of Submission	2-11-2020 (Dy. No.28943)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not Available

2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA of API (Batch # EPG20190101) from M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted. **Metformin hydrochloride:** Copy of COA of API (Batch# 4250/1203/18/A-0184PM) from M/s IOL Chemicals and Pharmaceutical Co., Ltd, India has been submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Provided
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The firm has submitted accelerated & real time stability studies for 3 batches by Zheijang Hongyuan China **Metformin hydrochloride:** The firm has submitted accelerated & real time stability studies for 3 batches by IOL chemicals and Pharmaceuticals Ltd. India
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** The firm has submitted copy of GMP certificate # ZJ20180032 of Zhejiang Hongyiaan pharma issued by China Food and Drug Administration valid upto 14-03-2023. **Metformin hydrochloride:** The firm has submitted copy of GMP certificate Pb.2018/ 1895 of API manufacturer issued by Food and Drug Administration Punjab, valid up to 31-12-2021.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** The firm has submitted copy of invoice for the purchase of Empagliflozin (450 gm) attested by Assistant Director (I & E) DRAP, dated 20-03-2019. **Metformin hydrochloride:** The firm has submitted copy of commercial invoice for the purchase of metformin hydrochloride (2225 Kg) attested by Assistant Director DRAP, Karachi dated 22-11-2018
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes
9.	Drug-excipients compatibility studies (where applicable)	No, as firm claims to use the same excipients as innovators.
10.	Complete batch manufacturing record of three stability batches.	yes
11.	Record of comparative dissolution data (where applicable)	Provided
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	HPLC software is 21 CFR compliant and it can be inspected at the time of inspection.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Stability chambers temperature and humidity is recorded by inbuild data logger and record is also monitored manually in log book.
REMARKS OF EVALUATOR		

S No	Deficiency	Response
1.	GMP certificate(s) of API manufacturers issued by regulatory authority of the country of origin is required.	Valid GMP copy of M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted.
2.	COA and import documents of impurity standards are required	Not available
3.	Provide complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods.	The complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods were provided
4.	Certificate of analysis of API from API manufacturer and finished product manufacturer is needed.	Provided
5.	Documents for the procurement of API with approval from DRAP for both empagliflozin and metformin	Commercial Invoice of both API empagliflozin and Metformin hydrochloride along with Form 6 was provided
6.	Record of comparative dissolution data	Provided
7.	It was mentioned that the method to quantifying the impurities in the API is not available how you will justify this	Firm claim that the method to quantifying the impurities in the API is available from API manufacturer
8.	Dissolution is not according to USFDA method justification is needed	Dissolution is performed as per innovators specification (Synjardy)at the time of submission of files its method of dissolution was not included in USFDA

Inspection Report

S.No.	Question	Remarks
1	Do you have documents confirming the import of Empagliflozin and Metformin API?	Yes, the firm has provided following documents Copy of raw material import attested invoice from AD (Peshawar) Empagliflozin = (Zhejiang hongyuan pharma china) API received date: 08/05/2019. API analysis and release date: 29/07/2019 Metformin = (IOL Lab India) API received date: 03/09/2018. API analysis and release date: 03/09/2018 Annexure-1
2	What was the rationale behind selecting the particular manufacturer of API?	Vendor is qualified internally against the Firm's internal SOP, and also having GMP issued by the local regulatory authority. Copy GMP certificate is attached. Annexure-2
3	Do you have documents confirming the import of Empagliflozin and Metformin reference standard and impurity standards?	Documents of reference standard and COAs are attached, impurity standards are not available. Annexure-3
4	Do you have certificate of Analysis of the API, reference standards and impurity standards?	Certificate of Analysis of the API and reference standards available. Impurities standards not available. Annexure-4
5	Do you have any approval of API or GMP certificate of API manufacturer issued by regulatory authority of country of origin?	GMP certificates of the company are available issued by the country of origin. Annexure-5
6	Do you use API manufacturer method of testing?	The Firm has used In-House Method for the testing of API and performed analytical method validation for review. Annexure-6
7	Do you have stability studies reports on API?	Yes The Firm has stability study reports from manufacturer for Metformin and Empagliflozin attached in the Master file. Annexure-7
8	If yes, whether the stability testing has	Yes quantification of the impurities has been done by the API

	been performed as per SIM method and degradation products have been quantified?	manufacturer using validated method and also quantified during stability study attached in the Master file. Annexure-8
9	Do you have method for quantifying the impurities in the API?	Method for the quantification of impurities from the manufacturer is available in the Master file. Annexure-9
10	Do you have some remaining quantities of the API, its reference standard and impurities standards?	Remaining quantity of Metformin reference standard : Nil Empagliflozin reference standard: 10mg API (Metformin): 18.8Kg API (Empagliflozin): Nil Impurities : Not available
11	Have you used pharmaceutical grade excipients?	Yes all the excipients used are of pharmaceutical grade listed as, Maize starch, MCC, Polyvinylpyrrolidone, Mg stearate, HPMC, PEG, titanium Dioxide and talcum. COA's are attached. Annexure-10
12	Do you have documents confirming the import of the used excipients?	Yes all the GRN/ invoices for import excipients are available and attached in the Master file. Annexure-11
13	Do you have test reports and other records on the excipients used?	Yes test records of the testing of excipients are available and attached in the Master file. Annexure-12
14	Do you have written and authorized protocols for the development of Empagliflozin and Metformin Tablets?	Yes the Firm have written and authorized protocol for the development of Empozin-M tablets attached in the Master file. Annexure-13
15	Have you performed Drug-excipient compatibility studies?	The Firm has used the formulation of innovator (Synjardy) manufactured by Boehringer ingelheim, Germany B # 90505 obtained from internet source.
16	Whether firm has performed comparative dissolution studies?	The Firm have Performed comparative dissolution with innovator; reports of comparative Dissolution are attached in the Master file. Packs of innovator product presented by the firm were also checked physically Annexure-14
17	Do you have product development (R&D) section	The product development section was not established during the period of stability studies and QC/ production equipment was utilized in process of development but now the firm has properly developed R&D section.
18	Do you have necessary equipments available in product development section for development of Empagliflozin and Metformin Tablets?	Yes, at present the Firm has all the necessary equipments available in product development section.
19	Are the equipments in product development section qualified	Yes all the equipments are qualified in product development section, qualification documents are attached in Master file. Annexure-15
20	Do you have proper maintenance / calibration /re-qualification program for the equipment used in PD section?	Yes The Firm have qualification; documents are attached in Master file. Annexure-16
21	Do you have qualified staff in product development section with proper knowledge and training in product development?	Yes the Firm have qualified staff in PDL section List is attached. Annexure-17
22	Have you manufactured three stability batches for the stability studies of Empagliflozin and Metformin Tablets as required	Yes The Firm has manufactured three batches of all strengths for stability study. i). 12.5/1000 mg/tab: Batch#(T-016,T-017, T-018) Dated: 17/01/2020 ii). 12.5/500 mg/tab: Batch#(T-028,T-029, T-030) Dated: 26/01/2020 iii). 5/500 mg/tab: Batch#(T-031, T-032, T-033) Dated: 26/01/2020 Stability start date: 21/01/2020

		Stability completion date: 29/07/2020
23	What were the criteria for fixing the batch size of stability batches?	The criteria for fixing the batch size of the stability batches is the quantity required for testing frequency and number of test to be performed during stability. The firm also provided remaining packs of stability batches and were physically verified placed in real time stability chamber.
24	Do you have complete record of production of stability batches?	Yes the Firm has complete batch record of the production of stability batches manufactured, and all BMR's are attached. Annexure-18
25	Do you have protocols for stability testing of stability batches?	Yes the Firm has stability protocols of the batches manufactured for stability study attached in the master file. Annexure-19
26	Do you have developed and validated the method for testing of stability batches?	Yes the Firm have developed and validated In house method of testing for Empozin-M and Validation data is attached in master file. Annexure-20
27	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Not available.
28	Do you have documents confirming the qualification of equipments/ instruments being used in the test and analysis of Empagliflozin and Metformin API and the finished drug?	Yes the Firm has all the qualification documents for the instrument used in the testing of Empagliflozin and Metformin API and finished drug attached in the master file. Annexure-21
29	Do your method of analysis stability indicating?	No, Method is not stability indicating.
30	Do your HPLC software is 21CFR compliant?	HPLC software is not 21CFR compliant but the firm has restricted access by the administrator and it is password controlled to avoid editing and data protection (Empower 2 software 2005 USA). Software 21CFR compliant certification was not available with the firm.
31	Can you show Audit Trail reports on Empagliflozin and Metformin testing?	Yes audit trail can be seen from the software and were shown by the firm on screen. The software does not provide print option. However, the firm has screen shot printouts.
32	Do you have some remaining quantities of degradation products and stability batches?	Degradation not checked through analysis in trial batches of finished products as the firm has no method of testing degradation products. Remaining quantity of Stability batches are available.
33	Do you have commitment batches kept on stability testing?	No., At the time of inspection, the Firm has following trial batches kept on stability testing i). 12.5/1000 mg/tab: Batch#(T-016,T-017,T-018) ii). 12.5/500 mg/tab: Batch# (T-028,T-029,T-030) iii). 5/500 mg/tab: Batch# (T-031, T-032, T-033)
34	Do you have valid calibration status for the equipments used in Empagliflozin and Metformin Tablets in analysis?	Yes the Firm have valid calibration record of the equipments used in analysis of stability batches calibration documents attached in master file. Annexure-23
35	Do proper and continuous monitoring and control are available for stability chamber?	Yes the Firm has proper and continuous monitoring of stability chambers and backup for power (UPS), temperature and humidity records are maintained in log books.
36	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Yes manufacturing area, equipment, personal and utilities are rated as GMP compliant by the DRAP in last GMP audit.
Conclusion: Data is verifiable and product is recommended		
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.

1. Dr. Qurban Ali
Member Registration Board

2. Faisal Shahzad
Federal Inspector of Drugs
DRAP, Peshawar

Report of Inspection: Verification of authenticity of stability data of Empozin 10 and 25 mg Tablet in reference to DRAP PEC Letter No. F.11-95/2014-Wnsfeild-DRAP (P) 4349

Name of Manufacturer	M/S Wnsfeild Pharmaceuticals,
Physical Address	Plot # 122, Block- A Phase-V, Industrial Estate, Hattar, Kpk
Date of Inspection	12-11-2021
Purpose of inspection	Verification of authenticity of stability data of Empozin 10 and 25 mg in reference to DRAP PEC Letter No. F.1-2/2020-PEC VII dated 15-11-2021.
Name of inspector	Dr. Qurban Ali, Member Registration Board Faisal Shahzad Federal Inspector of Drugs, DRAP, Peshawar.

20.	Name and address of manufacturer / Applicant	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar,Kpk
	Brand Name +Dosage Form + Strength	Empozin 10 mg Tablet
	Composition	Each film coated tablet contains: Empagliflozin……..10 mg
	Diary No. Date of R& I & fee	14542, dated 07/3/2019, Rs.20,000/- 05-03-2019 (1900582)
	Pharmacological Group	Antihyperglycemic
	Type of Form	Form-5D
	Finished product Specification	Innovator specifications
	Pack size & Demanded Price	As per brand leader
	Approval status of product in Reference Regulatory Authorities	Jardiance Tablets 10MG of Boehringer Ingelheim (USFDA Approved)
	Me-too status	Empa 10 mg by Weatherfold Pharma
	GMP status	Last GMP inspection was conducted on 18-01-2018 unanimously recommends the renewal of DML no. 000610 by way of formulation.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Empa 10 mg Tablet
Name of Manufacturer	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar, Kpk
Manufacturer of API	**Empagliflozin:** M/s Zhejiang Hongyuan Pharmaceutical Co., Ltd., Zhejiang, China.
API Lot No.	**Empagliflozin:** EPG20190101
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: 0,1,2,3,4,6 months Real Time: 0,3,6 months

Batch No.	T-07	T-08	T-09
Batch Size	1200	1200	1200
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	15-08-2020	15-08-2020	15-08-2020
No. of Batches	03		
Date of Submission	2-11-2020 (Dy. No.28941)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not provided
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA of API (Batch # EPG20190101) from M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Not provided
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The firm has submitted accelerated & real time stability studies for 3 batches by Zheijang Hongyuan China
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** The firm has submitted copy of GMP certificate # ZJ20180032 of Zhejiang Hongyiaan pharma issued by China Food and Drug Administration valid upto 14-03-2023.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** The firm has submitted copy of invoice for the purchase of Empagliflozin (450 gm) attested by Assistant Director (I & E) DRAP, dated 20-03-2019.
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes
9.	Drug-excipients compatibility studies (where applicable)	No, as firm claims to use same excipients as innovator
10.	Complete batch manufacturing record of three stability batches.	Yes
11.	Record of comparative dissolution data (where applicable)	Provided
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	HPLC software is 21 CFR compliant and it can be inspected at the time of inspection.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Stability chambers temperature and humidity is recorded by inbuild data logger and record is also monitored manually in log book.

REMARKS OF EVALUATOR

S No	Deficiency	Response
1.	GMP certificate(s) of API manufacturers issued by regulatory authority of the country of	Valid GMP copy of M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been

	origin is required.	submitted.
2.	COA and import documents of impurity standards are required	Not available
3.	Provide complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods.	The complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods were provided
4.	Certificate of analysis of API from API manufacturer and finished product manufacturer is needed.	Provided
5.	Documents for the procurement of API with approval from DRAP for both empagliflozin and metformin	Commercial Invoice of both API empagliflozin and Metformin hydrochloride along with Form 6 was provided
6.	Record of comparative dissolution data	Provided
7.	It was mentioned that the method to quantifying the impurities in the API is not available how you will justify this	Firm claim that the method to quantifying the impurities in the API is available from API manufacturer
8.	Dissolution is not according to USFDA method justification is needed	Dissolution is performed as per innovators specification (Synjardy)at the time of submission of files its method of dissolution was not included in USFDA

21.	Name and address of manufacturer / Applicant	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar,Kpk
	Brand Name +Dosage Form + Strength	Empozin 25 mg Tablet
	Composition	Each film coated tablet contains: Empagliflozin……..25 mg
	Diary No. Date of R& I & fee	14547, dated 07/3/2019, Rs.20,000/- 05-03-2019 (1900587)
	Pharmacological Group	Antihyperglycemic
	Type of Form	Form-5D
	Finished product Specification	Innovator specifications
	Pack size & Demanded Price	As per brand leader
	Approval status of product in Reference Regulatory Authorities	Jardiance Tablets 25 MG of Boehringer Ingelheim (USFDA Approved)
	Me-too status	Emazin 25 mg by Atco pharma
	GMP status	Last GMP inspection was conducted on 18-01-2018 unanimously recommends the renewal of DML no. 000610 by way of formulation.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Empa 25 mg Tablet
Name of Manufacturer	M/S Wnsfeild Pharmaceuticals, Plot # 122, Block- A Phase-V, Industrial Estate, Hattar, Kpk
Manufacturer of API	**Empagliflozin:** M/s Zhejiang Hongyuan Pharmaceutical Co., Ltd., Zhejiang, China.
API Lot No.	**Empagliflozin:** EPG20190101
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: 0,1,2,3,4,6 months Real Time: 0,3,6 months		
Batch No.	T-010	T-011	T-012
Batch Size	1200	1200	1200
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	15-08-2020	15-08-2020	15-08-2020
No. of Batches	03		
Date of Submission	2-11-2020 (Dy. No.28942)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not available
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA of API (Batch # EPG20190101) from M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Provided
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The firm has submitted accelerated & real time stability studies for 3 batches by Zheijang Hongyuan China
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** The firm has submitted copy of GMP certificate # ZJ20180032 of Zhejiang Hongyiaan pharma issued by China Food and Drug Administration valid upto 14-03-2023.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** The firm has submitted copy of invoice for the purchase of Empagliflozin (450 gm) attested by Assistant Director (I & E) DRAP, dated 20-03-2019.
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	Yes
9.	Drug-excipients compatibility studies (where applicable)	No, as firm claims to use same excipients as innovator
10.	Complete batch manufacturing record of three stability batches.	Yes
11.	Record of comparative dissolution data (where applicable)	Provided
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	HPLC software is 21 CFR compliant and it can be inspected at the time of inspection.
14.	Record of Digital data logger for temperature and	Stability chambers temperature and humidity is

	humidity monitoring of stability chambers (real time and accelerated)	recorded by inbuild data logger and record is also monitored manually in log book.

REMARKS OF EVALUATOR

S No	Deficiency	Response
1.	GMP certificate(s) of API manufacturers issued by regulatory authority of the country of origin is required.	Valid GMP copy of M/s Zhejiang Hongyuan Pharmaceutical Co, Ltd., Zhejiang, China has been submitted.
2.	COA and import documents of impurity standards are required	Not available
3.	Provide complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods.	The complete stability protocols along with detail protocols of trail batches and testing methods e.g., dissolution method and assay methods were provided
4.	Certificate of analysis of API from API manufacturer and finished product manufacturer is needed.	Provided
5.	Documents for the procurement of API with approval from DRAP for both empagliflozin and metformin	Commercial Invoice of both API empagliflozin and Metformin hydrochloride along with Form 6 was provided
6.	Record of comparative dissolution data	Not provided
7.	It was mentioned that the method to quantifying the impurities in the API is not available how you will justify this	Firm claim that the method to quantifying the impurities in the API is available from API manufacturer
8.	Dissolution is not according to USFDA method justification is needed	Dissolution is performed as per innovators specification at the time of submission of files its method of dissolution was not included in USFDA

S.No.	Question	Remarks
1	Do you have documents confirming the import of Empagliflozin API?	Yes, the firm has provided following documents Copy of raw material import attested invoice from AD (Peshawar) Empagliflozin = (Zhejiang hongyuan pharma china) Annexure-1 API received date: 08/05/2019. API analysis and release date: 29/07/2019
2	What was the rationale behind selecting the particular manufacturer of API?	Vendor is qualified internally against our internal SOP, and also having GMP issued by the local regulatory authority GMP certificate is attached. Annexure-2
3	Do you have documents confirming the import of Empagliflozin reference and impurity standard?	Documents of reference standard and COA's is attached, impurity standards are not available. Annexure-3
4	Do you have certificate of Analysis of the API, reference and impurity standard?	Certificate of Analysis of the API and reference standard available and impurities standard is not available. Annexure-4
5	Do you have any approval of API or GMP certificate of API manufacturer issued by regulatory authority of country of origin?	GMP certificates of the company are available issued by the country of origin. Annexure-5
6	Do you use API manufacturer method of testing?	The Firm has used In-House Method for the testing of API and performed analytical method validation for review. Annexure-6
7	Do you have stability studies reports on API?	Yes The Firm has stability study reports from manufacturer for Empagliflozin attached in the Master file. Annexure-7
8	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	Yes quantification of the impurities has been done by the API manufacturer using validated method and also quantified during stability study attached in the Master file. Annexure-8

9	Do you have method for quantifying the impurities in the API?	Method for the quantification of impurities from the manufacturer is available in the Master file. Annexure-9
10	Do you have some remaining quantities of the API, its reference standard and impurities standards?	Remaining quantity of reference standard Empagliflozin (RS): 10mg API (Empagliflozin): Nil Impurities: Not available.
11	Have you used pharmaceutical grade excipients?	Yes all the excipients used are of pharmaceutical grade listed as, lactose Monohydrate, MCC, Hydroxypropylcellose, Cross Carmellose Sodium, Aerosil-200, Mg-Stearate, HPMC, PEG, titanium Dioxide and talcum. COA's are attached. Annexure-10
12	Do you have documents confirming the import of the used excipients?	Yes all the GRN/ invoices for import of excipients are available and attached in the Master file. Annexure-11
13	Do you have test reports and other records on the excipients used?	Yes test records of the testing of excipients are available and attached in the Master file. Annexure-12
14	Do you have written and authorized protocols for the development of Empagliflozin Tablets?	Yes The Firm have written and authorized protocol for the development of Empozin tablets attached in the Master file. Annexure-13
15	Have you performed Drug-excipient compatibility studies?	The Firm has used the formulation of innovator (Jardiance) manufactured by Boehringer ingelheim, Germany B # 901762 obtained from internet.
16	Whether firm has performed comparative dissolution studies?	Yes, The Firm has Performed comparative dissolution with innovator; reports of comparative Dissolution are attached in the Master file. Packs of innovator product presented by the firm were also checked physically.Annexure-14
17	Do you have product development (R&D) section	The product development section was not established during the period of stability studies and QC/Production equipment was utilized in process of development but now the firm has properly developed R&D section.
18	Do you have necessary equipment available in product development section for development of Empagliflozin Tablets?	Yes, The Firm has all the necessary equipment available in product development section.
19	Are the equipment in product development section qualified	Yes, all the equipment are qualified in product development section, qualification documents are attached in Master file. Annexure-15
20	Do you have proper maintenance / calibration /re-qualification program for the equipment used in PD section?	Yes, The Firm has qualification of equipment, documents are attached in Master file. Annexure-16
21	Do you have qualified staff in product development section with proper knowledge and training in product development?	Yes, The Firm has qualified staff in PDL section List is attached. Annexure-17
22	Have you manufactured three stability batches for the stability studies of Empagliflozin and Metformin Tablets as required	Yes, The Firm have manufactured three batches of Empozin (10 and 25) mg/tab for stability studies. i). 10 mg/tab: Batch#(T-007,T-008, T-009) Dated: 13/08/2019 ii). 25 mg/tab: Batch#(T-010,T-011, T-012) Dated: 13/08/2019 Stability start date: 17/08/2019 Stability completion date: 17/02/2020
23	What were the criteria for fixing the batch size of stability batches?	The criteria for fixing the batch size of the stability batches is the quantity required for testing frequency and number of tests to be performed during stability.
24	Do you have complete record of production of stability batches?	Yes The Firm has complete batch record of the production of stability batches manufactured, and all BMR's are attached.

		Annexure-18
25	Do you have protocols for stability testing of stability batches?	Yes The Firm has stability protocols of the batches manufactured for stability study attached in the master file. Annexure-19
26	Do you have developed and validated the method for testing of stability batches?	Yes The Firm have developed and validated In house method of testing for Empozin tablets and Validation data is attached in master file. Annexure-20
27	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Not available.
28	Do you have documents confirming the qualification of equipment / instruments being used in the test and analysis of Empagliflozin API and the finished drug?	Yes, The Firm have all the qualification documents for the instrument used in the testing of Empagliflozin API and finished drug attached in the master file. Annexure-21
29	Do your method of analysis stability indicating?	No, method is not stability indicating.
30	Do your HPLC software is 21CFR compliant?	HPLC software is not 21CFR compliant but it has restricted access by the administrator and it is password controlled to avoid editing and data protection (Empower 2 software 2005 USA). Software 21CFR compliant certification was not available with the firm. Annex-22
31	Can you show Audit Trail reports on Empagliflozin testing?	Yes audit trail can be seen from the software and were shown by the firm on screen. The software does not provide print option. However, the firm has screen shot printouts.
32	Do you have some remaining quantities of degradation products and stability batches?	Degradation not checked through analysis in trial batches of finished products as the firm has no method of testing degradation products. Remaining quantity of Stability batches are available.
33	Do you have commitment batches kept on stability testing?	No., At the time of inspection, the Firm has following trial batches kept on stability testing i). 10 mg/tab: Batch#(T-007,T-008, T-009) ii). 25 mg/tab: Batch#(T-010,T-011, T-012).
34	Do you have valid calibration status for the equipments used in Empagliflozin Tablets in analysis?	Yes, The Firm have valid calibration record of the equipments used in analysis of stability batches calibration documents attached in master file. Annexure-23
35	Do proper and continuous monitoring and control are available for stability chamber?	Yes, The Firm have proper and continuous monitoring of stability chambers and backup for power (UPS), temperature and humidity records are maintained in log books.
36	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	Yes, manufacturing area, equipment, personal and utilities are rated as GMP compliant by the DRAP in last GMP audit.
Conclusion: Data is verifiable and product is recommended		
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.		

1. Dr. Qurban Ali
   Member Registration Board

2. Faisal Shahzad
   Federal Inspector of Drugs
   DRAP, Peshawar

Item No. I: Agenda of Evaluator PEC-IX

Case no. 01 Registration applications for local manufacturing of (Human) drugs

a. Deferred cases

22.	Name and address of manufacturer / Applicant	M/s Winbrains Research Laboratories. Plot No. 69/1, Block B, Phase I-II, Industrial Estate, Hattar, Pakistan
	Brand Name +Dosage Form + Strength	Azrocin Opthalmic Drops
	Composition	Each ml Contains: Azithromycin as Dihydrate…10mg
	Diary No. Date of R& I & fee	Dy No. 25952: 27.07.2018 PKR 20,000/-: 27.07.2018
	Pharmacological Group	Macrolides
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed innovator's specifications
	Pack size & Demanded Price	2.5ml; As per SRO
	Approval status of product in Reference Regulatory Authorities.	AzaSite® (azithromycin ophthalmic solution) 1% Sterile topical ophthalmic drops. USFDA approved.
	Me-too status	Could not be confirmed
	GMP status	The firm has been issued GMP certificate on the basis of inspection dated 20.05.2019
	Remarks of the Evaluator(IX)	•
	Previous 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 (M-307)
	Evaluation by PEC	Firm submitted the me-too product: Kraze ophthalmic drops Reg. No. 082125.
	Decision: Registration Board deliberated that applied product is me too / generic drug product and thus its product development data is required before sale of drug as done in all other cases. After thorough deliberation, the Board decided to approve the registration of Azrocin Ophthalmic Drops 10mg/ml (Azithromycin as dihydrate) based on availability of generic of applied drug Product.	
23.	Name and address of manufacturer/ Applicant	M/s Ethical Loboratories Pvt Ltd, 14 KM, Multan Road, Lahore
	Brand Name+ Dosage Form + Strength	OLO 0.1% eye drop solution
	Composition	Each ml contains: Olopatadine HCL…1mg
	Diary No. Date of R & I & fee	Dy. No. 3456; 25.01.2019 PKR. 20,000/-; 25.01.2019 PKR. 20,000/-; 07.05.2020
	Pharmacological Group	Other antiallergics
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	as per SRO
	Approval status of product in Reference Regulatory Authorities.	Pataday twice daily relief / Patanol (olopatadine hydrochloride ophthalmic solution) 0.1%. USFDA approved.
	Me-too status	Ogate 0.1% Ophthalmic Solution. Reg. No. 75915
	GMP status	The firm was inspected on 21.11.2017, wherein renewal of DML was recommended.
	Remarks of the Evaluator	• The firm revised the dosage form in line with the reference product with submission of Rs. 20000/- fee. The fee challan has not been endorsed by the Division of Budget and accounts. • Undertaking at the end of Form 5 is missing.
	Previous decision	Deferred for following: (M-295th) • Submission of fee for revision of formulation after getting endorsement from Budget and Account Division. • Submission of undertaking of Form 5.
	Evaluation by EPC	Firm submitted the required undertaking and copy of the challan (not been endorsed by the Division of Budget and accounts).
	Decision: Registration Board referred the case to QA & LT Division to conduct GMP inspection of	

	Firm on priority.

Item No. 6: Agenda of Evaluator PEC-XI

a. Deferred cases of Human drugs:

24.	Name and address of manufacturer / Applicant	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan
	Brand Name +Dosage Form + Strength	Paglif-M 5/500 mg Tablet
	Composition	Each film coated Tablet Contains: Empagliflozin ……5mg Metformin HCl ……500mg
	Diary No. Date of R& I & fee	Dy. No. 5189 dated 13-02-2018, Rs: 50,000/- dated 13-02-2018
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5D
	Finished product Specifications	Innovator's specifications
	Pack size & Demanded Price	10's, 14's, 30's; As per SRO
	Approval status of product in Reference Regulator Authorities	SYNJARDY (5mg/500mg, 5mg/1000mg, 12.5mg/500mg, 12.5 mg/1000 mg) film-coated tablet USFDA approved
	Me-too status	N/A
	GMP status	The firm was inspected on 05-08-2019 and conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Nabi Qasim Karachi is considered to be operating at an acceptable level of compliance of GMP requirements.
	Remarks of the Evaluator	

STABILITY STUDY DATA			
Drug			
Name of Manufacturer	M/s Nabiqasim Industries (Pvt) Ltd 17/24, Korangi Industrial Area Karachi Pakistan		
Manufacturer of API	**Empagliflozin:** Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China **Metformin HCl:** Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam-396155 Dist. Valsad Gujarat State, India		
API Lot No.	**Empagliflozin:** EPG20190101 **Metformin HCl:** MEF/19081807		
Description of Pack (Container closure system)	Alu-Alu; As per SRO		
Stability Storage Condition	Real time: 30˚C ± 2˚ C / 65% ± 5% RH Accelerated: 40 ℃ ± 2 ℃ / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (month) Real Time: 0, 3, 6 (month)		
Batch No.	361DS01	361DS02	361DS03
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	07-2020	07-2020	07-2020

Date of Initiation	10-08-2020	10-08-2020	10-08-2020
No. of Batches	03		
Date of Submission	05-03-2021 (7310)		

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	A Panel Inspection for the verification of authenticity of Stability Data of applied product on Form-5D "Sovir-C (Sofosbuvir) 400mg tablet" for Tablet Section has been conducted on 01st April, 2017. (Afternoon) and 27th October, 2020 and the Inspection Report included in the 297th DRB meeting held on 12-15th January, 2021. On the basis of Panel Inspection Report the applied product "Sofosbuvir 400mg Tablet" has been registered.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin:** Copy of COA (Batch# EPG20190101) of API from Zhejiang Hongyuan Pharmaceutical Co., Ltd. Chem&APIs Industrial zone, Linhai Zhejiang, China. and M/s Nabiqasim Industries is submitted **Metformin HCl:** Copy of COA (Batch# MEF/19081807) of API from Aarti Drugs Limited (Unit-II) Plot No. 211 & 213, Road - 2, G.I.D.C. AT & Post; Sarigam, City Sarigam-396155 Dist. Valsad Gujarat State, India and M/s Nabiqasim Industries is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of Empagliflozin from API Manufacturer and Finished Product Manufacturer is provided by the firm. Method used for analysis of Metformin from Finished Product Manufacturer is provided by the firm. Howevere Method used for analysis of Metformin by API Manufacturer is not provided
4.	Stability study data of API from API manufacturer	Incompletely submitted (accelerated stability study data of empgliflozin submitted and only six month real time stability study submitted while stability study data of metformin not submitted)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of certificate of GMP for Empagliflozin issued by Taizhou Drug Administration, is submitted. However, the GMP certificate could not be verified from China Food and Drug Administration (sfda) website. Copy of GMP certificate for Metformin HCl is submitted
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Commercial invoice for empafliflozin batch# EPG20190101 from Zhejiang Materials Industry Chemical Group Co., Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted **Invoice No** | **Quantity Imported** | **Date of attestation by DRAP** 30207132 | 0.5kg | 09.07.2019 Commercial invoice for Metformin HCl from Aarti Drugs Ltd issued in the name of M/s Nabiqasim Industries (Pvt). Ltd attested by AD DRAP Karachi is submitted **Invoice No** | **Quantity Imported** | **Date of attestation by DRAP** 1907074 | 1000kg | 08.11.2019 However, Batch No. is not mentioned on invoice.

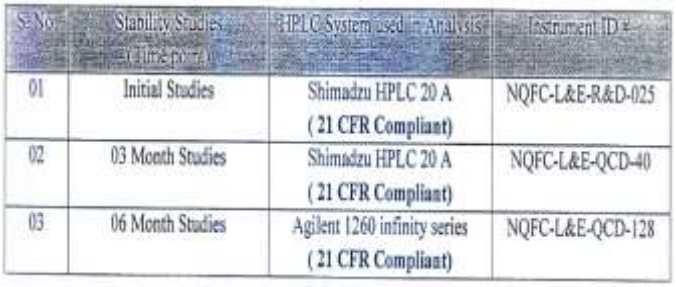
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted
9.	Drug-excipients compatibility studies (where applicable)	NA (The firm submitted that they have developed their product as per reference product Synjardy 12.5mg/1000mg. Formulation of applied drug product is qualitatively similar to that of innovator Brand Synjardy 12.5mg/1000mg tablet). However, firm have used povidone in formulation instead of copovidone as used by the innovator product
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted Batch Manufacturing record of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** 361DS01 / 1500 tablets / 07-2020 361DS02 / 1500 tablets / 07-2020 361DS03 / 1500 tablets / 07-2020
11.	Record of comparative dissolution data (where applicable)	The firm submitted that empagliflozin/metformin Hcl 5/500mg is dose proportional of higher strength i.e empagliflozin/metformin 12.5/1000 mg and that they have performed the test against the higher strength.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Incomplete Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

REMARKS OF EVALUATOR [XI]

S. No.	**Observations/ Deficiencies/ Short-Comings**	***Remarks/Justifications***

01	The registration board in its 293rd meeting decided as "Subsequent exemption will be considered after verification of CFR compliant status audit trail report on the testing of any product inspected either within three years", while the exemption report on the basis of which exemption is requested states that " Audit trail on the testing reports cannot be made as audit trail was not activated". Justification for your request for exemption is required as per above stated decision of registration board.	• Reference to the meeting minutes of 269th meeting held on 27-28th April 2017 deficiencies as pointed by panel of inspectors we have taken corrective action and removed all the deficiencies as pointed out by panel of inspectors and again panel inspection of Sofosbuvir 400mg Tablet conducted on 26th October 2020 and approved in 297th meeting with our product Navospet Gel 7.1%.
		• Reference to the Minutes of 297th Meeting of Registration Board, Report on investigation of Authenticity/ Genuineness of data submitted for registration of Navospet Gel 7.1% (Chlorhexidine digluconate) by M/s. Nabiqasim Industries, (Pvt). Ltd. Report mentioning as observed by panel against Q.No. 30 and 31
		  • The HPLC Software is 21CFR Complaint as per record of the firm.
		  • Audit trail was active on all HPLC systems used throughout stability study. Individual user login and IDs were available.
		• Audit trail reports were available and randomly

		checked.
02	Method used for analysis of Metformin API by API manufacturer is not submitted?	Method used for analysis of Metformin API by API manufacturer is submitted.
03	API manufacturer of Empagliflozin submitted only six months accelerated and real time stability study data while stability data of Metformin (both real time and accelerated) is not submitted by the API manufacturer.	Real Time Stability Data of API Manufacturers of Empagliflozin and Metformin HCl with full shelf life and Six Months Accelerated Stability Study Data by the API manufacturer as per zone IV-A are provided.
04	Submit GMP certificate of the Empagliflozin manufacturer, from the relevant (Federal or provincial) regulatory authority of China, since the submitted GMP certificate is issued by city drug administration.	Firm has submitted copy of GMP certificate (No. ZJ20180032) of Zhejiang Hongyuan Pharmaceutical co. Ltd issued by China Food and Drug Administration. The certificate is valid till 14-03-2023.
05	Submit analytical record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA.	Analytical Record including chromatograms and FTIR spectrum for identification of Empagliflozin and related substances by the firm for generated COA as well as analytical record including FTIR spectrum for identification of Metformin and related substances by the firm for generated COA are provided by the firm**.**
06	Batch size for each three trial is 1500 tablets as per your formulation; out of which 350 tablets for each batch were kept on real time stability while 150 tablets are sufficient for test/analysis of each of the trials at all time points up till proposed shelf life.	Firm has submitted calculation justifying that the batch size was sufficient enough to perform stability studies till shelf life.
07	You have not performed tests for heavy metals, residual solvents and chiral purity of Empagliflozin as mentioned in COA of drug substance, clarify?	Test for heavy metals, residual solvents and R-isomer has not been performed due to unavailability of testing supplies. These tests will be performed on commercial consignment. Revised specification is attached to be followed for commercial QC release.
08	You have mentioned dissolution specifications NLT 85%(Q+5) after 30 minutes in COA and in protocols, however , the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT(Q) in 20 minutes, Justify or revise your dissolution specifications as per innovator's product along with submission of applicable fee?	As per CDP report the dissolution of our product is more than 85% within 20 minutes for Metformin HCl and Empagliflozin. As your goodself informed us, the USFDA Biopharmaceutics review document of the innovator product specify dissolution specifications i.e. NLT(Q) in 20 minutes, we have revised our FP specifications for Paglif-M Tablet 5/500mg (Dissolution test interval from 30 minutes to 20 minutes).
09	You have not performed comparative dissolution studies for the applied product, Justify?	Justification Letter not performed comparative dissolution studies is enclosed that the study has been done on higher strength e.g. Empaglifozin 12.5mg & Metformin HCl 1000mg.
10	Justification for using Povidone in formulation instead of Copovidone.	Co povidone is also a binder and is analogue of povidone.
11	Test for impurity C of Empagliflozin not performed, clarify.	Impurity C of Eempagliflozin is a process related impurity not a degradant that's why its quantification is not required for Finished Product Testing.
12	Submit data of tests performed for	Tests performed for metformin HCl RC A and

	metformin HCl RC A and Empagliflozin impurity A mentioned in stability data sheet.	Empagliflozin impurity A mentioned in stability data sheets Of Paglif-M Tablet 5/1000 mg, chromatograms are provided
13	Submit readable copy of invoice mentioning the Batch No. of metformin HCl used in formulation. Submit form 5, form 3, form 7 of metformin HCl.	Clear copy of Metformin Invoice is provided
14	Submit COA of working standard and related substances/ impurity standards.	COA of working standard and related substances/ impurity standards is provided
15	You have performed stability study at initial time point 10.08.2020 and at six months time point 6.02.2021, five days before the completion of six months. Justification is required.	To conduct stability studies of products, we have monthly stability plan for that. As product appears in our monthly stability schedule/plan we have initiated its analytical testing.
16	The diluent used for analysis of metformin in dissolution make some disturbance of the baseline at the time at which metformin is detected. Justify that the interference due to diluent does not effect the peak area of metformin.	As per USP General Chapter <1092> the dissolution medium blank may not exceed 1% of the standard solution at the concentration used for analysis. In our case the blank absorbance is about 0.8% which lies within USP limit.
17	The submitted data for dissolution and assay of metformin does not show the peak of empagliflozin, although both are quantified by the same method and under similar conditions, clarify?	Traces of empagliflozin observed in metformin HCl assay sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 1mcg/ml. Traces of empagliflozin observed in metformin HCl dissolution sample because concentration of empagliflozin in metformin HCl sample is very low; i.e. 0.6mcg/ml.
18	The submitted data shows that stability is performed on two different HPLC system. Provide tabulated details of HPLC equipment used for stability study at different time point along with record of relevant audit trails. Also evidence that which HPLC system was used in previously approved product on basis of which exemption is applied.	 Shimadzu HPLC 20A system were used in previously approved product.
19	Submit compliance record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study as per submitted chromatograms.	The Compliance Record of HPLC software 21 CFR & Audit Trail reports on product testing for each analysis performed during the study is provided.
20	Submit record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The record of Digital data logger for temperature and humidity monitoring of stability chambers is provide.

S. No	Stability Studies (Time point)	HPLC System used in Analysis	Instrument ID #
01	Initial Studies	Shimadzu HPLC 20 A (21 CFR Compliant)	NQFC-L&E-R&D-025
02	03 Month Studies	Shimadzu HPLC 20 A (21 CFR Compliant)	NQFC-L&E-QCD-40
03	06 Month Studies	Agilent 1260 infinity series (21 CFR Compliant)	NQFC-L&E-QCD-128

Decision of 312th meeting of Registration Board:

Deferred for following:

- Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.
- Submission of applicable fee revision of specifications

Response by the firm:

Reason for deferment	Response by the firm
Submission of Comparative Dissolution Profile (CDP) data of the applied product along with innovator product.	Firm has submitted Comparative dissolution study of their product with reference Brand "Diampa-M 5/500 mg tablet" of M/s Getz Pharma (Pvt) Ltd.

	The details are as follows: <table><tr><th>Feature</th><th>Reference product</th><th>Product of Nabiqasim</th></tr><tr><td>Brand name</td><td>Diampa-M 5/500mg tablet</td><td>Empagliflozin/Metformin HCl tablet 5/500 mg (Test product)</td></tr><tr><td>Batch No.</td><td>003FC1</td><td>361DS01</td></tr></table>Comparative dissolution has been performed in pH 1.2 HCl, pH 4.5 buffer solution and pH 6.8 buffer solution. More than 85% of drug "Empagliflozin" and "Metformin HCl" releases in all three media in 15 minutes. Hence the dissolution profile of test product (Empagliflozin/Metformin HCl tablet 5/500 mg) found similar against data of reference product Diampa-M 5/500mg Tablet
Submission of applicable fee revision of specifications	Not submitted

Decision: Approved with innovator's specifications.

- **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.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.**

Item No. 7: Agenda of Evaluator AD PE&R (Mst. Saima Hussain)

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.

25.	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.24876 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: vide slip number 0927831457 dated 31/08/2021
	proposed proprietary name / brand name	Ensol- 5% IV Infusion 100mL
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Glucose Anhydrous …….5gm.
	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	100mL
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Glucose 5% Intravenous Infusion BP of Baxter Healthcare Ltd. Caxton Way, Thetford Norfolk IP24 3SE United Kingdom
	For generic drugs (me-too status)	Macsol 5% (Intravenous Infusion BP) of SEARLE IV SOLUTIONS (PVT) LTD. 1.5 Km Manga Raiwind Road, Manga Mandi, Distt. Lahore - Pakistan (Reg # 069132)
	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	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product 'Macsol 5% Infusion by Searle IV Solutions Pvt. Ltd." (Reg.no.069132)
	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)	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	19-07-2020	19-07-2020	19-07-2020
Date of Initiation	20-07-2020	20-07-2020	20-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable since it is a newly established license.
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.	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	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:

Shortcomings communicated	Response by the firm

Provide 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.

Firm provide the evidence of TGA Australia, detail of reference product is as under:

Name of Manufacturer	Active component and concentration in %	Pack size in ml
Baxter Glucose Infusion of Baxter Healthcare Pty Ltd 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA	Glucose 5%	50,100,250,500&1000
	Glucose 10%	500&1000
	Glucose 25%	1000
	Glucose 50%	500
	Glucose 70%	500

- 25% Glucose is not present in 25ml pack size.

COA of drug substance from drug substance manufacturer include pyrogen test 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	Firm has submitted the copy of COA of drug substance from drug product manufacturer in which the results of sterility test (including total bacterial/mold, total yeast count and E. coli test) and Bacterial Endotoxin test has been included.

<table>
<tr><td>manufacturer.</td><td></td></tr>
<tr><td>COA of drug substance from drug substance manufacturer include pyrogen test and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but the manufacturing method of drug substance did not include the step of sterilization.</td><td>The manufacturing method of drug substance did not include the step of sterilization by the vendor. As per DMF of Drug substance, the drug substance is nonsterile, and supporting documents are attached for total bacterial/mold and yeast count test of drug substance by drug product manufacturer.
The evidence from the DMF of dextrose is also attached, which clearly stated that the Dextrose anhydrous non-sterile drug substance.</td></tr>
<tr><td>Evidence of availability of HPLC equipped with refractometer.</td><td>Firm has submitted copy of purchase order invoice of water HPLC along with refractive index detector as an evidence of availability of HPLC equipped with refractometer.</td></tr>
<tr><td>COA of reference standard of anhydrous glucose is submitted, 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.</td><td>Firm has submitted that the COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.</td></tr>
<tr><td>Sterility test has not been performed during stability study of drug substance.</td><td>Firm has stated that Sterility test has not been performed of drug substance during the stability studies because the material is nonsterile as per DMF. Some microbial test was performed like BET test, total bacterial count, molds and yeasts count, E. Coli, mentioned in the COA of drug substance from drug substance manufacturer.</td></tr>
<tr><td>Provide the detail of composition of reference product against which pharmaceutical equivalence has been established.</td><td>Firm has provided details of the composition of reference product used for pharmaceutical equivalence for Ensol-5% (100ml), which is as under:
<table>
<tr><td rowspan="2">Component and quality standard (and grade, if applicable)</td><td rowspan="2">Function</td><td colspan="2">Strength (label claim)</td></tr>
<tr><td>Quantity per unit or per mL</td><td>%</td></tr>
<tr><td>Glucose Anhydrous</td><td>API</td><td>50mg/ml</td><td>5.0%</td></tr>
<tr><td>Water for injection</td><td>Solvent</td><td>q.s.*</td><td>N/A</td></tr>
</table>
The details of the manufacturer used for pharmaceutical equivalence for Ensol-5% (100mL) is given below.
Manufacturer Name: Searle IV Solutions Pvt. Ltd.
Brand Name: Mascol 5% infusion (Glucose anhydrous 5%)
Reg no.: 069132</td></tr>
<tr><td>According to BP for sample preparation volume of infusion containing the equivalent of 2g to 5g of glucose should be taken, justification is required for taking volume of infusion containing 10g of glucose for sample preparation.</td><td>Firm has submitted the same verification report in which the same quantity of sample has been taken for preparation of different sample concentration in performance of accuracy parameter.</td></tr>
<tr><td>Perform specificity parameter and provide results along with raw data sheets.</td><td>Firm has submitted the following comparison table to verify the specificity parameter:
<u>Specificity of Ensol- 5% (Glucose Anhydrous)</u>
<table>
<tr><td>Sr.#</td><td>Item</td><td>Specifications</td><td>Results</td></tr>
<tr><td>1</td><td>Blank (water)</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Not Complies</td></tr>
<tr><td>2</td><td>Sterifluid- 5</td><td>The solution prepared as</td><td>Complies</td></tr>
</table></td></tr>
</table>

	Standard	directed in the assay is dextrorotatory.	
3	Ensol- 10% Sample	The solution prepared as directed in the assay is dextrorotatory.	Complies

Limit: The solution prepared as directed in the assay is dextrorotatory.

Submitted AMV report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter.

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- 5% 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

Scientific justification is required regarding the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.

Firm submitted the following reply:

We performed stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH for our products packed in semi permeable containers instead of ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.

We adopted alternative approach to studying at the reference relative humidity as recommended in the table given below (for either long term or accelerated testing) is performing the stability studies under higher relative humidity and deriving the water loss at the reference relative humidity through calculation. This can be achieved by experimentally determining the permeation coefficient for the container closure system.

Alternative relative humidity	Reference relative humidity	Ratio of water loss rates at a given temperature
60% RH	25% RH	1.9
60% RH	40% RH	1.5
65% RH	35% RH	1.9
75% RH	25% RH	3.0

Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard.

Firm submitted the separate stability data for 100ml volume with the statement that "Same stability data was submitted for 100ml, 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."

Provide reference for the acceptance criteria of filled volume for applied drug product.

The reference for the acceptance criteria of filled volume for applied drug product is the general chapter of USP 1151. And the table is given below

	Recommended Excess Volume	
Labeled Size	For mobile liquids	For viscous liquid
0.5 ml	0.10 ml	0.12 ml
1 ml	0.10 ml	0.15 ml
2 ml	0.15 ml	0.25 ml
5 ml	0.30 ml	0.50 ml

10 ml	0.50 ml	0.70 ml
20 ml	0.60 ml	0.90 ml
30 ml	0.80 ml	1.20 ml
50ml or more	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

Firm has submitted the reply that, 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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

- Provide the evidence of reference product of dextrose infusion packed in LDPE plastic container.

Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis.

Firm provide the copy of COA of LDPE (Purell PE 3020D) resins of M/s. LyondellBasell, product description and properties are given as under:

Purell PE 3020D is a low-density polyethylene with high rigidity, good opticals and good chemical resistance. It is delivered in pellet form. The grade is used by our customers for small blow mouldings including packaging of pharmaceuticals in blow fill seal technology and injection moulding for medical devices, closures and seals.

Typical Properties	Nominal Value
Melt Flow Rate, (190 °C/2.16 kg)	0.3 g/10 min
Vicat Softening Temperature	102 °C
Peak Melting Point	114 °C
Recommended processing temperatures	170 °C to 220 °C

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.**

26.	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.24872 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: vide slip no.004131476 dated 31/08/2021
	proposed proprietary name / brand name	Ensol- 5% IV Infusion 500mL
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Glucose Anhydrous …….5gm.
	Pharmaceutical form of applied drug	Intravenous Injection
	Pharmacotherapeutic Group of (API)	Other IV Solution Additives ATC CODE: V06DC01
	Reference to Finished product specification	BP
	Proposed Pack size	500mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose 5% Intravenous Infusion BP of Baxter Healthcare Ltd. Caxton Way, Thetford Norfolk IP24 3SE United Kingdom
	For generic drugs (me-too status)	Sterifluid- 5 (Intravenous Infusion BP) of Frontier Dextrose Ltd. Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan (Reg # 049818)
	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	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product Sterifluid-5 of M/s. Frontier Dextrose Ltd. Reg.no.049818.
	Analytical method validation/verification	Method verification studies has been submitted including

	of product	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)	500mL 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	19-07-2020	19-07-2020	19-07-2020
Date of Initiation	20-07-2020	20-07-2020	20-07-2020
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable since it is a newly established license.	
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.	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	NA	
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.	
Remarks Of Evaluator:			

Shortcomings communicated	Response by the firm
Provide 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. Firm provide the evidence of TGA Australia, detail of reference product is as under:	

Name of Manufacturer	Active component and concentration in %	Pack size in ml

Baxter Glucose Infusion of Baxter Healthcare Pty Ltd 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA	Glucose 5%	50,100,250,500&1000
	Glucose 10%	500&1000
	Glucose 25%	1000
	Glucose 50%	500
	Glucose 70%	500

- 25% Glucose is not present in 25ml pack size.

COA of drug substance from drug substance manufacturer include pyrogen test 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.	Firm has submitted the copy of COA of drug substance from drug product manufacturer in which the results of sterility test (including total bacterial/mold, total yeast count and E. coli test) and Bacterial Endotoxin test has been included.
COA of drug substance from drug substance manufacturer include pyrogen test and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but the manufacturing method of drug substance did not include the step of sterilization.	The manufacturing method of drug substance did not include the step of sterilization by the vendor. As per DMF of Drug substance, the drug substance is nonsterile, and supporting documents are attached for total bacterial/mold and yeast count test of drug substance by drug product manufacturer. The evidence from the DMF of dextrose is also attached, which clearly stated that the Dextrose anhydrous non-sterile drug substance.
Evidence of availability of HPLC equipped with refractometer.	Firm has submitted copy of purchase order invoice of water HPLC along with refractive index detector as an evidence of availability of HPLC equipped with refractometer.
COA of reference standard of anhydrous glucose is submitted, 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.	Firm has submitted that the COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.
Sterility test has not been performed during stability study of drug substance.	Firm has stated that Sterility test has not been performed of drug substance during the stability studies because the material is nonsterile as per DMF. Some microbial test was performed like BET test, total bacterial count, molds and yeasts count, E. Coli, mentioned in the COA of drug substance from drug substance manufacturer.
Provide the detail of composition of reference product against which pharmaceutical equivalence has been established.	Firm has provided details of the composition of reference product used for pharmaceutical equivalence for Ensol-5% (500ml), which is as under:

Component and quality standard (and grade, if applicable)	Function	Strength (label claim)	
		Quantity per unit or per mL	%
Glucose Anhydrous	API	50mg/ml	5.0%
Water for injection	Solvent	q.s.*	N/A

The details of the manufacturer used for pharmaceutical equivalence for Ensol-5% (500mL) is given below.
Manufacturer Name: M/s. Frontier Dextrose Ltd.
Brand Name: Sterifluid-5 (500ml)
Reg.no. 049818
In reference product (sterifluid-5) glucose monohydrate has been used as an active material while in the applied product glucose anhydrous is

<table>
<tr><td></td><td>used as an active material.</td></tr>
<tr><td>According to BP for sample preparation volume of infusion containing the equivalent of 2g to 5g of glucose should be taken, justification is required for taking volume of infusion containing 10g of glucose for sample preparation.</td><td>Firm has submitted the same verification report in which the same quantity of sample has been taken for preparation of different sample concentration in performance of accuracy parameter.</td></tr>
<tr><td>Perform specificity parameter and provide results along with raw data sheets.</td><td>Firm has submitted the following comparison table to verify the specificity parameter:
<u>Specificity of Ensol- 5% (Glucose Anhydrous)</u>
<table>
<tr><th>Sr. No.</th><th>Item</th><th>Specifications</th><th>Results</th></tr>
<tr><td>1</td><td>Blank (water)</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Not Complies</td></tr>
<tr><td>2</td><td>Sterifluid- 5 Standard</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Complies</td></tr>
<tr><td>3</td><td>Ensol- 10% Sample</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Complies</td></tr>
</table>
Limit: The solution prepared as directed in the assay is dextrorotatory.</td></tr>
<tr><td>Submitted AMV report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter.</td><td>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- 5% 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</td></tr>
<tr><td>Scientific justification is required regarding the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.</td><td>Firm submitted the following reply:
We performed stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH for our products packed in semi permeable containers instead of ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.
We adopted alternative approach to studying at the reference relative humidity as recommended in the table given below (for either long term or accelerated testing) is performing the stability studies under higher relative humidity and deriving the water loss at the reference relative humidity through calculation. This can be achieved by experimentally determining the permeation coefficient for the container closure system.</td></tr>
</table>

Alternative relative humidity	Reference relative humidity	Ratio of water loss rates at a given temperature
60% RH	25% RH	1.9
60% RH	40% RH	1.5
65% RH	35% RH	1.9
75% RH	25% RH	3.0

Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard.	Firm submitted the separate stability data for 500ml volume with the statement that "Same stability data was submitted for 100ml, 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."

Provide reference for the acceptance criteria of filled volume for applied drug product.
The reference for the acceptance criteria of filled volume for applied drug product is the general chapter of USP 1151. And the table is given below

	Recommended Excess Volume	
Labeled Size	For mobile liquids	For viscous liquid
0.5 ml	0.10 ml	0.12 ml
1 ml	0.10 ml	0.15 ml
2 ml	0.15 ml	0.25 ml
5 ml	0.30 ml	0.50 ml
10 ml	0.50 ml	0.70 ml
20 ml	0.60 ml	0.90 ml
30 ml	0.80 ml	1.20 ml
50ml or more	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
Firm has submitted the reply that, 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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

- Provide the evidence of reference product of dextrose infusion packed in LDPE plastic container.

Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis.

Firm provide the copy of COA of LDPE (Purell PE 3020D) resins of M/s. LyondellBasell, product description and properties are given as under:
Purell PE 3020D is a low-density polyethylene with high rigidity, good opticals and good chemical resistance. It is delivered in pellet form. The grade is used by our customers for small blow mouldings including packaging of pharmaceuticals in blow fill seal technology and injection moulding for medical devices, closures and seals.

Typical Properties	Nominal Value
Melt Flow Rate, (190 °C/2.16 kg)	0.3 g/10 min
Vicat Softening Temperature	102 °C
Peak Melting Point	114 °C

	Recommended processing temperatures	170 °C to 220 °C	

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.**

27.	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. 24871 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: vide slip no.3378360866 dated 31/08/2021
	proposed proprietary name / brand name	Ensol- 5% IV Infusion 1000mL
	Strength/ concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Glucose Anhydrous …….5gm.
	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	1000mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose 5% Intravenous Infusion BP of Baxter Healthcare Ltd. Caxton Way, Thetford Norfolk IP24 3SE United Kingdom
	For generic drugs (me-too status)	Sterifluid- 5 (Intravenous Infusion BP) of Frontier Dextrose Ltd. Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan (Reg # 049818)
	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	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product Sterifluid-5 of M/s. Frontier Dextrose Ltd. Reg.no.049818.
	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)	1000mL 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	19-07-2020	19-07-2020	19-07-2020
Date of Initiation	20-07-2020	20-07-2020	20-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable since it is a newly established license.
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.	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	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:

Shortcomings communicated	Response by the firm

Provide 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.

Firm provide the evidence of TGA Australia, detail of reference product is as under:

Name of Manufacturer	Active component and concentration in %	Pack size in ml
Baxter Glucose Infusion of Baxter Healthcare Pty Ltd 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA	Glucose 5%	50,100,250,500&1000
	Glucose 10%	500&1000
	Glucose 25%	1000
	Glucose 50%	500
	Glucose 70%	500

25% Glucose is not present in 25ml pack size.

COA of drug substance from drug substance manufacturer include pyrogen test 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.	Firm has submitted the copy of COA of drug substance from drug product manufacturer in which the results of sterility test (including total bacterial/mold, total yeast count and E. coli test) and Bacterial Endotoxin test has been included.
COA of drug substance from drug substance manufacturer include pyrogen test and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but the manufacturing method of drug substance did not include the step of sterilization.	The manufacturing method of drug substance did not include the step of sterilization by the vendor. As per DMF of Drug substance, the drug substance is nonsterile, and supporting documents are attached for total bacterial/mold and yeast count test of drug substance by drug product manufacturer. The evidence from the DMF of dextrose is also attached, which clearly stated that the Dextrose anhydrous non-sterile drug substance.
Evidence of availability of HPLC equipped with refractometer.	Firm has submitted copy of invoice as an evidence of availability of HPLC equipped with refractometer.
COA of reference standard of anhydrous glucose is submitted, while according to BP glucose hydrous chemical reference standard is used to analyze the quality of glucose anhydrous.	Firm has submitted that the COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.

<table>
<tr><td>Justification is required for using glucose anhydrous reference standard for the assay.</td><td></td></tr>
<tr><td>Sterility test has not been performed during stability study of drug substance.</td><td>Firm has stated that Sterility test has not been performed of drug substance during the stability studies because the material is nonsterile as per DMF. Some microbial test was performed like BET test, total bacterial count, molds and yeasts count, E. Coli, mentioned in the COA of drug substance from drug substance manufacturer.</td></tr>
<tr><td>Provide the detail of composition of reference product against which pharmaceutical equivalence has been established.</td><td>Firm has provided details of the composition of reference product used for pharmaceutical equivalence for Ensol-5% (1000ml), which is as under:
<table>
<tr><td rowspan="2">Component and quality standard (and grade, if applicable)</td><td rowspan="2">Function</td><td colspan="2">Strength (label claim)</td></tr>
<tr><td>Quantity per unit or per mL</td><td>%</td></tr>
<tr><td>Glucose Anhydrous</td><td>API</td><td>50mg/ml</td><td>5.0%</td></tr>
<tr><td>Water for injection</td><td>Solvent</td><td>q.s.*</td><td>N/A</td></tr>
</table>
The details of the manufacturer used for pharmaceutical equivalence for Ensol-5% (1000mL) is given below.
Manufacturer Name: M/s. Frontier Dextrose Ltd.
Brand Name: Sterifluid-5 (500ml)
Reg.no. 049818
In reference product (sterifluid-5) glucose monohydrate has been used as an active material while in the applied product glucose anhydrous is used as an active material.</td></tr>
<tr><td>According to BP for sample preparation volume of infusion containing the equivalent of 2g to 5g of glucose should be taken, justification is required for taking volume of infusion containing 10g of glucose for sample preparation.</td><td>Firm has submitted the same verification report in which the same quantity of sample has been taken for preparation of different sample concentration in performance of accuracy parameter.</td></tr>
<tr><td>Perform specificity parameter and provide results along with raw data sheets.</td><td>Firm has submitted the following comparison table to verify the specificity parameter:
<u>Specificity of Ensol- 5% (Glucose Anhydrous)</u>
<table>
<tr><td>Sr. No.</td><td>Item</td><td>Specifications</td><td>Results</td></tr>
<tr><td>1</td><td>Blank (water)</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Not Complies</td></tr>
<tr><td>2</td><td>Sterifluid- 5 Standard</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Complies</td></tr>
<tr><td>3</td><td>Ensol- 10% Sample</td><td>The solution prepared as directed in the</td><td>Complies</td></tr>
</table></td></tr>
</table>

	assay is dextrorotatory. Limit: The solution prepared as directed in the assay is dextrorotatory.
Submitted AMV report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter.	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- 5% 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
Scientific justification is required regarding the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Firm submitted the following reply: We performed stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH for our products packed in semi permeable containers instead of ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers. We adopted alternative approach to studying at the reference relative humidity as recommended in the table given below (for either long term or accelerated testing) is performing the stability studies under higher relative humidity and deriving the water loss at the reference relative humidity through calculation. This can be achieved by experimentally determining the permeation coefficient for the container closure system.

Alternative relative humidity	Reference relative humidity	Ratio of water loss rates at a given temperature
60% RH	25% RH	1.9
60% RH	40% RH	1.5
65% RH	35% RH	1.9
75% RH	25% RH	3.0

Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard.	Firm submitted the separate stability data for 500ml volume with the statement that "Same stability data was submitted for 100ml, 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."

Provide reference for the acceptance criteria of filled volume for applied drug product.

The reference for the acceptance criteria of filled volume for applied drug product is the general chapter of USP 1151. And the table is given below

	Recommended Excess Volume	
Labeled Size	For mobile liquids	For viscous liquid
0.5 ml	0.10 ml	0.12 ml
1 ml	0.10 ml	0.15 ml
2 ml	0.15 ml	0.25 ml
5 ml	0.30 ml	0.50 ml
10 ml	0.50 ml	0.70 ml
20 ml	0.60 ml	0.90 ml
30 ml	0.80 ml	1.20 ml
50ml or more	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

Firm has submitted the reply that, 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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

- Provide the evidence of reference product of dextrose infusion packed in LDPE plastic container.

Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis.

Firm provide the copy of COA of LDPE (Purell PE 3020D) resins of M/s. LyondellBasell, product description and properties are given as under:

Purell PE 3020D is a low-density polyethylene with high rigidity, good opticals and good chemical resistance. It is delivered in pellet form. The grade is used by our customers for small blow mouldings including packaging of pharmaceuticals in blow fill seal technology and injection moulding for medical devices, closures and seals.

Typical Properties	Nominal Value
Melt Flow Rate, (190 °C/2.16 kg)	0.3 g/10 min
Vicat Softening Temperature	102 °C
Peak Melting Point	114 °C
Recommended processing temperatures	170 °C to 220 °C

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.**

28.	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. 24877 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: vide slip no. 49923360236 dated 31/08/2021
	proposed proprietary name / brand name	Ensol- 10% IV Infusion (500mL)
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Glucose Anhydrous …….10gm.

	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	500mL
	Proposed unit price	As per SRO
	status in reference regulatory authorities	Glucose 10% Intravenous Infusion BP of Baxter Healthcare Ltd. Caxton Way, Thetford Norfolk IP24 3SE United Kingdom
	For generic drugs (me-too status)	Sterifluid- 10 (Intravenous Infusion BP) of Frontier Dextrose Ltd. Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan (Reg # 049819)
	GMP status of the Finished product manufacturer	New DML issue dated w.e.f.13-02-2020. Last inspection conducted on 15-10-2020 & 16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Section Approval Status	The CLB approved in its 273rd approved the grant of Drug Manufacturing License (by way of formulation) vide letter no.F.1-29/2013-Lic dated 13th February,2020 with the following three section: Large Volume Parenteral (LVP) general section Small Volume Parenteral (SVP) general section Ampoule LDPE (General) section
	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	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product 'Sterifluid-10 Infusion by Frontier Dextrose

		Limited." (Reg.no.049819)		
	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)		500mL 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		22-07-2020	22-07-2020	22-07-2020
Date of Initiation		23-07-2020	23-07-2020	23-07-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable since it is a newly established license.		
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.	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	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:				

Shortcomings communicated	Response by the firm
Provide 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.	

Firm provide the evidence of TGA Australia, detail of reference product is as under:

Name of Manufacturer	Active component and concentration in %	Pack size in ml
Baxter Glucose Infusion of Baxter Healthcare Pty Ltd 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA	Glucose 5%	50,100,250,500&1000
	Glucose 10%	500&1000
	Glucose 25%	1000
	Glucose 50%	500
	Glucose 70%	500

25% Glucose is not present in 25ml pack size.

COA of drug substance from drug substance manufacturer include pyrogen test 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.	Firm has submitted the copy of COA of drug substance from drug product manufacturer in which the results of sterility test (including total bacterial/mold, total yeast count and E. coli test) and Bacterial Endotoxin test has been included.
COA of drug substance from drug substance manufacturer include pyrogen test and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but the manufacturing method of drug substance did not include the step of sterilization.	The manufacturing method of drug substance did not include the step of sterilization by the vendor. As per DMF of Drug substance, the drug substance is nonsterile, and supporting documents are attached for total bacterial/mold and yeast count test of drug substance by drug product manufacturer. The evidence from the DMF of dextrose is also attached, which clearly stated that the Dextrose anhydrous non-sterile drug substance.
Evidence of availability of HPLC equipped with refractometer.	Firm has submitted copy of purchase order invoice of water HPLC along with refractive index detector as an evidence of availability of HPLC equipped with refractometer.
COA of reference standard of anhydrous glucose is submitted, 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.	Firm has submitted that the COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.
Sterility test has not been performed during stability study of drug substance.	Firm has stated that Sterility test has not been performed of drug substance during the stability studies because the material is nonsterile as per DMF. Some microbial test was performed like BET test, total bacterial count, molds and yeasts count, E. Coli, mentioned in the COA of drug substance from drug substance manufacturer.
Provide the detail of composition of reference product against which pharmaceutical equivalence has been established.	Firm has provided details of composition of reference product used for pharmaceutical equivalence for Ensol-10% (500ml), which is as under:

Component and quality standard (and grade, if applicable)	Function	Strength (label claim)	
		Quantity per unit or per mL	%
Glucose Anhydrous	API	100mg/ml	10.0%

Water for injection	Solvent	q.s.*	N/A

The details of the manufacturer used for pharmaceutical equivalence for Ensol-10% (500mL) is given below.
Manufacturer Name: Frontier Dextrose Ltd.
Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan
Brand Name: Sterifluid- 10 (500ml)
Batch No.: 505720
Reg no.: 049819
In reference product (sterifluid-10) glucose monohydrate has been used as an active material while in the applied product glucose anhydrous is used as an active material.

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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

According to BP for sample preparation volume of infusion containing the equivalent of 2g to 5g of glucose should be taken, justification is required for taking volume of infusion containing 10g of glucose for sample preparation.

Firm has submitted the same verification report in which the same quantity of sample has been taken for preparation of different sample concentration in performance of accuracy parameter.

Perform specificity parameter and provide results along with raw data sheets.

Firm has submitted the following comparison table to verify the specificity parameter:
<u>Specificity of Ensol- 10% (Glucose Anhydrous)</u>

Sr. No.	Item	Specifications	Results
1	Blank (water)	The solution prepared as directed in the assay is dextrorotatory.	Not Complies
2	Sterifluid- 10 Standard	The solution prepared as directed in the	Complies

		assay is dextrorotatory.	
3	Ensol- 10% Sample	The solution prepared as directed in the assay is dextrorotatory.	Complies

Limit: The solution prepared as directed in the assay is dextrorotatory.

Submitted AMV report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter.	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- 5% 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
Scientific justification is required regarding the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Firm submitted the following reply: We performed stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH for our products packed in semi permeable containers instead of ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers. We adopted alternative approach to studying at the reference relative humidity as recommended in the table given below (for either long term or accelerated testing) is performing the stability studies under higher relative humidity and deriving the water loss at the reference relative humidity through calculation. This can be achieved by experimentally determining the permeation coefficient for the container closure system.

Alternative relative humidity	Reference relative humidity	Ratio of water loss rates at a given temperature
60% RH	25% RH	1.9
60% RH	40% RH	1.5
65% RH	35% RH	1.9
75% RH	25% RH	3.0

Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard.	• Firm submitted the separate stability data for 500ml 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." • According to the BMR, the filled bottles was terminally sterilized on 23-07-2020, while the submitted stability data indicated that date of initiation of stability is 22-07-2020.Clarification is required in this regard.

Provide reference for the acceptance criteria of filled volume for applied drug product.

The reference for the acceptance criteria of filled volume for applied drug product is the general chapter of USP 1151. And the table is given below

	Recommended Excess Volume	
Labeled Size	For mobile liquids	For viscous liquid

0.5 ml	0.10 ml	0.12 ml
1 ml	0.10 ml	0.15 ml
2 ml	0.15 ml	0.25 ml
5 ml	0.30 ml	0.50 ml
10 ml	0.50 ml	0.70 ml
20 ml	0.60 ml	0.90 ml
30 ml	0.80 ml	1.20 ml
50ml or more	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.

Firm has submitted the reply that, 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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

- Provide the evidence of reference product of dextrose infusion packed in LDPE plastic container.

Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis.

Firm provide the copy of COA of LDPE (Purell PE 3020D) resins of M/s. LyondellBasell, product description and properties are given as under:

Purell PE 3020D is a low-density polyethylene with high rigidity, good opticals and good chemical resistance. It is delivered in pellet form. The grade is used by our customers for small blow mouldings including packaging of pharmaceuticals in blow fill seal technology and injection moulding for medical devices, closures and seals.

Typical Properties	Nominal Value
Melt Flow Rate, (190 °C/2.16 kg)	0.3 g/10 min
Vicat Softening Temperature	102 °C
Peak Melting Point	114 °C
Recommended processing temperatures	170 °C to 220 °C

Decision: Deferred for clarification/justification from the firm regarding the commencement of stability study which was initiated before the terminal sterilization of drug product.

29.	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.24878 dated 08/09/2021
	Details of fee submitted	PKR 30,000/-: vide slip no.528291929 dated 31/08/2021
	The proposed proprietary name / brand name	Ensol- 10% IV Infusion (1000mL)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml contains: Glucose Anhydrous …….10gm.
	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	1000mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose 10% Intravenous Infusion BP of Baxter Healthcare Ltd.Caxton Way, Thetford Norfolk IP24 3SE United Kingdom
	For generic drugs (me-too status)	Sterifluid- 10 (Intravenous Infusion BP) of Frontier Dextrose Ltd. Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan (Reg # 049819)
	GMP status of the Finished product manufacturer	New DML issue dated w.e.f.13-02-2020. Last inspection conducted on 15-10-2020 & 16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Section Approval Status	The CLB approved in its 273rd approved the grant of Drug Manufacturing License (by way of formulation) vide letter no.F.1-29/2013-Lic dated 13th February,2020 with the following three section: Large Volume Parenteral (LVP) general section Small Volume Parenteral (SVP) general section Ampoule LDPE (General) section
	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	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product 'Sterifluid-10 Infusion by Frontier Dextrose Limited." (Reg.no.049819)
	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)	1000mL 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	22-07-2020	22-07-2020	22-07-2020
Date of Initiation	23-07-2020	23-07-2020	23-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable since it is a newly established license.
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.	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	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:

Shortcomings communicated	Response by the firm
Provide 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. Firm provide the evidence of TGA Australia, detail of reference product is as under: 25% Glucose is not present in 25ml pack size.	
COA of drug substance from drug substance manufacturer include pyrogen test 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.	Firm has submitted the copy of COA of drug substance from drug product manufacturer in which the results of sterility test (including total bacterial/mold, total yeast count and E. coli test) and Bacterial Endotoxin test has been included.
COA of drug substance from drug substance manufacturer include pyrogen test and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but the manufacturing method of drug substance did not include the step of sterilization.	The manufacturing method of drug substance did not include the step of sterilization by the vendor. As per DMF of Drug substance, the drug substance is nonsterile, and supporting documents are attached for total bacterial/mold and yeast count test of drug substance by drug product manufacturer. The evidence from the DMF of dextrose is also attached, which clearly stated that the Dextrose anhydrous non-sterile drug substance.
Evidence of availability of HPLC equipped with refractometer.	Firm has submitted copy of purchase order invoice of water HPLC along with refractive index detector as an evidence of availability of HPLC equipped with refractometer.
COA of reference standard of anhydrous glucose is submitted, 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.	Firm has submitted that the COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.
Sterility test has not been performed during stability study of drug substance.	Firm has stated that Sterility test has not been performed of drug substance during the stability studies because the material is nonsterile as per DMF. Some microbial test was performed like BET test, total bacterial count, molds and yeasts count, E. Coli, mentioned in the COA of drug substance from drug substance manufacturer.

Name of Manufacturer	Active component and concentration in %	Pack size in ml
Baxter Glucose Infusion of Baxter Healthcare Pty Ltd 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA	Glucose 5%	50,100,250,500&1000
	Glucose 10%	500&1000
	Glucose 25%	1000
	Glucose 50%	500
	Glucose 70%	500

<table>
<tr>
<td>Provide the detail of composition of reference product against which pharmaceutical equivalence has been established.</td>
<td>Firm has provided details of the composition of reference product used for pharmaceutical equivalence for Ensol-10% (1000ml), which is as under:
<table>
<tr><td rowspan="2">Component and quality standard (and grade, if applicable)</td><td rowspan="2">Function</td><td colspan="2">Strength (label claim)</td></tr>
<tr><td>Quantity per unit or per mL</td><td>%</td></tr>
<tr><td>Glucose Anhydrous</td><td>API</td><td>100mg/ml</td><td>10.0%</td></tr>
<tr><td>Water for injection</td><td>Solvent</td><td>q.s.*</td><td>N/A</td></tr>
</table>
The details of the manufacturer used for pharmaceutical equivalence for Ensol-10% (1000mL) is given below.
Manufacturer Name: Frontier Dextrose Ltd.
Plot No. 18/3, Phase- 1 Hatter Industrial Estate Haripur Pakistan
Brand Name: Sterifluid- 10 (1000ml)
Batch No.: 505720
Reg no.: 049819
In reference product (sterifluid-5) glucose monohydrate has been used as an active material while in the applied product glucose anhydrous is used as an active material.</td>
</tr>
<tr>
<td>According to BP for sample preparation volume of infusion containing the equivalent of 2g to 5g of glucose should be taken, justification is required for taking volume of infusion containing 10g of glucose for sample preparation.</td>
<td>Firm has submitted the same verification report in which the same quantity of sample has been taken for preparation of different sample concentration in performance of accuracy parameter.</td>
</tr>
<tr>
<td>Perform specificity parameter and provide results along with raw data sheets.</td>
<td>Firm has submitted the following comparison table to verify the specificity parameter:
<u>Specificity of Ensol- 10% (Glucose Anhydrous)</u>
<table>
<tr><th>Sr. No.</th><th>Item</th><th>Specifications</th><th>Results</th></tr>
<tr><td>1</td><td>Blank (water)</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Not Complies</td></tr>
<tr><td>2</td><td>Glucose Standard (sterifluid-10)</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Complies</td></tr>
<tr><td>3</td><td>Ensol- 10% Sample</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Complies</td></tr>
</table>
Limit: The solution prepared as directed in the assay is dextrorotatory.</td>
</tr>
<tr>
<td>Submitted AMV report describe the same procedure</td>
<td>Firm has submitted the following reply:
The details of accuracy parameter of drug product is given below.</td>
</tr>
</table>

<table>
<tr><td>for preparation of different sample concentration in performance of accuracy parameter.</td><td>ACCURACY/ RECOVERY
Prepared the three replicates of ENSOL- 10% 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</td></tr>
<tr><td>Scientific justification is required regarding the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.</td><td>Firm submitted the following reply:
We performed stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH for our products packed in semi permeable containers instead of ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.
We adopted alternative approach to studying at the reference relative humidity as recommended in the table given below (for either long term or accelerated testing) is performing the stability studies under higher relative humidity and deriving the water loss at the reference relative humidity through calculation. This can be achieved by experimentally determining the permeation coefficient for the container closure system.
<table>
<tr><th>Alternative relative humidity</th><th>Reference relative humidity</th><th>Ratio of water loss rates at a given temperature</th></tr>
<tr><td>60% RH</td><td>25% RH</td><td>1.9</td></tr>
<tr><td>60% RH</td><td>40% RH</td><td>1.5</td></tr>
<tr><td>65% RH</td><td>35% RH</td><td>1.9</td></tr>
<tr><td>75% RH</td><td>25% RH</td><td>3.0</td></tr>
</table></td></tr>
<tr><td>Same stability data has been submitted for 500ml &1000ml.Clarification required in this regard.</td><td>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.”
According to the BMR, the filled bottles was terminally sterilized on 23-07-2020, while the submitted stability data indicated that date of initiation of stability is 22-07-2020.Clarification is required in this regard.</td></tr>
<tr><td colspan="2">Provide reference for the acceptance criteria of filled volume for applied drug product.
The reference for the acceptance criteria of filled volume for applied drug product is the general chapter of USP 1151. And the table is given below
<table>
<tr><td></td><td colspan="2">Recommended Excess Volume</td></tr>
<tr><td>Labeled Size</td><td>For mobile liquids</td><td>For viscous liquid</td></tr>
<tr><td>0.5 ml</td><td>0.10 ml</td><td>0.12 ml</td></tr>
<tr><td>1 ml</td><td>0.10 ml</td><td>0.15 ml</td></tr>
<tr><td>2 ml</td><td>0.15 ml</td><td>0.25 ml</td></tr>
<tr><td>5 ml</td><td>0.30 ml</td><td>0.50 ml</td></tr>
<tr><td>10 ml</td><td>0.50 ml</td><td>0.70 ml</td></tr>
<tr><td>20 ml</td><td>0.60 ml</td><td>0.90 ml</td></tr>
<tr><td>30 ml</td><td>0.80 ml</td><td>1.20 ml</td></tr>
<tr><td>50ml or more</td><td>2%</td><td>3%</td></tr>
</table></td></tr>
<tr><td colspan="2">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</td></tr>
</table>

Firm has submitted the reply that, 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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

- Provide the evidence of reference product of dextrose infusion packed in LDPE plastic container.

Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis.
Firm provide the copy of COA of LDPE (Purell PE 3020D) resins of M/s. LyondellBasell, product description and properties are given as under:
Purell PE 3020D is a low-density polyethylene with high rigidity, good opticals and good chemical resistance. It is delivered in pellet form. The grade is used by our customers for small blow mouldings including packaging of pharmaceuticals in blow fill seal technology and injection moulding for medical devices, closures and seals.

Typical Properties	Nominal Value
Melt Flow Rate, (190 °C/2.16 kg)	0.3 g/10 min
Vicat Softening Temperature	102 °C
Peak Melting Point	114 °C
Recommended processing temperatures	170 °C to 220 °C

Decision: Deferred for clarification/justification from the firm regarding the commencement of stability study which was initiated before the terminal sterilization of drug product.

30.	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. 24879 dated 09/08/2021
	Details of fee submitted	PKR 30,000/-: vide slip no. 787539315 dated 09/08/2021
	proposed proprietary name / brand name	Ensol- 25% IV Infusion 25mL
	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	25mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glucose 25% Intravenous Infusion BP of Pharma Cure Laboratories. Near Govt. High School, Garha, Jalandhar, Punjab, 144022, India. Phone: +918037303733
	For generic drugs (me-too status)	Gee-Sol 25% (Intravenous Infusion BP) of Gallop Water Sciences (404- Sundar Industrial Estate, Lahore Pakistan) (Reg # 080474)
	GMP status of the Finished product manufacturer	New DML issue dated w.e.f.13-02-2020. Last inspection conducted on 15-10-2020 & 16-10-2020 and report concludes that overall evaluation of inspection report rating is Good
	Section Approval Status	The CLB approved in its 273rd approved the grant of Drug Manufacturing License (by way of formulation) vide letter no.F.1-29/2013-Lic dated 13th February,2020 with the following three section: Large Volume Parenteral (LVP) general section Small Volume Parenteral (SVP) general section Ampoule LDPE (General) section
	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	Firm has submitted results of pharmaceutical equivalence for all the quality tests defined in BP for their product against the reference product 'Gee-Sol 25% Infusion by Gallop Water

		Sciences (404- Sundar Industrial Estate, Lahore Pakistan)	
	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)	25mL LDPE 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.	A	B	C
Batch Size	50 L	50 L	50 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)	Not applicable since it is a newly established license.	
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.	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	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:			

Shortcomings communicated	Response by the firm
Provide 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.

Firm provide the evidence of TGA Australia, detail of reference product is as under:

Name of Manufacturer	Active component and concentration in %	Pack size in ml
Baxter Glucose Infusion of Baxter Healthcare Pty Ltd 1 Baxter Drive OLD TOONGABBIE NSW 2146 AUSTRALIA	Glucose 5%	50,100,250,500&1000
	Glucose 10%	500&1000
	Glucose 25%	1000
	Glucose 50%	500
	Glucose 70%	500

25% Glucose is not present in 25ml pack size.

COA of drug substance from drug substance manufacturer include pyrogen test 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.	Firm has submitted the copy of COA of drug substance from drug product manufacturer in which the results of sterility test (including total bacterial/mold, total yeast count and E. coli test) and Bacterial Endotoxin test has been included.
COA of drug substance from drug substance manufacturer include pyrogen test and total bacterial/mold and yeast count test for confirmation of sterility of drug substance but the manufacturing method of drug substance did not include the step of sterilization.	The manufacturing method of drug substance did not include the step of sterilization by the vendor. As per DMF of Drug substance, the drug substance is nonsterile. And supporting documents are attached for total bacterial/mold and yeast count test of drug substance by drug product manufacturer. The evidence from the DMF of dextrose is also attached, which clearly stated that the Dextrose anhydrous non-sterile drug substance.
Evidence of availability of HPLC equipped with refractometer.	Firm has submitted copy of purchase order invoice of water HPLC along with refractive index detector as an evidence of availability of HPLC equipped with refractometer.
COA of reference standard of anhydrous glucose is submitted, 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	Firm has submitted that the COA of reference standard of Glucose anhydrous is submitted instead of Glucose Monohydrate erroneously by our analyst, hence we are submitting the COA of reference standard of Glucose Monohydrate.

<table>
<tr><td>reference standard for the assay.</td><td></td></tr>
<tr><td>Sterility test has not been performed during stability study of drug substance.</td><td>Firm has stated that Sterility test has not been performed of drug substance during the stability studies because the material is nonsterile as per DMF. Some microbial test was performed like BET test, total bacterial count, molds and yeasts count, E. Coli, mentioned in the COA of drug substance from drug substance manufacturer.</td></tr>
<tr><td>Provide the detail of composition of reference product against which pharmaceutical equivalence has been established.</td><td>Firm has provided details of the manufacturer of reference product used for pharmaceutical equivalence Ensol-25% (25ml) which is as under:
<table>
<tr><td rowspan="2">Component and quality standard (and grade, if applicable)</td><td rowspan="2">Function</td><td colspan="2">Strength (label claim)</td></tr>
<tr><td>Quantity per unit or per mL</td><td>%</td></tr>
<tr><td>Glucose Anhydrous</td><td>API</td><td>250mg/ml</td><td>25%</td></tr>
<tr><td>Water for injection</td><td>Solvent</td><td>q.s.*</td><td>N/A</td></tr>
</table>
The details of the manufacturer used for pharmaceutical equivalence for Ensol-25% (25mL) is given below.
Manufacturer Name: Gallop Water Sciences
(404- Sundar Industrial Estate, Lahore Pakistan)
Brand Name: Gee-Sol 25%
Batch No.: 9AJ038
Mfg Date: 09-2019
Exp. Date: 08-2021
Mfg Lic No.: 000817
REG No.: 080474</td></tr>
<tr><td>According to BP for sample preparation volume of infusion containing the equivalent of 2g to 5g of glucose should be taken, justification is required for taking volume of infusion containing 25g of glucose for sample preparation.</td><td>Firm has submitted the same verification report in which the same quantity of sample has been taken for preparation of different sample concentration in performance of accuracy parameter.</td></tr>
<tr><td>Perform specificity parameter and provide results along with raw data sheets.</td><td>Firm has submitted the following comparison table to verify the specificity parameter:
<u>Specificity of Ensol- 25% (Glucose Anhydrous)</u>
<table>
<tr><td>Sr. No.</td><td>Item</td><td>Specifications</td><td>Results</td></tr>
<tr><td>1</td><td>Blank (water)</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Not Complies</td></tr>
<tr><td>2</td><td>Glucose Standard</td><td>The solution prepared as directed in the assay is dextrorotatory.</td><td>Complies</td></tr>
<tr><td>3</td><td>Ensol- 10%</td><td>The solution</td><td>Complies</td></tr>
</table></td></tr>
</table>

	Sample	prepared as directed in the assay is dextrorotatory.		

Limit: The solution prepared as directed in the assay is dextrorotatory.

Submitted AMV report describe the same procedure for preparation of different sample concentration in performance of accuracy parameter.	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.
Scientific justification is required regarding the performance of stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH being a product packed in LDPE (semi permeable) container, while ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers.	Firm submitted the following reply: We performed stability studies at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH for our products packed in semi permeable containers instead of ICH guidelines recommend performing stability studies at 30°C ± 2°C / 35% ± 5%RH and 40°C ± 2°C / NMT 25% RH for products packed in semi permeable containers. We adopted alternative approach to studying at the reference relative humidity as recommended in the table given below (for either long term or accelerated testing) is performing the stability studies under higher relative humidity and deriving the water loss at the reference relative humidity through calculation. This can be achieved by experimentally determining the permeation coefficient for the container closure system.

Alternative relative humidity	Reference relative humidity	Ratio of water loss rates at a given temperature
60% RH	25% RH	1.9
60% RH	40% RH	1.5
65% RH	35% RH	1.9
75% RH	25% RH	3.0

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." • According to the BMR, the filled bottles was terminally sterilized on 25-07-2020, while the submitted stability data indicated that date of initiation of stability is 24-07-2020.Clarification is required in this regard.

Provide detail information regarding the manufacturing facility of Large volume Parenteral/small volume parenteral since you have applied for glucose intravenous infusion ranging in fill volume from 25 ml to 1000ml.

Firm has submitted copy of inspection report for grant of new DML held on 05-12-2019 &12-12-2019, in which it was verified that the firm had following manufacturing facility along with detail of machines and their capacity:

1. LVP Fully automated Blow Fill and Seal Weiler USA machine capacity of producing 500/1000ml bottles at 1000 bottles per hour
2. SVP Weiler USA Blow Fill and Seal machine capacity of producing 1625 bottles of 100ml per

hour

3. LDPE Ampoule Weiler USA Blow Fill and Seal machine capacity of producing 2900 ampoules of 5ml to 25ml per hour.
4. Separate cap sealing machine has been provided for each BFS.

Provide reference for the acceptance criteria of filled volume for applied drug product.

The reference for the acceptance criteria of filled volume for applied drug product is the general chapter of USP 1151. And the table is given below

	Recommended Excess Volume	
Labeled Size	For mobile liquids	For viscous liquid
0.5 ml	0.10 ml	0.12 ml
1 ml	0.10 ml	0.15 ml
2 ml	0.15 ml	0.25 ml
5 ml	0.30 ml	0.50 ml
10 ml	0.50 ml	0.70 ml
20 ml	0.60 ml	0.90 ml
30 ml	0.80 ml	1.20 ml
50ml or more	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

Firm has submitted the reply that, 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/850374/201)*

No such data has been provided by the firm, which justify the conditions used for autoclaving of product other than the conventional condition.

- Provide the evidence of reference product of dextrose infusion packed in LDPE plastic container.

Describe the container closure system for applied product in detail, what is the exact material of construction, grade and density of the LDPE material along with its certificate of analysis.

Firm provide the copy of COA of LDPE (Purell PE 3020D) resins of M/s. LyondellBasell, product description and properties are given as under:

Purell PE 3020D is a low-density polyethylene with high rigidity, good opticals and good chemical resistance. It is delivered in pellet form. The grade is used by our customers for small blow mouldings including packaging of pharmaceuticals in blow fill seal technology and injection moulding for medical devices, closures and seals.

Typical Properties	Nominal Value
Melt Flow Rate, (190 °C/2.16 kg)	0.3 g/10 min
Vicat Softening Temperature	102 °C
Peak Melting Point	114 °C
Recommended processing temperatures	170 °C to 220 °C

Decision: Deferred for clarification/justification from the firm regarding the commencement of stability study which was initiated before the terminal sterilization of drug product.

31.	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. 14886 dated 31/05/2021
	Details of fee submitted	PKR 20,000/- vide slip no. 2073486 dated 16/03/2021
	The proposed proprietary name / brand name	Famoscot dry suspension 40mg/5ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Famotidine 40mg
	Pharmaceutical form of applied drug	Off white colored granular powder which on reconstitution gives flavored suspension.
	Pharmacotherapeutic Group of (API)	Short-term treatment of active duodenal ulcer. Short-term treatment of active benign gastric ulcer. Short-term treatment of gastroesophageal reflux disease. Treatment of pathological hypersecretory conditions
	Reference to Finished product specifications	USP
	Proposed Pack size	60ML
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pepcid manufactured by Salix Pharmaceuticals Inc. MERCK SHARP & DOHME Pty., Ltd. South Granville, NSW, Australia 2142.
	For generic drugs (me-too status)	Sofem Dry Suspension Manufacture by Roryan pharmaceuticals industries. DRAP Registration no. 082573
	GMP status of the Finished product manufacturer	New license granted on 17/12/2020 Suspension section approved.
	Name and address of API manufacturer.	NAME: Vaasavaa Pharmaceuticals Pvt. Limited, SITE OF MANUFACTURE: Plot no. C-216, MIDC-Chincholi, Solapur-413 255, Maharashtra, Ph: 02172357176 Contact person: Mr.K.M.K.Prasad/Mr.P.Narashima Rao Email: vaasavaa@yahoo.com OFFICE ADDRESS : Plot No. 623, Pent House, Vivekananda Nagar, Kukatpally, Hyderabad-500072, Telefax: 040-23061183, Contact Person: Mr. M. Subba Rao, Email: vaasavaa@yahoo.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 Famotidine 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: Long term: 30˚C ± 2˚C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 60 months Batches: FM-IV/05/001, FM-IV/05/005, FM IV/05/002)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its Validation /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 that is Sofem Dry Suspension by Roryan Pharmaceuticals industries performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form.) Reg.no.082573
	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: Vaasavaa Pharmaceuticals Pvt. Limited, SITE OF MANUFACTURE: Plot no. C-216, MIDC-Chincholi, Solapur-413 255, Maharashtra, Ph: 02172357176 Contact person: Mr.K.M.K.Prasad/Mr. P.Narashima Rao Email: vaasavaa@yahoo.com OFFICE ADDRESS: Plot No. 623, Pent House, Vivekananda Nagar, Kukatpally, Hyderabad-500072, Telefax: 040-23061183, Contact Person: Mr. M. Subba Rao, Email: vaasavaa@yahoo.com
API Lot No.	FAM-0120012 (Batch no.)
Description of Pack (Container closure system)	Pet bottles
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: 0,1, 2, 3, 4, 6 (Months) Long term: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	300 Bottles	300 Bottles	300 Bottles
Manufacturing Date	03/2020	03/2020	03/2020
Date of Initiation	06/03/2020	06/03/2020	06/03/2020
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. 6094634 issued by Food & Drugs Administration (Maharashtra state) Issue & Valid Upto Dt: 16/07/2020 – 15/07/2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Clearance certificate and commercial invoice attested by concerned officer of (I&E) DRAP dated 18/02/2020.
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 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	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.

Remarks of Evaluator:

Evidence of approval of manufacturing facility / Approved Section from Licensing Authority Dry powder suspension section has not been mentioned in the GMP certificate submitted along with the dossier. Section approval letter of dry powder suspension issued by Licensing Division is required.	Firm submitted the copy of panel inspection report, held for regularization of revised layout and grant of renewal of License on 17-11-2018 & 22-11-2018 in which it was endorsed that firm has Dry powder Suspension (general section).
Executed Production Documents: 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.	Firm has submitted the copy of filled BMR of all the batches of drug product for which stability studies data is provided. Weight of powder filled per bottle of 60ml has not been mentioned in the BMR.
Validation of analytical procedures Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Firm has submitted the analytical method verification studies data of drug substance performed by drug product manufacturer, in which the result of all three parameters has been given.
Batch analysis Provide results of analysis of relevant batches 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.	Firm has submitted the Batch analysis report of drug substance performed by drug product manufacturer, in which all the quality test has been performed as per USP.
Description of accompanying reconstitution diluent(s) Provide information including type of diluent, its composition, quantity or volume which is to be	Firm has submitted the specimen of label of bottle on which it is mentioned that 46ml of boiled water has been added in the bottle for 60ml pack size of Famotidine for

provided along with the applied drug. As it is mentioned in the method of preparation of suspension written on inner carton that "Put the premium hygienic water given in the pack to reconstitute the suspension".	oral suspension containing 480mg famotidine per 60ml. While, the innovator product Pepcid (Famotidine) for oral suspension contain 400mg famotidine per 50ml bottle and for reconstitution, 46ml of purified water is added to obtained the concentration of 40mg/5ml famotidine.
Compatibility studies of dry powder for suspension with its diluent shall be performed as per the instructions provided in individual label of the drug product and submit the obtained results.	Firm has not submitted the data of compatibility studies with its diluent.
Detailed analytical procedure as per USP monograph of famotidine for oral suspension is required.	Firm has submitted the analytical procedure of drug product as per USP.
Provide certificate of analysis of reference standard /working standard used for testing of the product.	Firm provided the certificate of analysis of USP reference standard of famotidine.
In-use stability studies of reconstituted suspension is required along with proposed in-use storage statement and in-use shelf-life. Firm performed the in-use stability studies of reconstituted suspension at room temperature for 14 days (proposed shelf life).	
Discussion: The Board was apprised that the innovator product i.e Pepcid for suspension approved by USFDA has used 46ml of purified water for reconstitution of 400mg of Famotidine powder for suspension to attain the final concentration of 40mg/5ml while the applicant has used same volume of diluent (i.e 46ml) for reconstitution of 480mg of Famotidine. The final reconstituted concentration is 40mg/5ml which cannot be attained by using the volume of diluent used by the applicant. **Decision: Registration Board after thorough deliberation decided to deferred the case for clarification/justification of using 46ml of diluent for reconstitution of the drug product containing 480mg of Famotidine per bottle.**	

32.	Name and address of manufacturer / Applicant	M/s. Allmed (Private) Limited Plot no.590 Sundar Industrial Estate, Lahore
	Brand Name +Dosage Form + Strength	Bioral Concentrate for solution for infusion 50mg/ml
	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No.5134 dated 11/06/2012 Rs.8,000/- (photocopy) R&I verified Differential fee (photocopy) of Rs.12,000/- submitted on 11/10/2012 Dy.No.7940 R&I verified
	Composition	Each Ampoule contains: Cyclosporin ….50mg/ml
	Pharmacological Group	Immunosuppressant
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1ml and 5ml ampoule, As per S.R. O
	Approval Status of Product in Reference Regulatory Authorities	USFDA approved (Sandimmune® Injection (cyclosporine injection, USP) is available in a 5 mL sterile ampul for intravenous (IV) administration.)
	Me-too Status	Cyclocon Injection of M/s. Pharmedic Pharmaceutical Industries
	GMP Status	GMP Inspection report dated 01-01-2020 concluded with the following remarks: Firm M/s. Allmed (pvt.) Ltd., Lahore was GMP compliant on the day of inspection. Firm has Liquid Injectable Ampoule Section (general) as evident from the aforesaid GMP inspection report.
	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. • Firm applied for pack size of 5ml and 1ml ampoule in the single registration dossier.

	Decision of 312th meeting of Registration Board	Deferred for submission of evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm OR else application on Form 5-D along with submission of differential fee and stability study data as per the requirements of 293rd meeting of registration Board.
	Reply of the firm	Firm has submitted evidence of Me-Too registered in Pakistan detail are as under: Cyclocon Injection of M/s. Pharmedic Pharmaceutical Industries (Reg.no. 024074) Each 5ml contains: cyclosporin….250mg (50mg/ml)
	Decision: Approved with innovator's specification. Moreover, 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.	
33.	Name and address of manufacturer / Applicant	M/s. Allmed (Private) Limited Plot no.590 Sundar Industrial Estate, Lahore
	Brand Name +Dosage Form + Strength	Nephrotec Infusion (500ml)
	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No.3812 dated 24/03/2011 Rs.8,000/- (photocopy) R&I verified Differential fee (photocopy) of Rs.12,000/- submitted on 11/10/2012 Dy.No.7327 R&I verified
	Composition	Each vial contains: L-Lysine Acetate….5.005gm L-Histidine….2.15gm L-Isoleucine….2.55gm L-leucine…5.15gm L-Methionine….1.4gm L-Phenylalamine….1.9gm L-Threonine….2.4gm L-Tryptophan…0.95gm L-Valine….3.1gm L-Arginine…2.45gm L-Alanine….3.15gm L-Proline…2.15gm L-Serine…2.25gm Acetylcysteine…0.25gm
	Pharmacological Group	Amino acids
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack Size & Demanded Price	As per S.R. O
	Approval Status of Product in Reference Regulatory Authorities	Approved in DMDI (Germany) (Nephrosterile Infusion) 1000 ml infusion solution contain: Isoleucine 5.10 g Leucine 10.30 g Lysine acetate eq to Lysine 7.1 g Methionine 2.80 g Acetylcysteine eq. to Cysteine 0.37 g Phenylalanine 3.80 g Threonine 4.80 g Tryptophan 1.90 g Valine 6.20 g Arginine 4.90 g Histidine 4.30 g Glycine 3.20 g Alanine 6.30 g Proline 4.30 g

		Serine 4.50 g L-malic acid 1.50 g Acetic acid 99% 1.38 g
	Me-too Status	Nephrosterile Infusion of M/s. Fresenius Kabi Pakistan (Reg.no.095879)
	GMP Status	GMP Inspection report dated 01-01-2020 concluded with the following remarks: Firm M/s. Allmed (pvt.) Ltd., Lahore was GMP compliant on the day of inspection. Firm has Liquid Injectable Ampoule Section (general) as evident from the aforesaid GMP inspection report.
	Remarks of the Evaluator.	Applied formulation is different from the reference formulation, so correction is required accordingly. Section approval for large volume parental (LVP) is required.
	Decision of 312th meeting of Registration Board	Deferred for revision of formulation as per reference product along with the requisite fee, revised Form-5, master formulation and outline of method of manufacturing.
	Reply of the firm	Firm has revised the formulation as per the reference product along with fee of Rs.30,000/- vide slip no. 0483390971 dated 04-11-2021.Detail of composition is as under: 1000 ml infusion solution contain: L-Isoleucine 5.10 g L-Leucine 10.30 g L-Lysine Monoacetate 10.1g eq to Lysine 7.1 g L-Methionine 2.80 g Acetylcysteine eq. to L-Cysteine 0.37 g L-Phenylalanine 3.80 g L-Threonine 4.80 g L-Tryptophan 1.90 g L-Valine 6.20 g L-Arginine 4.90 g L-Histidine 4.30 g Glycine (Amino acetic acid) 3.20 g L-Alanine 6.30 g L-Proline 4.30 g L-Serine 4.50 g L-malic acid 1.50 g Glacial Acetic acid 99% 1.38 g • For evidence of having Large volume parenteral section, firm submitted the copy of transfer of registration letter of product Maxon (Moxifloxacin) Infusion 400mg/250ml Reg.no. 062620 registered in their name dated 21, june,2011 vide letter no. F.13-8/2011-R-V.
	Decision: Approved with innovator's specification.	
34.	Name and address of manufacturer / Applicant	M/s Jawa Pharmaceuticals Pvt Ltd 112/10, Quaid-e-Azam Industrial Area, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Fusdic-B Cream
	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No. 5249 dated 11/05/2011 Rs.8,000/- (photocopy fee challan) Dy. No. dated 10/12/2015 Rs.12,000/- (photocopy fee challan) (Receipt of application verified by R&I)
	Composition	Each gram contains: - Fusidic Acid ……. 20mg Betamethasone Valerate …. 1mg
	Pharmacological Group	Antibacterial & Corticosteroid
	Type of Form	Form-5
	Finished Product Specification	Manufacturer Specification

	Pack Size & Demanded Price	5gm & 15gm
	Approval Status of Product in Reference Regulatory Authorities	Fucibet ® Lipid Cream contains the active ingredients fusidic acid 2% (20mg/g) and betamethasone 0.1% (1mg/g), as betamethasone valerate.
	Me-too Status	Baxidin B Cream, Baxter Pharmaceuticals, Reg. No. 067597.
	GMP Status	Panel inspection for renewal of DML conducted on 15-12-2020,16-12-2020,26-01-2021 concluded with the following remarks: "The panel recommends the renewal of Drug Manufacturing License to M/s. Jawa Pharmaceuticals (Pvt.) Ltd., Lahore by way of formulation"
	Remarks of the Evaluator.	• Applied formulation is different from the reference product. Quantity of betamethasone valerate used in the reference product is betamethasone 1mg as betamethasone valerate while in the applied formulation quantity of betamethasone valerate is 1mg. • Separate dispensing booth is available for steroid products dispensing according to the panel inspection report dated 15-12-2020,16-12-2020,26-01-2020.
	Decision of 308th meeting of Registration Board	Deferred for the revision of formulation as per the reference product i.e. Betamethasone 1mg as betamethasone valerate along with submission of applicable fee, revised Form-5, master formulation and manufacturing method.
	Reply of the Firm	Firm has revised the formulation as per reference product i.e. Fusidic acid…20mg + Betamethasone valerate eq. to Betamethasone 1mg along with fee of Rs.7500/- vide slip no. 01682345272 dated 29/09/2021 and requisite documents.
	Decision: Approved with innovator's specification.	
35.	Name and address of manufacturer / Applicant	M/s Jawa Pharmaceuticals Pvt Ltd 112/10, Quaid-e-Azam Industrial Area, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Betavat Cream
	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No. 5281 dated 11/05/2011 Rs.8,000/- (photocopy fee challan) Dy. No. dated 16/12/2015 Rs.12,000/- (photocopy fee challan) (Receipt of application verified by R&I)
	Composition	Each gram contains: - Betamethasone Valerate BP ……. 1mg
	Pharmacological Group	Corticosteroid
	Type of Form	Form-5
	Finished Product Specification	BP
	Pack Size & Demanded Price	5gm & 15gm
	Approval Status of Product in Reference Regulatory Authorities	Audavate 0.1% w/w Cream (One gram of cream contains 1 mg of betamethasone (0.1% w/w) as valerate) (Emc approved)
	Me-too Status	Betnovate Cream by GSK Pharma (Reg#000256)
	GMP Status	Panel inspection for renewal of DML conducted on 15-12-2020,16-12-2020,26-01-2021 concluded with the following remarks: "The panel recommends the renewal of Drug Manufacturing License to M/s. Jawa Pharmaceuticals (Pvt.) Ltd., Lahore by way of formulation"
	Remarks of the Evaluator.	• Applied formulation is different from the reference product. Quantity of betamethasone valerate used in the reference product is betamethasone 1mg as betamethasone valerate while in the applied formulation quantity of betamethasone valerate is 1mg. • Separate dispensing booth is available for steroid

		products dispensing according to the panel inspection report dated 15-12-2020,16-12-2020,26-01-2020.
	Decision of 308th meeting of Registration Board	Deferred for the revision of formulation with reference to quantity of Betamethasone as per the reference product i.e. Betamethasone 1mg as betamethasone valerate along with submission of applicable fee, revised Form-5, master formulation and manufacturing method.
	Reply of the Firm	Firm has revised the formulation as per reference product i.e. Betamethasone valerate eq. to Betamethasone 1mg along with fee of Rs.7500/- vide slip no. 4251163006 dated 29/09/2021 and requisite documents.
	Decision: Approved with BP specification.	
36.	Name and address of manufacturer / Applicant	M/s Jawa Pharmaceuticals Pvt Ltd 112/10, Quaid-e-Azam Industrial Area, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Betavat-N Cream
	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No.5261 dated 11/05/2011 Rs.8,000/- (Photocopy fee challan) Dy. No. dated 16/12/2015 Rs.12,000/- (Photocopy fee challan) (Receipt of application verified by R&I)
	Composition	Each gram contains: - Betamethasone Valerate ……. 1mg Neomycin Sulphate ……. 5mg
	Pharmacological Group	Antibacterial & Corticosteroid
	Type of Form	Form-5
	Finished Product Specification	Manufacturer Specification
	Pack Size & Demanded Price	5gm & 15gm
	Approval Status of Product in Reference Regulatory Authorities	Betamethasone valerate/Neomycin Sulphate 1mg/5mg cream of Essential generics (MHRA Approved)
	Me-too Status	Betasone-N cream of M/s. Sharex Laboratories (Reg.no. 009062)
	GMP Status	Panel inspection for renewal of DML conducted on 15-12-2020,16-12-2020,26-01-2021 concluded with the following remarks: "The panel recommends the renewal of Drug Manufacturing License to M/s. Jawa Pharmaceuticals (Pvt.) Ltd., Lahore by way of formulation".
	Remarks of the Evaluator.	• Applied formulation is different from the reference product. Quantity of betamethasone valerate used in the reference product is betamethasone 1mg as betamethasone valerate while in the applied formulation quantity of betamethasone valerate is 1mg. • Separate dispensing booth is available for steroid products dispensing according to the panel inspection report dated 15-12-2020,16-12-2020,26-01-2020.
	Decision of 308th meeting of Registration Board	Deferred for the revision of formulation with reference to quantity of Betamethasone as per the reference product i.e. Betamethasone 1mg as betamethasone valerate along with submission of applicable fee, revised Form-5, master formulation and manufacturing method.
	Reply of the Firm	Firm has revised the formulation as per reference product i.e. Betamethasone valerate eq. to Betamethasone 1mg+Neomycin Sulphate 5mg along with fee of Rs.7500/- vide slip no. 1680637275 dated 29/09/2021 and requisite documents.
	Decision: Approved with innovator's specification.	
37.	Name and address of manufacturer / Applicant	M/s Jawa Pharmaceuticals Pvt Ltd 112/10, Quaid-e-Azam Industrial Area, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Flunide-N Cream

	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No. 5255 dated 11/05/2011 Rs.8,000/- (photocopy fee challan) Dy. No. dated 16/12/2015 Rs.12,000/- (photocopy fee challan) (Receipt of application verified by R&I)
	Composition	Each gram contains: - Fluocinolone Acetonide ……. 0.25mg (0.025%) Neomycin Sulphate ……. 3250 IU
	w/w	Antibacterial & Corticosteroids
	Type of Form	Form-5
	Finished Product Specification	USP
	Pack Size & Demanded Price	5gm, 15gm & 30gm
	Approval Status of Product in Reference Regulatory Authorities	Approved in USFDA (FLUOCINOLONE ACETONIDE; NEOMYCIN SULFATE) (0.025%; EQ 3.5MG BASE/GM)
	Me-too Status	Synalar-N Cream by Mass Pharma (Reg No.002511)
	GMP Status	Panel inspection for renewal of DML conducted on 15-12-2020,16-12-2020,26-01-2021 concluded with the following remarks: "The panel recommends the renewal of Drug Manufacturing License to M/s. Jawa Pharmaceuticals (Pvt.) Ltd., Lahore by way of formulation"
	Remarks of the Evaluator.	Applied formulation is not as per the reference formulation approved in USFDA Separate dispensing booth is available for steroid products dispensing according to the panel inspection report dated 15-12-2020,16-12-2020,26-01-2020.
	Decision of 308th meeting of Registration Board	Deferred for revision of formulation as per the reference product i.e. Each gram contains: Fluocinolone Acetonide…0.025% and Neomycin Sulphate eq. to 3.5mg base/gm along with submission of applicable fee, revised Form-5, master Formulation and manufacturing method.
	Reply of the Firm	Firm has revised the formulation as per reference product i.e. Each gram contains: Fluocinolone Acetonide…0.025% and Neomycin Sulphate eq. to 3.5mg base/gm along with fee of Rs.7500/- vide slip no. 1680637275 dated 29/09/2021 and requisite documents.
	Decision: Approved with USP specification.	
38.	Name and address of manufacturer / Applicant	M/s Jawa Pharmaceuticals Pvt Ltd 112/10, Quaid-e-Azam Industrial Area, Kot Lakhpat, Lahore
	Brand Name +Dosage Form + Strength	Clinaderm Gel
	Diary No. Date of R& I & fee	(Duplicate Dossier) Dy. No.5283 dated 11/05/2011 Rs.8,000/- (photocopy fee challan) Dy. No. dated 16/12/2015 Rs.12,000/- (photocopy fee challan) (Receipt of application verified by R&I)
	Composition	Each Gram contains: - Clindamycin Phosphate …… 10mg
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished Product Specification	USP
	Pack Size & Demanded Price	10gm, 15gm & 20gm, As per SRO
	Approval Status of Product in Reference Regulatory Authorities	CLEOCIN T Topical Gel contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per gram of Pfizer (USFDA Approved)
	Me-too Status	Acsolve Gel by Atco Laboratories (Reg No.067527)
	GMP Status	Panel inspection for renewal of DML conducted on 15-12-2020,16-12-2020,26-01-2021 concluded with the following remarks:

		"The panel recommends the renewal of Drug Manufacturing License to M/s. Jawa Pharmaceuticals (Pvt.) Ltd., Lahore by way of formulation"
	Remarks of the Evaluator.	Applied formulation is not according to the reference product i.e. each gram contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per gram. While the applied formulation contains clindamycin phosphate 10mg According to the above said inspection report the firm has cream/ointment section.
	Decision of 308th meeting of Registration Board	Deferred for revision of formulation as per the reference product i.e. each gram contains clindamycin phosphate at a concentration equivalent to 10 mg clindamycin per gram while the applied formulation contains clindamycin phosphate 10mg along with submission of requisite fee, revise Form-5, master formulation and manufacturing method.
	Reply of the firm	Firm has revised the formulation as per reference product i.e. Gel contains Clindamycin phosphate equivalent to 10mg clindamycin per gram along with fee of Rs. 7,500/- vide slip no. 19228160 Dated 29/09/2021 and requisite documents.
	Decision: Approved with USP specification.	

Agenda of Evaluator PEC-I

Registration application of priority molecules:

Assistant Director (I&E) (QA&LT) vide letter No 05-12/2021 I&E dated 16-08-2021 informed that Authority in its 111th meeting decided as follows:

"A list be prepared by I&E section and be presented to the Registration Board for its consideration to register these drugs on priority"

In light of decision of Authority, Assistant Director (I&E) (QA&LT) has also forwarded list of unregistered / not-available drugs for necessary action.

Accordingly, following applications from above list are presented before the Registration Board for its consideration, please:

39.	Name, address of Applicant / Importer	M/s Lab Diagnostic Systems Pvt Ltd 111-B Hali Road Westridge 1 Cantt District Rawalpindi.
	Details of Drug Sale License of importer	License No: 01-374-0176-041296D Address: 111-B Hali Road Westridge 1 Cantt District Rawalpindi. Address of Godown: NA Validity: 07-03-2023. Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	NAPROD LIFE SCIENCES PVT. LTD., **Factory:** G-17/1, M.I.D.C. Tarapur industrial area, Boisar, dist – thane – 401506 Maharashtra state, India **Office:** 304, town centre, Andheri kurla road, andheri (east), Mumbai – 400 059 India.
	Name, address of manufacturer(s)	NAPROD LIFE SCIENCES PVT. LTD., **Factory:** G-17/1, M.I.D.C. Tarapur industrial area, Boisar, dist – thane – 401506 Maharashtra state, India **Office:** 304, town centre, Andheri kurla road, andheri (east), Mumbai – 400 059 India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate) • Firm has submitted legalized copy of CoPP certificate (No. COPP/CERT/ KD/85896/ 2019/11/28425/146234) dated 13-06-2019 issued by Food and Drug Administration Mahrashtra Estate Mumbai valid till 03/04/2022 for Dacarbazine for Injection USP 200 mg. 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.	
	Details of letter of authorization / sole agency agreement Firm has submitted copy of letter of distribution certificate from Naprod Life Sciences Pvt. Ltd. The letter specifies that M/s Lab Diagnostic Systems Pvt Ltd. Is authorized for registration of the applied product in Pakistan. The authorization letter is valid till 11-04-2024.	
	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 ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 5668: 09-05-2019
	Details of fee submitted	PKR 50,000/-: 09-05-2019
	proposed proprietary name / brand name	Dacarbazine for IV Injection 200mg
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains Dacarbazine (As Dacarbazine citrate, formed in-Situ)...200mg
	Pharmaceutical form of applied drug	A white to yellowish white lyophilised mass for solution for IV injection
	Pharmacotherapeutic Group of (API)	L01AX04 – Dacarbazine
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	650/- per single dose vial
	The status in reference regulatory authorities	Dacarbazine lipomed 200 mg **(HPRA** Approved).
	For generic drugs (me-too status)	Dacarb-200 Injection (registration number 052260) for A.J. Mirza Pharma 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 validation (for drug substance and for impurities), batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Mac Chem Products (India) Pvt. Ltd. 304, Town Centre, Andheri - Kurla Road, Andheri (East), Mumbai–400059, 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)	• Accelerated stability studies have been conducted at 25ºC±2 and 60%RH±5% for 6 months of 3 batches • Real time stability studies have been conducted at 5ºC±3 for 24 months of 3 batches Batch size: DAC0211010, DAC0211011, DAC0211012
	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. The product is stable for 8hours when reconstituted with WFI (20ml) stored at 30ºC. Further dilution with 0.9% sodium chloride/5% Dextrose, the solution is stable for 8 hours when store at 30ºC.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is established against Dacarbazine Lipomed 200mg by M/s Lipomed UK by performing all the quality tests.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Dacarbazine for Injection USP 200 mg/vial is packed in 20 ml 20 mm Amber Type –I vial with 20 mm Grey Bromo Butyl Slotted Rubber Stopper & Aluminium Seal.
	Stability study data of drug product, shelf life and storage conditions	• Accelerated stability studies have been conducted at 25ºC±2 and 60%RH±5% for 6 months of 3 batches • Real time stability studies have been conducted at 5ºC±3 for 24 months of 24 batches Batch size: NN0268, NN0193, K10079, NN5001

Evaluation by PEC:

- Initially the firm has submitted the application for registration on form 5A along with PKR 50,000/- fee. Later one, upon communication, the firm submitted complete Form 5F along with the annexures vide diary No. 19150 dated 08/07/2021.
- The firm has submitted long term stability studies at 5ºC±3ºC while the reference product (MHRA & Ireland approved product) are stable at 25ºC.
- Pharmaceutical equivalence not provided
- **Reconstitution:**
  Under aseptic conditions, the contents of one vial of Dacarbazine Injection 200 mg is first dissolved with 20 ml of water for injections. The density of the solution is 1.007 g/ml. This freshly prepared solution, containing 10 mg/ml of dacarbazine, can be administered by slow intravenous injection.

In order to prepare an intravenous infusion solution, the solution has to be further diluted in 200 – 300 ml sodium chloride solution or glucose 5%. The solution is given as a short term infusion over a period between 15 and 30 minutes (MHRA, HPRA Ireland).

Decision: The Board was apprised that Dacarbazine 200mg for injection by M/s Hikma is approved by USFDA (ANDA-075812) with storage conditions to 2° to 8°C. The Board after thorough deliberation, decided to approve the case as per Policy for inspection of Manufacturer abroad and verification of local storage facility. Furthermore, the Board directed the firm to maintain the cold chain storage strictly during transportation.

Agenda of Evaluator PEC-VI:

40.	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 Stallion Pharmaceuticals (pvt.) Ltd. 581-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 11273 , dated 13/04/2021
	Details of fee submitted	PKR 50,000/-: dated 08/06/2020
	proposed proprietary name / brand name	ZOBAC 4.5g Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Piperacillin (as piperacillin sodium)……..4gm Tazobactam (as Tazobactam sodium)…….0.5gm (USP Specification)
	Pharmaceutical form of applied drug	Powder for Injection White or almost white colored dry powder for injection filled in 20ml glass vial with rubber stopper and aluminum seal
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's & 5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zosyn injection 4.5g by M/s Pfizer injectables , USFDA Approved.
	For generic drugs (me-too status)	Tanzo injection 4.5g by M/s Bosch Pharmaceuticals, R.No.039439
	GMP status of the Finished product manufacturer	License granted on 22/09/2020 Dry powder injectable (carbapenem) section approved.
	Name and address of API manufacturer.	Shandong Anxin Pharmaceutical CO. LTD (Previously Qilu Tianhe Pharmaceutical CO. LTD Address : 849, Dongjia town, Licheng district, Jinan, 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 Piperacillin & Tazobactam are 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,B,C,D,E,F,J & 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% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (HF7001D1, HF7002D2, HF7003D3)
	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 TANZO 4.5g sterile dry powder injection by M/s Bosch Pharmaceuticals by performing quality tests (Description, Ph, water content, reconstitution time, clarity of solution, endotoxin, sterility test & assay). CDP is Not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA

Manufacturer of API	Shandong Anxin Pharmaceutical CO. LTD (Previously Qilu Tianhe Pharmaceutical CO. LTD		
API Lot No.	KA1007150022		
Description of Pack (Container closure system)	20ml glass vial with rubber stopper and aluminum 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 1, 2,3,4,5,6 (Months) Real Time: 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	P5001	P5002	P5003
Batch Size	8600 Vials	8600 Vials	10630 Vials
Manufacturing Date	03-2015	03-2015	04-2015
Date of Initiation	-	-	-
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. 2018001 issued by PEOPLE'S REPUBLIC OF CHINA valid till 24/07/2023.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has imported PIPERACILLIN (as piperacillin sodium) TAZOBACTAM (as Tazobactam sodium) manufactured by SHANDONG ANXIN PHARMACEUTICAL CO. LTD (Previously Qilu Tianhe Pharmaceutical CO. LTD) through invoice number SL150202- Z dated: 04-02-2015 duly verified by ADC on dated 09-02-2015.
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)
Remarks OF Evaluator:		
Decision: Approved. • **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.** • **Manufacturer will perform process validation of first three batches of both products as per the commitment submitted in the registration application.**		
41.	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 Stallion Pharmaceuticals (pvt.) Ltd. 581-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 11274 dated 13/04/2021
	Details of fee submitted	PKR 50,000/-: dated 08/06/2020
	proposed proprietary name / brand name	ZOBAC 2.25g
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Piperacillin (as piperacillin sodium)……..2gm Tazobactam (as Tazobactam sodium)…….0.25gm (USP Specification)
	Pharmaceutical form of applied drug	Powder for Injection White or almost white colored dry powder for injection filled in 20ml glass vial with rubber stopper and aluminum seal
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP

	Proposed Pack size	1's & 5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zosyn injection 2.25g by M/s Pfizer injectable , USFDA Approved.
	For generic drugs (me-too status)	Tanzo injection 2.25g by M/s Bosch Pharma Reg. No. 039593
	GMP status of the Finished product manufacturer	GMP License granted on 22/09/2020 Dry powder injectable (carbapenem) section approved.
	Name and address of API manufacturer.	Shandong Anxin Pharmaceutical CO. LTD (Previously Qilu Tianhe Pharmaceutical CO. LTD Address : 849, Dongjia town, Licheng district, Jinan, 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 Piperacillin & Tazobactam are 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,B,C,D,E,F,J & 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% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (HF7001D1, HF7002D2, HF7003D3)
	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 TANZO 2.25 sterile dry powder injection by M/s Bosch Pharmaceuticals by performing quality tests (Description, Ph, water content, reconstitution time, clarity of solution, endotoxin, sterility test & 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	Shandong Anxin Pharmaceutical CO. LTD (Previously Qilu Tianhe Pharmaceutical CO. LTD
API Lot No.	KA1007150022
Description of Pack (Container closure system)	20ml glass vial with rubber stopper and aluminum 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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 1, 2,3,4,5,6 (Months) Real Time: 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	N5001	N5002	N5003
Batch Size	4250 Vials	4160 Vials	6380 Vials
Manufacturing Date	03-2015	03-2015	04-2015
Date of Initiation	-	-	-
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. 2018001 issued by PEOPLE'S REPUBLIC OF CHINA valid till 24/07/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has imported PIPERACILLIN (as piperacillin sodium) TAZOBACTAM (as Tazobactam sodium) manufactured by SHANDONG ANXIN PHARMACEUTICAL CO. LTD (Previously Qilu Tianhe Pharmaceutical CO. LTD) through invoice number SL150202- Z dated: 04-02-2015 duly verified by ADC on dated 09-02-2015.
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)

S.No	Sections	Observations/Deficiencies/Shortcoming	Response
A	1.6.5	Valid GMP Certificate of Product & API manufacturer are required.	Submitting Valid GMP Certificate of Product & API.
B	2.3. P.2.6	Compatibility studies for the dry powder for injections & dry powder for suspensions shall be performed as per the instructions provided in individual label of the drug product.	WFI Compatibility checked with FPP Batch in which the API from Qilu China Pharma is used and the results are found satisfactory and diluent (WFI) from Shahzaib pharma is compatible with product of above said vendor API.
C	2.3. P.3.2	Justify the theoretical quantity of 4.7056gm per vial of Piperacillin sodium + Tazobactam Sodium	Detailed Calculation is submitted to justify the theorical quantity of 4.7056gm per vial of Piperacillin sodium + Tazobactam Sodium.
D	3.2. S.2	Details of any buffer or stabilized added in the drug substance has not been provided.	In the manufacturing process of API, Sodium bicarbonate is used by Shandong Anxin China the sodium bicarbonate is not buffer or stabilizer it is used for salification with Piperacillin acid & Tazobactam acid & made the product to salification status and can be used for medical purpose
E	3.2.P.1(c)	Provide information including type of diluent, its composition, quantity or	Certificate of analysis of WFI is provided along with details of approvals.

		volume, specification (as applicable) & regulatory status in Pakistan (as applicable) for the diluent which is to be provided along with the applied drug.	
F	3.2. P.2.3	The selection & optimization of the manufacturing process described in 3.2. P.3.3, in particular its critical aspects, shall be explained. Any specific manufacturing process development shall be provided e.g. sterilization shall be explains & justified. Where relevant, justification for the selection of aseptic processing or other sterilization methods over terminal sterilization shall be provided.	Complete manufacturing process is submitted.
H	3.2. P.5.2	Evidence of availability of HPLC with refrigerated autosampler (with temperature range of 5 $\pm$ 3°) shall be submitted.	Evidence has been submitted.
J	3.2. P.8	Documents for the procurement of API with approval from DRAP is required.	Submitting Procurement document along with COA.

Remarks OF Evaluator:

Decision: Approved.

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

42.	Name, address of Applicant / Marketing Authorization Holder	M/s Cherwel Pharmaceuticals (Pvt.) Ltd., Plot # 20, Phase 4, Hattar Industrial Estate, Hattar KPK.
	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)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11387; dated 14-4-2021.
	Details of fee submitted	PKR 50,000/-: dated 24-02-2021.
	The proposed proprietary name / brand name	Ketora 30mg Injection IM/IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1ml ampoule contains: Ketorolac Tromethamine …….. 30mg
	Pharmaceutical form of applied drug	Clear colorless liquid filled in glass ampoule
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	Innovator's Specifications.
	Proposed Pack size	1ml x 5's
	Proposed unit price	As per SRO.

	The status in reference regulatory authorities	US FDA approved.
	For generic drugs (me-too status)	Tekac 30mg/ml Injection, Sami Pharma, Reg. No. 092855.
	GMP status of the Applicant.	GMP certificate issued on 26-03-2019 on the basis of inspection conduct 04-02-2019.
	GMP status of the Finished product manufacturer	GMP certificate issued on 21-05-2019 on the basis of inspection conduct 23-4-2019, valid up to 22-04-2022.
	Evidence of section approval of the Finished product manufacturer.	Liquid ampoule (from GMP certificate.) Ampoule general vide letter No. F. 1-12/89-Lic (Vol-II) dated 23-07-2012.
	Name and address of API manufacturer.	M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab 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, 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 60 months. (Batch No. KTM06130016, KTM06130017 & KTM06130018)
	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	Firm has performed pharmaceutical equivalence against the product Toradol Ampoule 30mg, B. No. C2436, Mfg. date 01, 2020 by Barrett Hodgson by performing quality tests (Description, Identification, pH, Assay, Sterility, Bacterial endotoxin.)
	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. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India		
API Lot No.	KM-0100918, KTM-180015 & KTM180015.		
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: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	A-439	A-596	A-611
Batch Size	46,200 Ampoules	16,000 Ampoules	33,000 Ampoules
Manufacturing Date	05-2018	03-2019	03-2019
Date of Initiation	25-06-2018	22-04-2019	20-05-2019
No. of Batches	03		

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. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India. Valid till 25-06-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice# SCL2018/18-19 dated 29-01-2019.
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 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)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Sr.#	Section#	Observations	Firm's Response
1	1.5.6	Official monograph is available in USP. Firm has claimed innovator's specifications in "1.5.6" section of form 5F.	Firm has provided new Form 5F wherein they have revised their specifications from innovator's specifications to USP specifications without submission of applicable fee.

2	1.4.3	Number of approved sections of the applicant and total number of approved registered products on contract basis could not be confirmed.	As per submitted details, the applicant has 02 approved sections and 10 registered products on contract basis.
3	1.6.5	Valid GMP certificate of API manufacturer issued by regulatory body of country shall be submitted.	Valid GMP certificate of API manufacturer is provided. Valid till 25-06-2023.
4	3.2. S.4	• Results of analysis of relevant batch(es) of drug substance performed by drug product manufacturer used during product development and stability studies along with COA of the same batch from drug substance/Active Pharmaceutical ingredient manufacturer. • Detailed analytical procedure for the drug substance by the drug product manufacturer shall be provided. • Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the drug product 5manufacturer shall be submitted.	Batch No. A-439 has been manufactured by API lot No. KM-0100918 while COA has only been submitted for API Lot No. KTM-180015 Submitted. Firm has submitted analytical method verification studies but chromatograms for finished product has been submitted.
5	3.2. P.8.1	ADC attested invoices of the drug substance used during product development and stability studies shall be submitted.	ADC attested invoice for API Lot No. KM-0100918 used in Batch No. A-439 has not been provided by the firm.
6	3.2. P.2.1	Justification of not performing terminal sterilization of the drug product.	Firm has submitted that we cannot perform terminal sterilization of ketorolac injection because it is heat sensitive product. *Melting point of the API mentioned in DMF is 165-170 ^{o}C.*
7	3.2. P.5.2	Detailed analytical procedure for the drug product by the drug product manufacturer shall be provided.	Submitted.
8	3.2. P.5.1	In process validation protocol 30.45mg of ketorolac tromethamine is used. Justification is required whether overage or potency adjustment?	Firm has submitted that it is potency adjustment.
9	3.2. P.8.1	Submit 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.	Submitted.

Decision: Deferred for following;

- **Submission of documents/commercial invoice for the procurement of API Lot No. KM-0100918 wi approval from DRAP.**
- **Submission of scientific justification for not performing terminal sterilization of the drug product.**
- **Submission of 7500/- fee for revision of finished product specifications as per notification No. F. 11/2012-B&A/DRAP dated 07-05-2021.**

Case No.1. Request for Change in Registration Status of Products from M/s OBS Pakistan (Pvt.) Ltd., Karachi to M/s Aspin Pharma (Pvt.) Ltd., Karachi

Registration Board in its 289th meeting held on 14th – 16th May, 2019 deferred the request of M/s. Aspin Pharma (Pvt.) Ltd; Plot No. 10 & 25, Sector 20, Korangi Industrial Area Karachi-74900 for change in registration status of following products from M/s. OBS Pakistan (Pvt.) Ltd; Karachi to their name **for confirmation of renewal status & submission of complete documents/information regarding source of pellets**:

The firm has now submitted evidence for submission of differential fee (of Rs.10000/each) deposited for renewal of registration (Dy.No.11584 (R&I) dated 11-07-2019 along-with following information/ documents:

Administrative Documents in the light of SOP approved by the Registration Board in its 283rd meeting
i. Copy of last GMP inspection report dated 01-06-2020 (**Good** Level of Compliance).
ii. Panel Inspection report for renewal of DML dated 26-01-2021.
iii. Section approval of M/s Aspin verified from Licensing Division's letter for renewal of DML (dated 09th June, 2016) confirming following sections; ➢ Tablet (General) ➢ Capsule (General) ➢ Liquid Syrup ➢ Ointment/ Cream.
iv. NOC from M/s. OBS Pakistan (Pvt.) Ltd; Karachi dated 07-01-2021.
v. Relevant undertakings & commitments.

I	II	III	IV	V
S. No.	**Name of Drug(s)**	**Reg. No.**	**Registration History**	**Previous Remarks**
1.	C-Yalta 20mg Capsule Each capsule contains: Duloxetine HCl enteric coated pellets eq. to Duloxetine … 20mg (Manufacturer's Specifications)	076116	Initial date of Reg. 25-10-2013 (Source of Pellets: M/s Spansules formulation, India) Last Renewal applied on 27-09-2018 With fee of Rs.10,000/-Pellets are being imported from India and the firm has submitted renewal fee of Rs.10,000/- only	Dy.No.3318 (R&I) 11-04.2019 Rs.20,000/- Dy.No.4923 (R&I) 30-04.2019 Rs.100,000/- *Applied Source of Pellets:* *M/s Spansules, India*

	Name, address of Applicant / Marketing Authorization Holder	M/s Aspin Pharma (Pvt.) Ltd., Plot No. 10 & 25, Sector No. 20, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	Aspin Pharma (Pvt.) Ltd., Plot No. 10 & 25, Sector No. 20, 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. 3318 (R&I) : 11-04-2019

	Details of fee submitted	PKR 20,000/-: 11-04-2019
	The proposed proprietary name / brand name	**C-Yalta 20mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Duloxetine HCl enteric coated pellets eq. to Duloxetine … 20mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Antidepressant
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	10's
	Proposed unit price	474.01
	The status in reference regulatory authorities	Approved by MHRA
	For generic drugs (me-too status)	Hapibar 20mg per Capsule Barrett Hodgson Pakistan (Pvt.) Ltd.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted in 14-05-2020
	Name and address of API manufacturer.	M/s SURGE Laboratories (Pvt.) Ltd., Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Remarks: Firm has performed comparative dissolution profile against the innovator's product i.e, Cymbalta Capsule manufactured by Lilly Del Caribe, Inc. and the results are within acceptable limit of f2 value.	
	Module-III (Drug Product):	Firm has submitted relevant information against the Module III, including Comparative Dissolution Profile studies, Process validation protocol, Finished product analytical method validation report & stability studies data (6M Acc. & 6M RT).

STABILITY STUDY DATA			
Manufacturer of API	M/s SURGE Laboratories (Pvt.) Ltd., Pakistan.		
API Lot No.	DXP-17-054		
Description of Pack (Container closure system)	Alu-Alu 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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	199DS04	199DS05	199DS06
Batch Size	2500 Capsules	2500 Capsules	2500 Capsules
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	02-2020	02-2020	02-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable as the said product is Me-Too
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Manufacturing License for M/s SURGE Laboratories (Pvt.) Ltd., Pakistan, issued by DRAP valid Up to 03-07-2022.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Not applicable since the API is procured locally form M/s Surge Laboratories.
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
Shortcomings		**Replies**
3.2.S.4 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 shall be submitted.		The firm has submitted protocol and report for analytical method verification performed by M/s Aspin of C-yalta capsules.

I	II	III	IV	V
S. No.	**Name of Drug(s)**	**Reg. No.**	**Registration History**	**Previous Remarks**
2.	C-Yalta 30mg Capsule Each capsule contains: Duloxetine HCl enteric coated pellets eq. to Duloxetine … 30mg (Manufacturer's Specifications)	076118	Initial date of Reg. 25-10-2013 (Source of Pellets: M/s Spansules formulation, India) Last Renewal applied on 27-09-2018 With fee of Rs.10,000/-Pellets are being imported from India and the firm has submitted renewal fee of Rs.10,000/-only	Dy.No.3319 (R&I) 11-04.2019 Rs.20,000/- Dy.No.4922 (R&I) 30-04.2019 Rs.100,000/- *Applied Source of Pellets: M/s Spansules, India*

688.	Name, address of Applicant / Marketing Authorization Holder	M/s Aspin Pharma (Pvt.) Ltd., Plot No. 10 & 25, Sector No. 20, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	Aspin Pharma (Pvt.) Ltd., Plot No. 10 & 25, Sector No. 20, 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. 3319 (R&I) : 11-04-2019
	Details of fee submitted	PKR 20,000/-: 11-04-2019
	proposed proprietary name / brand name	C-Yalta 30mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Duloxetine HCl enteric coated pellets eq. to Duloxetine … 30mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Antidepressant
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	10's
	Proposed unit price	614.73
	status in reference regulatory authorities	Approved by MHRA
	For generic drugs (me-too status)	Hapibar 30mg per Capsule Barrett Hodgson Pakistan (Pvt.) Ltd.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted in 14-05-2020
	Name and address of API manufacturer.	M/s SURGE Laboratories (Pvt.) Ltd., Pakistan.
	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 Comparative Dissolution Profile studies, Process validation protocol, Finished product analytical method validation report & stability studies data (6M Acc. & 6M RT).
	Remarks: Firm has performed comparative dissolution profile against the innovator's product i.e, Cymbalta Capsule manufactured by Lilly Del Caribe, Inc. and the results are within acceptable limit of f2 value.	

STABILITY STUDY DATA

Manufacturer of API	M/s SURGE Laboratories (Pvt.) Ltd., Pakistan.		
API Lot No.	DXP-17-054		
Description of Pack (Container closure system)	Alu-Alu 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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	200DS04	200DS05	200DS06
Batch Size	2500 Capsules	2500 Capsules	2500 Capsules
Manufacturing Date	03-2020	03-2020	03-2020

Date of Initiation	03-2020	03-2020	03-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable as the said product is Me-Too
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Manufacturing License for M/s SURGE Laboratories (Pvt.) Ltd., Pakistan, issued by DRAP valid Up to 03-07-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not applicable since the API is procured locally.
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

Shortcomings	**Replies**
3.2.S.4 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 shall be submitted.	The firm has submitted protocol and report for analytical method verification performed by M/s Aspin of C-yalta capsules.

I	**II**	**III**	**IV**	**V**
S. No.	**Name of Drug(s)**	**Reg. No.**	**Registration History**	**Previous Remarks**
3.	C-Yalta 60mg Capsule Each capsule contains: Duloxetine HCl enteric coated pellets eq. to Duloxetine … 60mg (Manufacturer's Specifications)	076117	Initial date of Reg. 25-10-2013 (Source of Pellets: M/s Spansules formulation, India) Last Renewal applied on 27-09-2018 With fee of Rs.10,000/-Pellets are being imported from India and the firm has submitted renewal fee of Rs.10,000/- only	Dy.No.3320 (R&I) 11-04.2019 Rs.20,000/- Dy.No.4941(R&I) 30-04.2019 Rs.100,000/- *Applied Source of Pellets:* *M/s Spansules, India*

	Name, address of Applicant / Marketing Authorization Holder	M/s Aspin Pharma (Pvt.) Ltd., Plot No. 10 & 25, Sector No. 20, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	Aspin Pharma (Pvt.) Ltd., Plot No. 10 & 25, Sector No. 20, 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.3320 (R&I) : 11-04-2019
	Details of fee submitted	PKR 20,000/-: 11-04-2019
	proposed proprietary name / brand name	**C-Yalta 60mg Capsule**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Duloxetine HCl enteric coated pellets eq. to Duloxetine … 60mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Antidepressant
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	10's
	Proposed unit price	1022.04
	status in reference regulatory authorities	Approved by MHRA
	For generic drugs (me-too status)	Hapibar 60mg per Capsule Barrett Hodgson Pakistan (Pvt.) Ltd.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted in 14-05-2020
	Name and address of API manufacturer.	M/s SURGE Laboratories (Pvt.) Ltd., Pakistan.
	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 Comparative Dissolution Profile studies, Process validation protocol, Finished product analytical method validation report & stability studies data (6M Acc. & 6M RT).
	Remarks: Firm has performed comparative dissolution profile against the innovator's product i.e, Cymbalta 60mg Capsule manufactured by Lilly Del Caribe, Inc. and the results are within acceptable limit of f2 value.	

STABILITY STUDY DATA			
Manufacturer of API	M/s SURGE Laboratories (Pvt.) Ltd., Pakistan.		
API Lot No.	DXP-17-054		
Description of Pack (Container closure system)	Alu-Alu 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: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	201DS04	201DS05	201DS06
Batch Size	2500 Capsules	2500 Capsules	2500 Capsules
Manufacturing Date	03-2020	03-2020	03-2020
Date of Initiation	03-2020	03-2020	03-2020
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 the following documents in conjunction with the checklist approved by the Registration Board.		
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable as the said product is Me-Too
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Manufacturing License for M/s SURGE Laboratories (Pvt.) Ltd., Pakistan, issued by DRAP valid Up to 03-07-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not applicable since the API is procured locally.
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

Shortcomings	**Replies**
3.2.S.4 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 shall be submitted.	The firm has submitted protocol and report for analytical method verification performed by M/s Aspin of C-yalta capsules.

Decision **Registration Board decided as under:**

i. Cancelled registration of following products from the name of M/s OBS Pakistan (Pvt.) Ltd., C-14, Manghopir Road, S.I.T.E. Karachi:

S. No.	Reg. No.	Product Name & Composition
i.	076116	C-Yalta 20mg Capsule Each capsule contains:- Duloxetine HCl enteric coated pellets eq. to Duloxetine……..20mg (Manufacturer's Specification)
ii.	076118	C-Yalta 30mg Capsule Each capsule contains:- Duloxetine HCl enteric coated pellets eq. to Duloxetine.....30mg (Manufacturer's Specification)
iii.	076117	C-Yalta 60mg Capsule Each capsule contains:- Duloxetine HCl enteric coated pellets eq. to Duloxetine…….60mg (Manufacturer's Specification)

ii. Approved registration of following products in the name of M/s Aspin Pharma (Pvt.) Ltd; Plot No. 10 & 25, Sector 20, Korangi Industrial Area Karachi:

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
i.	C-Yalta 20mg Capsule Each capsule contains: Duloxetine HCl Enteric Coated Pellets eq. to Duloxetine…..20mg (USP Specifications) Source of Pellets: M/s Surge Laboratories (Pvt) Ltd, 10th Km Faisalabad Road, Bikhi, District Sheikhupura
ii.	C-Yalta 30mg Capsule Each capsule contains: Duloxetine HCl Enteric Coated Pellets eq. to Duloxetine…..30mg (USP Specifications) Source of Pellets: M/s Surge Laboratories (Pvt) Ltd, 10th Km Faisalabad Road, Bikhi, District Sheikhupura
iii.	C-Yalta 60mg Capsule Each capsule contains: Duloxetine HCl Enteric Coated Pellets eq. to Duloxetine…..60mg (USP Specifications) Source of Pellets: M/s Surge Laboratories (Pvt) Ltd, 10th Km Faisalabad Road, Bikhi, District Sheikhupura

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.2. Request for Change in Registration Status of Products from M/s The Searle Company Limited Karachi to M/s OBS Pakistan (Pvt.) Ltd., Karachi

M/s. OBS Pakistan (Pvt.) Ltd., C-14, Manghopir Road, S.I.T.E, Karachi has requested for change in registration of two products (Ezium 20mg; 035621 and 40mg Capsules; 035622) from M/s The Searle Company Ltd., F-319, S.I.T.E Karachi to their name as per following details:

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 07-10-2020. (Rating: Good)
ii. Copy of DML 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 07-10-2020 confirming "Capsule (General) Section"
iv. NOC from M/s. The Searle Company Ltd; Karachi dated 15-10-2021 for transfer of Ezium 20mg (Reg.035621) and Ezium 40mg (Reg. 035622).
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	V
S. No.	**Reg. No.**	**Product Name & Composition (As per initial Registration letter)**	**Registration Trail**	**Dy. No./ Fee/ Date** Remarks
1.	035621	Ezium 20mg Capsule Each capsule contains:- Esomeprazole Magnesium 22.5% Pellets eq. to Esomeprazole ……20mg	Initial Reg. Date: **30-12-2004** Change of Name: **07-02-2005** Renewal Submitted: **10-02-2010** Change of registration status	Dy.No.16315 Dated 11-06-2021 Fee of Rs.20,000/-(1940937) dated 17-04-2020 Rs. 80,000/-(1986664) dated 17-03-2021

			to new title: **19-03-2018** Last Renewal: **09-08-2019**	
	Name, address of Applicant / Marketing Authorization Holder		M/s OBS Pakistan (Pvt.) Ltd. Address: C-14, Manghopir Road, S.I.T.E, Karachi	
	Name, address of Manufacturing site.		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 22-03-2021]*	
	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 copies of letter for grant of additional section mentioning Capsule (General) 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.16315 (R&I) dated 11-06-2021	
	Details of fee submitted		For transfer of registration: PKR 100,000/- DS# 1986664 dated 14-04-2021 DS# 1940937 dated 30-06-2020	
	proposed proprietary name / brand name		Ezium 20 mg Capsule	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit		Each capsule contains: 96mg Esomeprazole Magnesium Pellets (22.5% w/w) equivalent to 20mg of Esomeprazole	
	Pharmaceutical form of applied drug		Delayed Release Capsule Hard gelatin capsule size # 4, opaque amethyst color cap and body imprinted "EZIUM" containing white to off-white enteric coated spherical pellets.	
	Pharmacotherapeutic Group of (API)		Proton Pump Inhibitor	
	Reference to Finished product specifications		USP Specification	
	Proposed Pack size		2 x 7's	
	Proposed unit price		As per DPC	
	status in reference regulatory authorities		Nexium 20mg Capsule, AstraZeneca Pharmaceuticals,	
	For generic drugs (me-too status)		Ecorox 20mg Capsule, Atco laboratories Ltd, (Reg#035721)	
	Name and address of API manufacturer.		M/s Murli Krishna Pharma Pvt Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, 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, character elucidations using various techniques, solubility, physical forms, manufacturing process of finish product, USP specification, impurities characterizations, analytical procedures and its validation, drug excipients compatibility studies by pellets manufacturer using HPLC and FTIR, batch analysis and specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, impurities elucidation, physical form, DS and raw material specifications, manufacturer, quantitative composition of esomeprazole pellets, excipients specifications, analytical methods and its validation, certificate of analysis, impurities, specifications based on USP, analytical procedures, batch analysis, reference standard, 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 (4.5 kg each) 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 and the real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months. The esomeprazole 22.5% Pellets are packed in a double polyethylene bag which was sealed with plastic fastener and placed in fibre board drum. The product was remain within specified limits as tested on defined intervals.
	Module-III Drug Product:	Firm has submitted data of drug product including its composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocol, control of excipients, control of drug product, specifications, analytical procedures and its verification, batch analysis, justification of specifications, analytical procedure for organic impurities, reference standard or materials, container closure system and stability. The Specifications and control tests comply to USP.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The comparative dissolution profile was performed for Ezium 20mg Capsule against the Nexum 20mg Capsule, manufactured by AstraZeneca. Comparison was performed using 12 samples in acidic medium for 120min which revealed that less than 3% results, and in in the buffer medium at 10, 15,20, 25, and 30 minutes. Calculation of value was f1=8 and f2=53.
	Analytical method validation/verification of product	Firm has claimed USP specifications for which report of verification of analytical method for the drug product has been provided.

STABILITY STUDY DATA

Manufacturer of API	M/s Murli Krishna Pharma Pvt Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, India.
API Lot No.	MKPPLR-ESF-19044
Description of Pack	Alu/PVC blister in unit carton

(Container closure system)			
Stability Storage Condition	Real time: 30˚C ± 2˚C / 75% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time:06 months (Continue for 36 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 and 36(Months)		
Batch No.	03DT01	03DT02	03DT03
Batch Size	3000 Capsules	3000 Capsules	3000 Capsules
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	23-06-2020	23-06-2020	23-06-2020
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)	-
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 Office of the commissioner, Food & Drug Administration, Government of Maharashtra, Mumbai, dated 20-04-2019. The GMP certificate was granted based on inspection dated 1st – 2nd March, 2019. (Valid up to 03-04-2022).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	API purchased from M/s Murli Krishna Pvt Ltd, India invoice dated 30-11-2019, cleared 01-01-2020 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	
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.

I	II	III	IV	V
S.No.	**Reg. No.**	**Product Name & Composition (As per initial Registration letter)**	**Registration Trail**	**Dy. No./ Fee/ Date**
2.	035622	Ezium 40mg Capsule Each capsule contains:- Esomeprazole Magnesium 22.5% Pellets eq. to Esomeprazole ……40mg	Initial Reg. Date: **30-12-2004** Change of Name: **07-02-2005** Renewal Submitted: **10-02-2010** Change of registration status to new title: **19-03-2018** Last Renewal: **09-08-2019**	Dy.No.16316 Dated 11-06-2021 Fee of Rs.20,000/-(1940938) dated 17-04-2020 Rs. 80,000/-(1986663) dated 17-03-2021
	Name, address of Applicant / Marketing Authorization Holder		M/s OBS Pakistan (Pvt.) Ltd. Address: C-14, Manghopir Road, S.I.T.E, Karachi	

	Name, address of Manufacturing site.	M/s OBS Pakistan (Pvt.) Ltd. Address: C-14, Manghopir Road, S.I.T.E, Karachi **(DML 000012)** ***(Transfer of Registration from M/s Searle Pakistan to M/s OBS Pakistan Pvt. Ltd Karachi,*** ***[NOC attached dated 22-03-2021]***
	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 copies of letter for grant of additional section mentioning Capsule (General) 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.16316 (R&I) dated 11-06-2021
	Details of fee submitted	**For transfer of registration:** PKR 100,000/- DS# 1940398 dated 14-04-2021 DS# 1986663 dated 30-06-2020
	proposed proprietary name / brand name	Ezium 40 mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: 192mg Esomeprazole Magnesium Pellets (22.5% w/w) equivalent to 40mg of Esomeprazole
	Pharmaceutical form of applied drug	Delayed Release Capsule Hard gelatin capsule size # 3, opaque dark purple color cap and body imprinted “EZIUM 40” containing white to off-white enteric coated spherical pellets.
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	2 x 7’s
	Proposed unit price	As per DPC
	status in reference regulatory authorities	Nexium 40mg Capsule, AstraZeneca Pharmaceuticals,
	For generic drugs (me-too status)	Nexum 40mg Capsule, Getz Pharma Ltd, (Reg#033891)
	Name and address of API manufacturer.	M/s Murli Krishna Pharma Pvt Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, 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, character elucidations using various techniques, solubility, physical forms, manufacturing process of finish product, USP specification, impurities

		characterizations, analytical procedures and its validation, drug excipients compatibility studies by pellets manufacturer using HPLC and FTIR, batch analysis and specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted data for drug substance related to nomenclature, structure, general properties, solubilities, impurities elucidation, physical form, DS and raw material specifications, manufacturer, quantitative composition of esomeprazole pellets, excipients specifications, analytical methods and its validation, certificate of analysis, impurities, specifications based on USP, analytical procedures, batch analysis, reference standard, 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 (4.5 kg each) 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 and the real time stability data is conducted at 30ºC ± 2ºC / 65% ± 5% RH for 36 months. The esomeprazole 22.5% Pellets are packed in a double polyethylene bag which was sealed with plastic fastener and placed in fibre board drum. The product was remain within specified limits as tested on defined intervals.
	Module-III Drug Product:	Firm has submitted data of drug product including its composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocol, control of excipients, control of drug product, specifications, analytical procedures and its verification, batch analysis, justification of specifications, analytical procedure for organic impurities, reference standard or materials, container closure system and stability. The Specifications and control tests comply to USP.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The comparative dissolution profile was performed for Ezium 40mg Capsule against the Nexum 40mg Capsule, manufactured by AstraZeneca. Comparison was performed using 12 samples in acidic medium for 120min which revealed that less than 3% results, and in in the buffer medium at 10, 15,20, 25, and 30 minutes. Calculation of value was f1=8 and f2=57.
	Analytical method validation/verification of product	Firm has claimed USP specifications for which report of verification of analytical method for the drug product has been provided.

STABILITY STUDY DATA	
Manufacturer of API	M/s Murli Krishna Pharma Pvt Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, India.
API Lot No.	MKPPLR-ESF-19044
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:06 months (Continue for 36 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 and 36(Months)		
Batch No.	03DT01	03DT02	03DT03
Batch Size	3000 Capsules	3000 Capsules	3000 Capsules
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	23-06-2020	23-06-2020	23-06-2020
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)	-
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 Office of the commissioner, Food & Drug Administration, Mumbai, dated 20-04-2019. The GMP certificate was granted based on inspection dated 1st – 2nd March, 2019. (Valid up to 03-04-2022).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	API purchased from M/s Murli Krishna Pvt Ltd, India invoice dated 30-11-2019, cleared 01-01-2020 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	
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.

Decision **Registration Board decided as under:**

i. Cancelled registration of following products from the name of M/s The Searle Company Ltd., F-319, S.I.T.E Karachi:

S. No.	Reg. No.	Product Name & Composition
i.	035621	Ezium 20mg Capsule Each capsule contains:- Esomeprazole Magnesium 22.5% Pellets eq. to Esomeprazole ……...…20mg
ii.	035622	Ezium 40mg Capsule Each capsule contains:- Esomeprazole Magnesium 22.5% Pellets eq. to Esomeprazole ……...…40mg

ii. Approved registration of following products in the name of M/s OBS Pakistan (Pvt.) Ltd., C-14, Manghopir Road, S.I.T.E. Karachi:

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.

c) Furthermore, the firm shall submit valid and legalized GMP certificate of pellets manufacturer i.e., M/s Murli Krishna Pharma Pvt Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, India.

S. No.	Product Name & Composition
i.	Ezium 20mg Capsule Each capsule contains: Esomeprazole Magnesium Pellets (22.5% w/w) equivalent to Esomeprazole……20mg (USP Specifications) Source of Pellets: M/s Murli Krishna Pharma Pvt. Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, India.
ii.	Ezium 20mg Capsule Each capsule contains: Esomeprazole Magnesium Pellets (22.5% w/w) equivalent to Esomeprazole……20mg (USP Specifications) Source of Pellets: M/s Murli Krishna Pharma Pvt. Ltd., D 98, Ranjangaon MIDC, Pune, Maharashtra, India.

iii. Reference will be sent to Costing and Pricing Division for confirmation of maximum retail price (MRP).

Case No.3. Irrational combination - Drug Safety Threats of Drug (Paracetamol 500mg, Thioridazine 3mg And Caffeine 70mg).

Registration Board in its 293rd meeting held on 6th – 8th January, 2020 considered the subject mentioned case as per following details:

A combination of Paracetamol 500mg, Thioridazine 3mg and Caffeine is registered in Pakistan by the name of tablet Diagesic P of Wilson's Pharmaceutical Islamabad Registration no. 015654 and tablet Pregesic of Cirin Pharmaceutical Hattar Registration no.063092. The said combination is routinely prescribed by the physicians as analgesic and also is sold as OTC medicine by the pharmacies and medical store.

Thioridazine, a conventional anti-psychotic drug which was used in Schizophrenia and was discontinued in most of the western countries. Novartis had issued dear health care professional letter in July, 2000 for its research product Mallaril (thioridazine) regarding black box warning of QTc interval prolongation, arrhythmia (abnormal heart rhythm that can lead to sudden cardiac arrest), sudden death and limit its use only for schizophrenic patients who fail to show an acceptable response to adequate courses of treatment with other anti-psychotic drugs. In 2005 Novartis announced to discontinue all form of Thioridazine worldwide due to its questionable benefit risk profile. Moreover, the said combination is not registered in any stringent regulatory authorities (Canada, EU, FDA, PMDA, TGA and MHRA).

Rule 30(10)[a] of Drug (Licensing, Registering & Advertising), 1976 in respect of registered drugs shall be complied with the following provisions of the rule, stated as under:

"30(10). If a drug or any of its ingredients, which is imported or manufactured by a company in Pakistan is also approved for registration and free sale by its subsidiary, sister concern, associate or parent company in the country where it was originally developed or in any of the countries namely, U.S.A, European Union Countries, Canada, Japan, Australia and—

a. if that drug at any time, for safety reasons is withdrawn or banned or certain restrictions are imposed in any of the said countries, then it shall be the responsibility of the manufacturer in Pakistan or the case may be, the inventors, to immediately withdraw the drug from the market in Pakistan or, as the case may be to impose similar restriction and to inform the Registration Board within fourteen days of such an information having come to his knowledge and having taken the necessary action. The Registration Board after getting the said intimation shall take similar action for the same drugs available from other sources with the shortest possible time;"

The case was placed in 263rd meeting of Registration Board and Board decided as under;

Decision of 263rd Meeting: Registration Board deliberated the case and decided that:

i. The combination (Paracetamol 500mg, Thioridazine 3mg and Caffeine 70mg) is not available in any of the reference regulatory authorities as approved by the Board i.e. FDA, TGA, EMA, PMDA, MHRA, Health Canada, Germany, France, Switzerland, Sweden, Norway, Denmark, Austria and Netherland. Since, it is reported vide WHO newsletter no.1, 2005 about voluntary withdrawn of Thioridazine worldwide by the brand leader Novartis, hence all irrational combinations containing Thioridazine, which are also not existent worldwide be also withdrawn throughout the country.

ii. Show cause notice will be served by the concerned Registration section to Wilson's Pharmaceutical Islamabad and Cirin Pharmaceutical Hattar for de-registration of drug.

iii. Advised PE & R Division to confirm/status of registration of the said combination (other than two brands i.e. Diagesic-P and Pregesic) and inform Registration Board to initiate process for de-registration of products.

Accordingly show cause notices were served to M/s. Wilson Pharmaceutical, Islamabad and M/s. Cirin pharmaceutical, Hattar regarding cancellation of registration under Drugs Act 1976 and rules framed there under. Then M/s. Wilson Pharmaceutical, Islamabad had filed a case in the Court of Senior Civil Judge (West) Islamabad. The Court vide their order dated 01-11-2018 rejected plaint under order VII rule 11 of CPC.

It is pertinent to mention here that Provincial Drug Inspector, Nowshera has informed that the Registration Board in its 263rd meeting decided regarding the registration of Tablet Diagesic-P of M/s. Wilson Pharmaceuticals, Islamabad on account of safety and efficacy concerns. He has seized the said drug product from multiple sales outlets at district Nowshera and then served show cause notice to M/s. Wilson, Islamabad. In response, Mr. Tepu Sultan Akram, General Manager of M/s. Wilson Pharmaceuticals Islamabad replied him that registration of Diagesic-P Tablet (Reg.No.015654) is still intact and renewed regularly from the DRAP and no proceeding regarding the cancellation/de-registration of Diagesic-P Tablet is initiated by DRAP. He has therefore, requested for final decision by DRAP in the case to further proceed in the matter.

Decision of M-293:

Registration Board deliberated on the matter in details and decided to give an opportunity of personal hearing as per Drug Act, 1976 and Rules framed there under to both the firms i.e M/s. Wilson Pharmaceuticals, Islamabad & M/s. Cirin Pharmaceuticals, Hattar in forthcoming meeting of Registration Board.

Decision: **Registration Board discussed that as show-cause notices have already been issued to M/s Wilson Pharmaceuticals, Islamabad and M/s Cirin Pharmaceuticals (New Title: ICI Pakistan Ltd.), Hattar, therefore, Registration Board decided that management of above-mentioned firms shall be given the opportunity of personal hearing in the forthcoming meeting of the Board under section 42 of the Drugs Act, 1976.**

Case No. 01 Transfer of Products From M/s. Indus Pharma Karachi to M/s. Dynatis Pakistan (Pvt.) Ltd. Lahore.

M/s Dynatis Pakistan (Pvt) Ltd, Lahore have applied for transfer of their following products, on Form 5 F, from Indus Pharma Karachi to their name:

1.	Name, address of Applicant / Marketing Authorization Holder	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, Sundar Industrial Estate, Lahore, Pakistan
	Name, address of Manufacturing site.	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, 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. 24023 dated 31/08/2021
	Details of fee submitted	PKR 30,000/-: dated 30/07/2021
	The proposed proprietary name / brand name	Tofranil 25 mg Tablets (*Dynatis has submitted an NOC for transferring Tofranil- Reg. No. 000644- from Indus Pharma Karachi to Dynatis Lahore dated 06th August 2021*)
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each sugar-coated tablet contains: Imipramine Hydrochloride … ……..25mg
	Pharmaceutical form of applied drug	Oral; Tablets, Sugar-coated
	Pharmacotherapeutic Group of (API)	Anti-depressive agent; Tricyclic; Non-selective monoamine reuptake inhibitors;
	Reference to Finished product specifications	USP
	Proposed Pack size	200's Tablets (10's x 20's Blister Strips)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Tofranil 25 mg Tablet manufactured by Novartis Pharma (Australia) Pvt. Ltd; Approved status in TGA Australia
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	cGMP certificate issued by FID Lahore Majida Mujahid Ref. No. 29/2021-DRAP (FID-2065251-174) dated 01-07-2021.
	Name and address of API manufacturer.	R.L FINE CHEM PVT LTD; Plot No. IP No. 27-29 PARTS of SY. No.s 18 273 274 & 313 KIADB INDUSTRIAL AREA, I PHASE KUDUMALAKUNTE VILLAGE GOWRIBIDANOOR, TALIK, CHIKKABALLAPUR, DISTRICT -561208, INDIA.
	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,

<table>
<tr><td></td><td></td><td>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>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</td></tr>
<tr><td></td><td>Stability studies</td><td>DS Imipramine Hydrochloride stability by DS Manufacturer RL Fine Chem submitted.
Accelerated: 40 ± 2 °C and 75 % ± 5 % RH, Packed in double LDPE bags in HDPE containers.
Batches: 01: No. Pr/1495 Mfg. Date: December 2008: 02: No. Pr/1496 Mfg. Date: December 2008: 03: No. Pr/1497 Mfg. Date: December 2008
Long term: 30 ± 2 °C and 65 % ± 5 % RH, Packed in double LDPE bags in HDPE containers.
Batches: 01: No. Pr/1495 Mfg. Date: December 2008: 02: No. Pr/1496 Mfg. Date: December 2008: 03: No. Pr/1497 Mfg. Date: December 2008
Forced degradation studies have been performed in June 2018 by the manufacturer of DS with conclusion that DS imipramine HCL under stress maximum degradation occurred of unknown impurity whereas Iminodibenzyl was observed 0.356 %.</td></tr>
<tr><td></td><td>Module-III (Drug Product):</td><td>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.</td></tr>
<tr><td></td><td>Pharmaceutical equivalence and comparative dissolution profile</td><td>Submitted Comparative Dissolution Profile of:
<table>
<tr><th>Product</th><th>B #, Mfg. Date</th><th>Manuf.</th></tr>
<tr><td>Tofranil Tablets 25 mg</td><td>Batch No. 002 Mfg. Date: Not specified in report</td><td>Dynatis Pakistan Pvt. Ltd., Lahore</td></tr>
<tr><td>Tofranil Tablets 25 mg</td><td>Batch No. 084 Mfg. Date: Not specified in report</td><td>Indus Pharma (Pvt.) Ltd., Karachi</td></tr>
</table>
Buffers Used: i. HCl Buffer pH 1.2
ii. Acetate Buffer pH 4.5
iii. Phosphate Buffer pH 6.8
<table>
<tr><th>Factor</th><th>pH 1.2</th><th>pH 4.5</th><th>pH 6.8</th></tr>
<tr><td>Difference Factor f1</td><td>Not calculated</td><td>9</td><td>Not calculated</td></tr>
<tr><td>Similarity Factor f2</td><td>Not calculated due to 88.87 % release of reference and 98.32% of test product after 15 mins.</td><td>55</td><td>Not calculated due to 99.60 % release of reference and 99.69 % of test product after 15 mins.</td></tr>
</table></td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Method verification studies has been submitted including linearity, accuracy, precision, specificity and robustness.</td></tr>
<tr><td colspan="3">STABILITY STUDY DATA</td></tr>
<tr><td colspan="2">Manufacturer of API</td><td>R.L FINE CHEM PVT LTD; Plot No. IP No. 27-29 PARTS of SY. No.s 18 273 274 & 313 KIADB INDUSTRIAL AREA, I PHASE KUDUMALAKUNTE</td></tr>
</table>

	VILLAG/E GOWRIBIDANOOR, TALIK, CHIKKABALLAPUR, DISTRICT - 561208, INDIA.		
API Lot No.	IMP P/1597		
Description of Pack (Container closure system)	ALU-PVC Foil in unit carton comprising of 200 Tablets (20's 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.	001	002	003
Batch Size	5000 Tablets	5000 Tablets	5000 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)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	License of RL Fine Chem Pvt Ltd is issued by Drugs Controller (I/c) & Licensing Authority, Karnataka dated 01-12-2016 which is valid till 30-11-2021. Same department has also issued GMP certificate of RL Fine Chem Pvt Ltd valid up to 30-11-2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy invoices of Imiparamine HCl for Indus Pharma Karachi.
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:

The drug substance for Tofranil 25 mg Tablet is manufactured by R.L Fine Chem Pvt Ltd; plot no. IP no. 27-29 parts of SY. No.s 18 273 274 & 313 Kiadb Industrial area, I Phase Kudumalakunte villag/e Gowribidanoor, Talik, Chikkaballapur, District -561208, India (License and GMP certified by Drugs Controller (I/c) & Licensing Authority, Karnataka, India) on USP specifications. Manufacturing and controls, comparability protocols, structural characterization, and stability protocol has been submitted. Specification is considered adequate with respect to USP monograph. Process impurity Iminodibenzyl has been shown to be in acceptable limits. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications except impurity estimation.

The drug product is tablet of 25 mg manufactured by Dynatis Pakistan (Pvt) Ltd., Lahore DML 000891 (Formulation) (reddish-brown, round biconvex, sugar-coated tablet). The method of manufacturing is standard

wet granulation, compression, and sugar coating with adequate in process controls. Submitted regulatory specifications have been verified as per USP monograph and submitted stability data shows no degradation product at specified time points. Labelling is submitted that meets the requirements of respective rules.

Dynatis Pakistan (Pvt) Ltd., is GMP complaint as per certificate issued by DRAP, Lahore office on 01-07-2021. Tofranil 25mg Tablets' pharmaceutical equivalence has been established against the Tofranil oral sugar-coated Tablets approved (September 1997) by the TGA. The clinical particulars and pharmacological properties of the Imipramine HCl, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for (i) Major depression, and (ii) Nocturnal enuresis (from the age of 5 years onwards and provided the possibility of organic causes has first been excluded).

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.

Chemistry manufacturing and control is satisfactory as per CTD guidelines PE&R/GL/AF/004 effective 1st October 2020. The firm shall ensure boxed information on "Suicidality and Antidepressant Drugs" in the beginning of the leaflet.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above-mentioned product from the name of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi.**
b. **Approved registration of above-mentioned product in the name of M/s Dynatis Pakistan (Pvt) Ltd. Plot No. 710, Sundar Industrial Estate, Lahore.**
c. **Reference will be sent to Cost and Pricing division for confirmation of maximum retail price (MRP).**
d. **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.**
e. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
f. **New registration numbers are issued in cases where registration is cancelled from one manufacturer and fresh registration is issued in the name of another manufacturer. In response to decision of 312th meeting of Registration Board, Legal Affair's Division opined that same registration numbers shall be issued in such cases where no change in name/ title of registration holder/ manufacturer and management occurs. However, since, the instant case pertains to change in registration status of products from one DML to another DML without any change in management only, therefore, as per discussion regarding issuance of registration with same registration numbers, Registration Board decided to seek opinion from Legal Affairs Division, DRAP and advised to proceed accordingly.**

2.	Name, address of Applicant / Marketing Authorization Holder	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, Sundar Industrial Estate, Lahore, Pakistan
	Name, address of Manufacturing site.	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, 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. 22706 dated 17/08/2021
	Details of fee submitted	PKR 30,000/-: dated 16/06/2021

	The proposed proprietary name / brand name	**Dynagab Capsule 50 mg** (*Dynatis has submitted an NOC for transferring Dynagab Capsule 50 mg-Registration number 083776- from Indus Pharma Karachi to Dynatis Lahore dated 15th November 2021*)
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin capsule: Pregabalin … 50 mg
	Pharmaceutical form of applied drug	Oral; Capsule; hard gelatin
	Pharmacotherapeutic Group of (API)	Anti-epileptics’;
	Reference to Finished product specifications	Innovator
	Proposed Pack size	10’s,14’s, 20’s, 30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lyrica Capsules 50 mg, manufactured by Pfizer Upjohn UK Limited, approved by US FDA
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	cGMP certificate issued by FID Lahore Majida Mujahid Ref. No. 29/2021-DRAP (FID-2065251-174) dated 01-07-2021.
	Name and address of API manufacturer.	Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India
	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	DS Pregabalin stability by DS Manufacturer Atlas Life Sciences **Accelerated:** 40 ± 2 °C and 75 % ± 5 % RH, **Batches: 01:** No. PG-035/13 Mfg. Date: 26-12-2013: **02:** No. PG-036/13 Mfg. Date: 28-12-2013: **03:** No. PG-037/13 Mfg. Date: 29-12-2013 **Long term**: 30 ± 2 °C and 65 % ± 5 % RH, **Batches: 01:** No. PG-035/13 Mfg. Date: 26-12-2013: **02:** No. PG-036/13 Mfg. Date: 28-12-2013: **03:** No. PG-037/13 Mfg. Date: 29-12-2013
	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	Submitted Comparative Dissolution Profile of:

Product	**B #, Mfg. Date**	**Manuf.**
Dynagab Capsule 50	Batch No. 002 Mfg. Date: Not	Dynatis Pakistan Pvt.

mg	specified in report	Ltd., Lahore
Lyrica capsule 50 mg	Batch No. EP0925 Mfg. Date: Not specified in report	Pfizer Upjohn UK Limited

Buffers Used: i. HCl Buffer pH 1.2
ii. Acetate Buffer pH 4.5
iii. Phosphate Buffer pH 6.8

Factor	**pH 1.2**	**pH 4.5**	**pH 6.8**
Difference Factor f1	Not calculated	Not calculated	Not calculated
Similarity Factor f2	Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.	Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.	Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.

	Analytical method validation/verification of product	Method validation studies has been submitted including linearity, range, Accuracy (recovery), Precision (repeatability & intermediate precision), LOD & LOQ, Robustness, Solution stability, system suitability and specificity.

STABILITY STUDY DATA

Manufacturer of API	Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India		
API Lot No.	PG-0090419		
Description of Pack (Container closure system)	size 4 hard-gelatin capsule with standard scarlet OP cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board 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.	001	002	003
Batch Size	6000 Capsules	6000 Capsules	6000 Capsules
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	09-11-2020	11-11-2020	13-11-2020
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	Food and Drug Administration, Gujrat State of India has issued GMP certificate to Altas Life Sciences Private Limited valid up to 10-02-2022.

	country of origin.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice no. 004 dated 25-04-2019 of Pregabalin batch number PG-0090419 to Indus Pharma, Karachi cleared by Assistant Director, DRAP Karachi office.
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:

The drug substance for Dynagab 50 mg Capsules is manufactured by Atlas Life Sciences Pvt Ltd 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India (GMP by FDA Gujrat, India) on inhouse specifications. Manufacturing and controls, comparability protocols, structural characterization, and stability protocol has been submitted. Specification is considered adequate with respect to general monographs of USP and European Pharmacopoeias and inhouse specification sets by the DS manufacturer. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications except impurity estimation.

The drug product is 50 mg capsule manufactured by Dynatis Pakistan (Pvt) Ltd., Lahore DML 000891 (Formulation) (size 4 hard-gelatin capsule with standard scarlet OP cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board unit carton with leaf insert). The method of manufacturing is blend mixing and capsule filling with adequate in process controls. Submitted regulatory specifications have been validated and submitted stability data shows no degradation product at specified time points. Labelling is submitted that meets the requirements of respective rules.

Dynatis Pakistan (Pvt) Ltd., is GMP complaint as per certificate issued by DRAP, Lahore office on 01-07-2021.

Dynagab 50 mg Capsules' pharmaceutical equivalence has been established against the Lyrica oral Capsule that was approved (December 2004) by the USFDA. The clinical particulars and pharmacological properties of Pregabalin, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy.

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.

Chemistry manufacturing and control is satisfactory as per CTD guidelines PE&R/GL/AF/004 effective 1st October 2020. However, the invoice submitted for Pregabalin batch number PG-0090419 (from which stability batches have been manufactured) is at the name of Indus Pharma Karachi.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above-mentioned product from the name of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi.**
b. **Approved registration of above-mentioned product in the name of M/s Dynatis Pakistan (Pvt) Ltd. Plot No. 710, Sundar Industrial Estate, Lahore.**
c. **Reference will be sent to Cost and Pricing division for confirmation of maximum retail price (MRP).**
d. **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.**
e. **Manufacturer will perform process validation of first three batches as per the commitment**

submitted in the registration application.

f. New registration numbers are issued in cases where registration is cancelled from one manufacturer and fresh registration is issued in the name of another manufacturer. In response to decision of 312th meeting of Registration Board, Legal Affair's Division opined that same registration numbers shall be issued in such cases where no change in name/ title of registration holder/ manufacturer and management occurs. However, since, the instant case pertains to change in registration status of products from one DML to another DML without any change in management only, therefore, as per discussion regarding issuance of registration with same registration numbers, Registration Board decided to seek opinion from Legal Affairs Division, DRAP and advised to proceed accordingly.

3.	Name, address of Applicant / Marketing Authorization Holder	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, Sundar Industrial Estate, Lahore, Pakistan
	Name, address of Manufacturing site.	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, 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. 22389 dated 13/08/2021
	Details of fee submitted	PKR 30,000/-: dated 16/06/2021
	The proposed proprietary name / brand name	Dynagab Capsule **75** mg (*Dynatis has submitted an NOC for transferring Dynagab Capsule 75 mg-Registration number 083777- from Indus Pharma Karachi to Dynatis Lahore dated 15th November 2021*)
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin capsule: Pregabalin … 75 mg
	Pharmaceutical form of applied drug	Oral; Capsule; hard gelatin
	Pharmacotherapeutic Group of (API)	Anti-epileptics';
	Reference to Finished product specifications	Innovator
	Proposed Pack size	10's,14's, 20's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lyrica Capsules 75mg, manufactured by Pfizer Upjohn UK Limited, approved by US FDA
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	cGMP certificate issued by FID Lahore Majida Mujahid Ref. No. 29/2021-DRAP (FID-2065251-174) dated 01-07-2021.
	Name and address of API manufacturer.	Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India
	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,

<table>
<tr><td></td><td></td><td>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>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</td></tr>
<tr><td></td><td>Stability studies</td><td>DS Pregabalin stability by DS Manufacturer Atlas Life Sciences
Accelerated: 40 ± 2 °C and 75 % ± 5 % RH,
Batches: 01: No. PG-035/13 Mfg. Date: 26-12-2013: 02: No. PG-036/13 Mfg. Date: 28-12-2013: 03: No. PG-037/13 Mfg. Date: 29-12-2013
Long term: 30 ± 2 °C and 65 % ± 5 % RH,
Batches: 01: No. PG-035/13 Mfg. Date: 26-12-2013: 02: No. PG-036/13 Mfg. Date: 28-12-2013: 03: No. PG-037/13 Mfg. Date: 29-12-2013</td></tr>
<tr><td></td><td>Module-III (Drug Product):</td><td>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.</td></tr>
<tr><td></td><td>Pharmaceutical equivalence and comparative dissolution profile</td><td>Submitted Comparative Dissolution Profile of:
<table>
<tr><th>Product</th><th>B #, Mfg. Date</th><th>Manuf.</th></tr>
<tr><td>Dynagab Capsule 75 mg</td><td>Batch No. EA002 Mfg. Date: Not specified in report</td><td>Dynatis Pakistan Pvt. Ltd., Lahore</td></tr>
<tr><td>Lyrica capsule 75 mg</td><td>Batch No. EP0902 Mfg. Date: Not specified in report</td><td>Pfizer Upjohn UK Limited</td></tr>
</table>
Buffers Used: i. HCl Buffer pH 1.2
ii. Acetate Buffer pH 4.5
iii. Phosphate Buffer pH 6.8
<table>
<tr><th>Factor</th><th>pH 1.2</th><th>pH 4.5</th><th>pH 6.8</th></tr>
<tr><td>Difference Factor f1</td><td>Not calculated</td><td>Not calculated</td><td>Not calculated</td></tr>
<tr><td>Similarity Factor f2</td><td>Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.</td><td>Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.</td><td>Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.</td></tr>
</table></td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Method validation studies has been submitted including linearity, range, Accuracy (recovery), Precision (repeatability & intermediate precision), LOD & LOQ, Robustness, Solution stability, system suitability and specificity.</td></tr>
<tr><td colspan="3">STABILITY STUDY DATA</td></tr>
<tr><td colspan="2">Manufacturer of API</td><td>Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India</td></tr>
<tr><td colspan="2">API Lot No.</td><td>PG-0090419</td></tr>
<tr><td colspan="2">Description of Pack (Container closure system)</td><td>size 3 hard-gelatin capsule with standard blue TR cap and white OP body containing white granular powder packed in 2 x 7’s Alu-Alu blister packed in</td></tr>
</table>

	bleach board 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.	EA001	EA002	EA003
Batch Size	6000 Capsules	6000 Capsules	6000 Capsules
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	16-11-2020	16-11-2020	16-11-2020
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.	Food and Drug Administration, Gujrat State of India has issued GMP certificate to Altas Life Sciences Private Limited valid up to 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice no. 004 dated 25-04-2019 of Pregabalin batch number PG-0090419 to Indus Pharma, Karachi cleared by Assistant Director, DRAP Karachi office.
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:

The drug substance for Dynagab 75 mg Capsules is manufactured by Atlas Life Sciences Pvt Ltd 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India (GMP by FDA Gujrat, India) on inhouse specifications. Manufacturing and controls, comparability protocols, structural characterization, and stability protocol has been submitted. Specification is considered adequate with respect to general monographs of USP and European Pharmacopoeias and inhouse specification sets by the DS manufacturer. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications except impurity estimation.

The drug product is 75 mg capsule manufactured by Dynatis Pakistan (Pvt) Ltd., Lahore DML 000891 (Formulation) (size 3 hard-gelatin capsule with standard blue TR cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board unit carton with leaf insert). The method of manufacturing is blend mixing and capsule filling with adequate in process controls. Submitted regulatory specifications have been validated and submitted stability data shows no degradation product at specified time points. Labelling is submitted that meets the requirements of respective rules.

Dynatis Pakistan (Pvt) Ltd, is GMP complaint as per certificate issued by DRAP, Lahore office on 01-07-2021.

Dynagab 75 mg Capsules' pharmaceutical equivalence has been established against the Lyrica oral Capsule that was approved (in December 2004) by the USFDA. The clinical particulars and pharmacological properties of Pregabalin, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy.

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.
Chemistry manufacturing and control is satisfactory as per CTD guidelines PE&R/GL/AF/004 effective 1st October 2020. However, the invoice submitted for Pregabalin batch number PG-0090419 (from which stability batches have been manufactured) is at the name of Indus Pharma Karachi.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above-mentioned product from the name of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi.**
b. **Approved registration of above-mentioned product in the name of M/s Dynatis Pakistan (Pvt) Ltd. Plot No. 710, Sundar Industrial Estate, Lahore.**
c. **Reference will be sent to Cost and Pricing division for confirmation of maximum retail price (MRP).**
d. **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.**
e. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
f. **New registration numbers are issued in cases where registration is cancelled from one manufacturer and fresh registration is issued in the name of another manufacturer. In response to decision of 312th meeting of Registration Board, Legal Affair's Division opined that same registration numbers shall be issued in such cases where no change in name/ title of registration holder/ manufacturer and management occurs. However, since, the instant case pertains to change in registration status of products from one DML to another DML without any change in management only, therefore, as per discussion regarding issuance of registration with same registration numbers, Registration Board decided to seek opinion from Legal Affairs Division, DRAP and advised to proceed accordingly.**

4.	Name, address of Applicant / Marketing Authorization Holder	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, Sundar Industrial Estate, Lahore, Pakistan
	Name, address of Manufacturing site.	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, 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. 22705 dated 17/08/2021
	Details of fee submitted	PKR 30,000/-: dated 16/06/2021
	The proposed proprietary name / brand name	Dynagab Capsule **100** mg (*Dynatis has submitted an NOC for transferring Dynagab Capsule 100 mg-Registration number 083778- from Indus Pharma Karachi to Dynatis Lahore dated 15th November 2021*)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin capsule: Pregabalin … 100 mg
	Pharmaceutical form of applied drug	Oral; Capsule; hard gelatin
	Pharmacotherapeutic Group of (API)	Anti-epileptics';
	Reference to Finished product specifications	Innovator

<table>
<tr><td></td><td>Proposed Pack size</td><td>10’s,14’s, 20’s, 30’s</td></tr>
<tr><td></td><td>Proposed unit price</td><td>As per SRO</td></tr>
<tr><td></td><td>The status in reference regulatory authorities</td><td>Lyrica Capsules 100 mg, manufactured by Pfizer Upjohn UK Limited, approved by US FDA</td></tr>
<tr><td></td><td>For generic drugs (me-too status)</td><td></td></tr>
<tr><td></td><td>GMP status of the Finished product manufacturer</td><td>cGMP certificate issued by FID Lahore Majida Mujahid Ref. No. 29/2021-DRAP (FID-2065251-174) dated 01-07-2021.</td></tr>
<tr><td></td><td>Name and address of API manufacturer.</td><td>Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India</td></tr>
<tr><td></td><td>Module-II (Quality Overall Summary)</td><td>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.</td></tr>
<tr><td></td><td>Module III (Drug Substance)</td><td>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</td></tr>
<tr><td></td><td>Stability studies</td><td>DS Pregabalin stability by DS Manufacturer Atlas Life Sciences
Accelerated: 40 ± 2 °C and 75 % ± 5 % RH,
Batches: 01: No. PG-035/13 Mfg. Date: 26-12-2013: 02: No. PG-036/13 Mfg. Date: 28-12-2013: 03: No. PG-037/13 Mfg. Date: 29-12-2013
Long term: 30 ± 2 °C and 65 % ± 5 % RH,
Batches: 01: No. PG-035/13 Mfg. Date: 26-12-2013: 02: No. PG-036/13 Mfg. Date: 28-12-2013: 03: No. PG-037/13 Mfg. Date: 29-12-2013</td></tr>
<tr><td></td><td>Module-III (Drug Product):</td><td>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.</td></tr>
<tr><td></td><td>Pharmaceutical equivalence and comparative dissolution profile</td><td>Submitted Comparative Dissolution Profile of:
<table>
<tr><th>Product</th><th>B #, Mfg. Date</th><th>Manuf.</th></tr>
<tr><td>Dynagab Capsule 100 mg</td><td>Batch No. TA002 Mfg. Date: Not specified in report</td><td>Dynatis Pakistan Pvt. Ltd., Lahore</td></tr>
<tr><td>Lyrica capsule 100 mg (in QOS firm has stated Lyrica 75 mg instead of 100 mg)</td><td>Batch No. EP0801 Mfg. Date: Not specified in report</td><td>Pfizer Upjohn UK Limited</td></tr>
</table>
Buffers Used: i. HCl Buffer pH 1.2
ii. Acetate Buffer pH 4.5
iii. Phosphate Buffer pH 6.8
<table>
<tr><th>Factor</th><th>pH 1.2</th><th>pH 4.5</th><th>pH 6.8</th></tr>
<tr><td>Difference Factor f1</td><td>Not calculated</td><td>Not calculated</td><td>Not calculated</td></tr>
<tr><td>Similarity Factor f2</td><td>Not calculated due as Pregabalin</td><td>Not calculated due as Pregabalin</td><td>Not calculated due as Pregabalin</td></tr>
</table></td></tr>
</table>

			dissolution in both reference and test products is more than 85 % after 15 minutes.	dissolution in both reference and test products is more than 85 % after 15 minutes.	dissolution in both reference and test products is more than 85 % after 15 minutes.
	Analytical method validation/verification of product	Method validation studies has been submitted including linearity, range, Accuracy (recovery), Precision (repeatability & intermediate precision), LOD & LOQ, Robustness, Solution stability, system suitability and specificity.			

STABILITY STUDY DATA			
Manufacturer of API	Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India		
API Lot No.	PG-0090419		
Description of Pack (Container closure system)	size 3 hard-gelatin capsule with dark yellow TR cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board 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.	TA001	TA002	EA003
Batch Size	6000 Capsules	6000 Capsules	6000 Capsules
Manufacturing Date	08-2020	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)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Food and Drug Administration, Gujrat State of India has issued GMP certificate to Altas Life Sciences Private Limited valid up to 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice no. 004 dated 25-04-2019 of Pregabalin batch number PG-0090419 to Indus Pharma, Karachi cleared by Assistant Director, DRAP Karachi office.
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:

The drug substance for Dynagab 100 mg Capsules is manufactured by Atlas Life Sciences Pvt Ltd 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India (GMP by FDA Gujrat, India) on inhouse specifications. Manufacturing and controls, comparability protocols, structural

characterization, and stability protocol has been submitted. Specification is considered adequate with respect to general monographs of USP and European Pharmacopoeias and inhouse specification sets by the DS manufacturer. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications except impurity estimation.

The drug product is capsule of 100 mg manufactured by Dynatis Pakistan (Pvt) Ltd., Lahore DML 000891 (Formulation) (size 3 hard-gelatin capsule with dark yellow TR cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board unit carton with leaf insert). The method of manufacturing is blend mixing and capsule filling with adequate in process controls. Submitted regulatory specifications have been validated and submitted stability data shows no degradation product at specified time points. Labelling is submitted that meets the requirements of respective rules.

Dynatis Pakistan (Pvt) Ltd., is GMP complaint as per certificate issued by DRAP, Lahore office on 01-07-2021.

Dynagab 100 mg Capsules' pharmaceutical equivalence has been established against the Lyrica oral Capsule that was approved (December 2004) by the USFD. The clinical particulars and pharmacological properties of Pregabalin, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy.

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.

Chemistry manufacturing and control is satisfactory as per CTD guidelines PE&R/GL/AF/004 effective 1st October 2020. However, the invoice submitted for Pregabalin batch number PG-0090419 (from which stability batches have been manufactured) is at the name of Indus Pharma Karachi.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above-mentioned product from the name of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi.**
b. **Approved registration of above-mentioned product in the name of M/s Dynatis Pakistan (Pvt) Ltd. Plot No. 710, Sundar Industrial Estate, Lahore.**
c. **Reference will be sent to Cost and Pricing division for confirmation of maximum retail price (MRP).**
d. **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.**
e. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
f. **New registration numbers are issued in cases where registration is cancelled from one manufacturer and fresh registration is issued in the name of another manufacturer. In response to decision of 312th meeting of Registration Board, Legal Affair's Division opined that same registration numbers shall be issued in such cases where no change in name/ title of registration holder/ manufacturer and management occurs. However, since, the instant case pertains to change in registration status of products from one DML to another DML without any change in management only, therefore, as per discussion regarding issuance of registration with same registration numbers, Registration Board decided to seek opinion from Legal Affairs Division, DRAP and advised to proceed accordingly.**

5.	Name, address of Applicant / Marketing Authorization Holder	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, Sundar Industrial Estate, Lahore, Pakistan
	Name, address of Manufacturing site.	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, 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. 23630 dated 27/08/2021
	Details of fee submitted	PKR 30,000/-: dated 16/06/2021
	The proposed proprietary name / brand name	Dynagab Capsule **1**50 mg (*Dynatis has submitted an NOC for transferring Dynagab Capsule 150 mg-Registration number 08377*9*- from Indus Pharma Karachi to Dynatis Lahore dated 15th November 2021*)
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin capsule: Pregabalin … 150 mg
	Pharmaceutical form of applied drug	Oral; Capsule; hard gelatin
	Pharmacotherapeutic Group of (API)	Anti-epileptics';
	Reference to Finished product specifications	Innovator
	Proposed Pack size	10's,14's, 20's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lyrica Capsules 150 mg, manufactured by Pfizer Upjohn UK Limited, approved by US FDA
	For generic drugs (me-too status)	
	GMP status of the Finished product manufacturer	cGMP certificate issued by FID Lahore Majida Mujahid Ref. No. 29/2021-DRAP (FID-2065251-174) dated 01-07-2021.
	Name and address of API manufacturer.	Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India
	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	DS Pregabalin stability by DS Manufacturer Atlas Life Sciences **Accelerated:** 40 ± 2 °C and 75 % ± 5 % RH, **Batches: 01:** No. PG-035/13 Mfg. Date: 26-12-2013: **02:** No. PG-036/13 Mfg. Date: 28-12-2013: **03:** No. PG-037/13 Mfg. Date: 29-12-2013 **Long term**: 30 ± 2 °C and 65 % ± 5 % RH, **Batches: 01:** No. PG-035/13 Mfg. Date: 26-12-2013: **02:** No. PG-036/13 Mfg. Date: 28-12-2013: **03:** No. PG-037/13 Mfg. Date: 29-12-2013
	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	Submitted Comparative Dissolution Profile of: **Product** | **B #, Mfg. Date** | **Manuf.** Dynagab Capsule 150 mg | Batch No. AU002 Mfg. Date: Not specified in report | Dynatis Pakistan Pvt. Ltd., Lahore Lyrica capsule 150 mg | Batch No. EP00825 Mfg. Date: Not specified in report | Pfizer Upjohn UK Limited Buffers Used: i. HCl Buffer pH 1.2 ii. Acetate Buffer pH 4.5 iii. Phosphate Buffer pH 6.8

Factor	pH 1.2	pH 4.5	pH 6.8
Difference Factor f1	Not calculated	Not calculated	Not calculated
Similarity Factor f2	Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.	Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.	Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.

	Analytical method validation/verification of product	Method validation studies has been submitted including linearity, range, Accuracy (recovery), Precision (repeatability & intermediate precision), LOD & LOQ, Robustness, Solution stability, system suitability and specificity.

STABILITY STUDY DATA

Manufacturer of API	Atlas Life Sciences Pvt. Ltd., 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India		
API Lot No.	PG-0090419		
Description of Pack (Container closure system)	size 2 hard-gelatin capsule with standard green OP cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board 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.	AU001	AU002	AU003
Batch Size	6000 Capsules	6000 Capsules	6000 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)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Food and Drug Administration, Gujrat State of India has issued GMP certificate to Altas Life Sciences Private Limited valid up to 10-02-2022.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice no. 004 dated 25-04-2019 of Pregabalin batch number PG-0090419 to Indus Pharma, Karachi cleared by Assistant Director, DRAP Karachi office.
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:

The drug substance for Dynagab 150 mg Capsules is manufactured by Atlas Life Sciences Pvt Ltd 3, Harshad Industrial Estate, Opp. Mamta Nagar, Bapunagar, Ahmedabad – 380024 Gujrat, India (GMP by FDA Gujrat, India) on inhouse specifications. Manufacturing and controls, comparability protocols, structural characterization, and stability protocol has been submitted. Specification is considered adequate with respect to general monographs of USP and European Pharmacopoeias and inhouse specification sets by the DS manufacturer. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications except impurity estimation.

The drug product is capsule of 150 mg manufactured by Dynatis Pakistan (Pvt) Ltd., Lahore DML 000891 (Formulation) (size 2 hard-gelatin capsule with standard green OP cap and white OP body containing white granular powder packed in 2 x 7's Alu-Alu blister packed in bleach board unit carton with leaf insert). The method of manufacturing is blend mixing and capsule filling with adequate in process controls. Submitted regulatory specifications have been validated and submitted stability data shows no degradation product at specified time points. Labelling is submitted that meets the requirements of respective rules.

Dynatis Pakistan (Pvt) Ltd., is GMP complaint as per certificate issued by DRAP, Lahore office on 01-07-2021.

Dynagab 150 mg Capsules' pharmaceutical equivalence has been established against the Lyrica oral Capsule that was approved (in December 2004) by the USFDA. The clinical particulars and pharmacological properties of Pregabalin, based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy.

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.

Chemistry manufacturing and control is satisfactory as per CTD guidelines PE&R/GL/AF/004 effective 1st October 2020. However, the invoice submitted for Pregabalin batch number PG-0090419 (from which stability batches have been manufactured) is at the name of Indus Pharma Karachi.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above-mentioned product from the name of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi.**
b. **Approved registration of above-mentioned product in the name of M/s Dynatis Pakistan (Pvt) Ltd. Plot No. 710, Sundar Industrial Estate, Lahore.**
c. **Reference will be sent to Cost and Pricing division for confirmation of maximum retail price (MRP).**
d. **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.**
e. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
f. **New registration numbers are issued in cases where registration is cancelled from one manufacturer and fresh registration is issued in the name of another manufacturer. In response to decision of 312th meeting of Registration Board, Legal Affair's Division opined that same registration numbers shall be issued in such cases where no change in name/ title of registration**

	holder/ manufacturer and management occurs. However, since, the instant case pertains to change in registration status of products from one DML to another DML without any change in management only, therefore, as per discussion regarding issuance of registration with same registration numbers, Registration Board decided to seek opinion from Legal Affairs Division, DRAP and advised to proceed accordingly.	
6.	Name, address of Applicant / Marketing Authorization Holder	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, Sundar Industrial Estate, Lahore, Pakistan
	Name, address of Manufacturing site.	Dynatis Pakistan (Pvt) Ltd., Plot no. 710, 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. 17416 dated 22/06/2021
	Details of fee submitted	PKR 20,000/-: 30/04/2021 PKR 10,000/-: 05/05/2021
	The proposed proprietary name / brand name	Misartan Tablets 20 mg (*Dynatis has submitted an NOC for transferring Misartan Tablets 20 mg-Registration number 055937- from Indus Pharma Karachi to Dynatis Lahore dated 27th May 2021*)
	Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Telmisartan … 20 mg
	Pharmaceutical form of applied drug	Oral; Tablet;
	Pharmacotherapeutic Group of (API)	Angiotension II Antagonist
	Reference to Finished product specification	USP
	Proposed Pack size	10’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Micardis 20 mg Tablet, manufactured by Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, CT 06877 USA approved by US FDA.
	For generic drugs (me-too status)	Telsitan 20 mg tablets Reg. No 044215, manufactured by Macter International Limited
	GMP status of the Finished product manufacturer	cGMP certificate issued by Additional Director Lahore Ref. No. 07/2020-DRAP (AD-1961363-1079) dated 02-01-2020.
	Name and address of API manufacturer.	Jiangsu Zhongbang Pharmaceutical Co., Ltd., 36 Shuanggao Rd., Goachun District, Nanjing, Jiangsu, 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.

<table>
<tr><td></td><td>Module III (Drug Substance)</td><td>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</td></tr>
<tr><td></td><td>Stability studies</td><td>DS Telmisartan stability by DS Manufacturer Jiangsu Zhongbang Pharmaceutical Co., Ltd
Accelerated: 40 ± 2 °C and 75 % ± 5 % RH,
Batches: 01: D1002-20131001 production date 29-10-2013: 02: No. D1002-20131002 production date 07/11/2013: 03: D1002-20131003 production date 10/11/2013
Long term: 30 ± 2 °C and 65 % ± 5 % RH,
Batches: 01: D1002-20131001 production date 29-10-2013: 02: No. D1002-20131002 production date 07/11/2013: 03: D1002-20131003 production date 10/11/2013
Forced degradation studies have also been performed.</td></tr>
<tr><td></td><td>Module-III (Drug Product):</td><td>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.</td></tr>
<tr><td></td><td>Pharmaceutical equivalence and comparative dissolution profile</td><td>Submitted Comparative Dissolution Profile of:
<table>
<tr><th>Product</th><th>B #, Mfg. Date</th><th>Manuf.</th></tr>
<tr><td>Misartan 20 mg Tablet</td><td>Batch No. 003
Mfg. Date: 08-2020</td><td>Dynatis Pakistan Pvt. Ltd., Lahore</td></tr>
<tr><td>Micardis 20 mg Tablet</td><td>Batch No. 26441
Mfg. Date: Oct 2019</td><td>Boehringer Ingelheim Pharmaceuticals, Germany</td></tr>
</table>
Buffers Used: i. HCl Buffer pH 1.2
ii. Acetate Buffer pH 4.5
iii. Phosphate Buffer pH 6.8
iv. Phosphate Buffer pH 7.5
(release medium)
<table>
<tr><th>Factor</th><th>pH 1.2</th><th>pH 4.5</th><th>pH 6.8</th></tr>
<tr><td>Difference Factor f1</td><td>Not calculated</td><td>Not calculated</td><td>Not calculated</td></tr>
<tr><td>Similarity Factor f2</td><td>Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.</td><td>Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.</td><td>Not calculated due as Pregabalin dissolution in both reference and test products is more than 85 % after 15 minutes.</td></tr>
</table></td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Method verification studies has been submitted including linearity, accuracy, precision, specificity and robustness.</td></tr>
</table>

STABILITY STUDY DATA

Manufacturer of API	Jiangsu Zhongbang Pharmaceutical Co., Ltd., 36 Shuanggao Rd., Goachun District, Nanjing, Jiangsu, China
API Lot No.	D10011-20190702
Description of Pack (Container closure system)	Alu Alu blister strip of 1 x 10's 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.	003	004	005
Batch Size	12000 Tablets	12000 Tablets	12000 Tablets
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	15-08-2020	19-08-2020	25-08-2020
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.	License issued by Jiangsu Drug Administration dated Dec 17 2020 with expiry date of Dec 16 2025 has been provided. Jiangsu Medical Products Administration website shows that inspection was conducted from 20-22 November 2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of to Indus Pharma, Karachi.
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:

The drug substance for Misartan Tablets 20 mg is manufactured Jiangsu Zhongbang Pharmaceutical Co., Ltd., 36 Shuanggao Rd., Goachun District, Nanjing, Jiangsu, China (Licensed and GMP by Jiangsu Medical Products Administration) on USP specifications. Manufacturing and controls, comparability protocols, structural characterization, and stability protocol has been submitted. Specification is considered adequate with respect to general monographs of USP and European Pharmacopoeias USP specification. Finished Pharmaceutical Product (FPP) manufacturer has also performed analysis of Drug Substance (DS) according to provided specifications except impurity estimation.

The drug product is Misartan Tablets 20 mg manufactured by Dynatis Pakistan (Pvt) Ltd., Lahore DML 000891 (Formulation) (white to off-white round biconvex uncoated tablets packed in 1 x 10's Alu-Alu blister packed in bleach board unit carton with leaf insert). The method of manufacturing is standard wet granulation and compression with adequate in process controls. Submitted regulatory specifications have been verified as per USP monograph and submitted stability data shows no degradation product at specified time points. Labelling is submitted that meets the requirements of respective rules.

Misartan 20mg Tablets' pharmaceutical equivalence has been established against the Micardis 20 mg Tablets approved (in November 1998) by the USFDA. The clinical particulars and pharmacological properties of the Telmisartan, also based on the reliance principle, are as per the reference regulatory authority's product. This product is mainly indicated for the treatment of hypertension.

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.
Chemistry manufacturing and control is satisfactory as per CTD guidelines PE&R/GL/AF/004 effective 1st October 2020. Telmisartan do not contain tetrazole group in its structure, therefore, EMA in its assessment report EMA/217823/2019 excluded Telmisartan from assessment of nitrosamine impurities procedure. However, the invoice submitted for Telmisartan (from which stability batches have been manufactured) is at the name of Indus Pharma Karachi.

Decision: Registration Board decided as follows:

a. **Cancellation of registration of above-mentioned product from the name of M/s Indus Pharma (Pvt) Ltd. Plot No. 26, 27, 63, 64, 65, 66 & 67 Sector 27 Korangi Industrial Area Karachi.**
b. **Approved registration of above-mentioned product in the name of M/s Dynatis Pakistan (Pvt) Ltd. Plot No. 710, Sundar Industrial Estate, Lahore.**
c. **Reference will be sent to Cost and Pricing division for confirmation of maximum retail price (MRP).**
d. **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.**
e. **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
f. **New registration numbers are issued in cases where registration is cancelled from one manufacturer and fresh registration is issued in the name of another manufacturer. In response to decision of 312th meeting of Registration Board, Legal Affair's Division opined that same registration numbers shall be issued in such cases where no change in name/ title of registration holder/ manufacturer and management occurs. However, since, the instant case pertains to change in registration status of products from one DML to another DML without any change in management only, therefore, as per discussion regarding issuance of registration with same registration numbers, Registration Board decided to seek opinion from Legal Affairs Division, DRAP and advised to proceed accordingly.**

ITEM NO:-1 **Following cases are not recommended by Expert Working Group on Veterinary Drugs.**

Case No. 01:- Registration of products containing Novaminsulfon/Dipyrone/ Metamizole for Veterinary Use.

Registration Board in its 289th meeting decided to call up all the firms, having registered veterinary products containing Novaminsulfon (metamizole), for personal hearing after serving them a show cause for cancellation of registration.

Initially, Registration Board in its 277th meeting held on 27-29th December, 2017 meeting, while rejecting registration applications of veterinary drugs containing Novaminsulfon, due to earlier decisions of cancelling registration of metamizole for being associated with serious adverse effects like agranulocytosis. Accordingly, show cause notices were issued to the firms having registrations of aforementioned drug formulation. A number of firms have responded with their point of view including request for personal hearings.

It has been discussed during 289th meeting, while considering registration applications of veterinary products containing "antipyrine", that Metamizole Sodium is an organic sodium salt of antipyine. Furthermore, it is pertinent to mention that a number of products are registered with DRAP having antipyrine as active pharmaceutical ingredient.

Registration Board in its 291st meeting referred the case to Expert Working Group on veterinary drugs for further deliberation.

DEPARTMENT OF
MEDICINES
VETERINARIANS **SPAIN**

1. BUSCAPINA COMPOSITUM VETERINARY USE solution for injection for horse.

Each ml contains:
Active substances:
Scopolamine butylbromide ..... 4.00 mg
(equivalent to 3.27 mg scopolamine)
Metamizole sodium .... 500.00 mg
(equivalent to 443.10 mg of metamizole

2. ESPASMODIAN solution for injection FOR Cattle and horses

Each ml contains:
Active substances:
Sodium metamyzole monohydrate..... 500.00 mg
(equivalent to 467.03 mg metamizol)
Scopolamine Butyl Bromide ..... 4.00 mg
(equivalent to 2.76 mg scopolamine)

Data access on 05-03-2021 from official website of Spanish authority .:: CIMAVET ::. Resultados de la búsqueda de medicamentos (aemps.es)

Recommendation of 10th EWG:-

The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Novaminsulfom/Dipyrone/ Metamizole for Veterinary drugs for being associated with serious adverse effects like agranulocytosis.

Decision:- On the recommendation of the Expert Working Group on Veterinary Drugs that drugs containing Novaminsulfom/Dipyrone/ Metamizole etc. for Veterinary drugs are associated with serious adverse effects like agranulocytosis; Registration Board considered and decided to issue show cause notices for cancellation of registration as per law.

Case No.2

1.	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, Anti-inflammatory
	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 3years or 36months a) 0111 Manufacturing dated March 2011 b) 0211 Manufacturing dated March 2011 c) 0311Manufacturing dated 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.
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Novaminsulfom/Dipyrone/ Metamizole for Veterinary drugs for being associated with serious adverse effects like agranulocytosis.* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	
2.	Name and address of manufacturer / Applicant	M/s. Izfaar Pharmaceutical Pvt Ltd. 542-A & B, Sundar Industrial Estate, Lahore.
	Brand Name +Dosage Form + Strength	Furol Powder
	Composition	Each gm contains:-

		Furazolidone…....950mg.
	Diary No. Date of R& I & fee	Dy. No.290; 7-9-2015; Rs.20,000/- (7-9-2015)
	Pharmacological Group	Antiprotozoal
	Type of Form	Form-5
	Finished product Specifications	In house specification
	Pack size & Demanded Price	20gm, 50gm, 100gm, 250gm, 500gm, 1000gm, 2.5kg, 5kg 10Kg, Decontrolled
	Approval status of product in Reference Regulatory Authorities	NA
	Me-too status (with strength and dosage form)	Furasym Powder by Syman Pharmaceuticals Reg # 023435
	GMP status	New Section Veterinary Powder (General & General Antibiotic)
	Remarks of the Evaluator	
	Previous Decision	Registration Board referred the case to Expert Working Group on Veterinary Drugs.
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs formulation containing Furazolidone due to strong potential of causing genotoxicity, cytotoxicity and possible residual effects* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	
3.	Name and address of Applicant	M/s. Huzaifa International Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan
	Detail of Drug Sale License	DSL by way of distribution no. 0011000 0001489 valid upto20-Nov-2019
	Name and address of manufacturer	M/s. Super's Diana S.L CTRA C. 17, km 17, 08150 Parets Del Valles, (Barcelona), Spain
	Marketing authorization holder	M/s Super's Diana S.L CTRA C. 17, km 17, 08150 Parets Del Valles, (Barcelona), Spain
	Name of exporting country	Spain
	Type of Form	Form 5-A
	Diary No. & Date of R& I	Dy. No 19409 Dated 30-10-2017
	Fee including differential fee	Rs. 100,000/- Dated 30-10-2017
	Brand Name +Dosage Form + Strength	ESPASMODIAN Solution for Injection
	Composition	Each 100ml contains:- Hyoscine (N-Butyl Bromide)……4gm Metamizole (Sodium)……..50gm
	Finished Product Specification	Innovator specification
	Pharmacological Group	Antispasmodic
	Shelf life	24Months
	Demanded Price	Decontrolled
	Pack size	20ml, 50ml, 100ml
	International availability	Spain
	Me-too status	N/A
	Stability studies	Firm has submitted long term (24 months) at 30°C 65% RH & accelerated (06 months) stability data at 40°C, 75% RH for three batches. (50ml, 100ml)
	Detail of certificates attached	Legalized GMP No. ES/073HV/17 date of inspection 16/02/2017 valid for three year from date of inspection. Legalized FSC dated 30th June 2017. Sole agency agreement between manufacturer M/s Super's Diana S.L CTRA C. 17, km 17, 08150 Parets Del Valles, (Barcelona), Spain and Importer M/s Huzaifa international

		commercial area, Aziz Bhatti town, Sargodha, Pakistan
	Previous Decisions:	Decision of 291st meeting of Registration Board: 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. Moreover, registration status of metamizole shall also be verified as generic product. Registration Board referred the case regarding the composition to the expert working group on veterinary drugs **(M-293)**.
	Firm submitted that our applied veterinary medicine Espasmodian Injection is mainly for use in Dogs and Horses. Target species as per Summary of Product Characteristics Horses, cattle, pigs, dogs. Generic/Me-too status not confirmed	
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Novaminsulfom/Dipyrone/ Metamizole for Veterinary drugs for being associated with serious adverse effects like agranulocytosis.* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	
4.	Name and address of manufacturer / Applicant	M/s. Evergreen Pharmaceuticals, 69-70/B, Main Glaxo Town, Industrial Area, 20th Km Ferozepur Road, Lahore.
	Brand Name +Dosage Form + Strength	Bromant-D Oral Powder
	Composition	Each 1000gm contains:- Doxycycline HCL…..…….200gm Tylosine Tartrate…….…...100gm Colistine Sulphate……500 MIU Bromhexine HCl……..…5gm Amantadine HCL……...40gm
	Diary No. Date of R& I & fee	Dy.No. 33575 dated 10-10-2018 Rs.20,000/- 10-10-2018
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	500gm, 1kg, 5kg,10kg,25kg: Decontrolled
	Me-too status	Bronco Mars Water Soluble Powder M/S D-Maarson Pharmaceuticals, (Reg # 072683)
	GMP status	Last GMP inspection conducted on 03-01-2018 and report concludes that panel recommend renewal of DML
	Remarks of the Evaluator	
	Previous Decision:	Registration Board deferred for consideration by expert working group.
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Amantadine in combination with antibiotic/ antibacterials in absence of any recognized scientific rational, regarding simultaneous use of antibiotic with antiviral drugs, all such combination are recommended to be withdrawn."* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	
5.	Name and address of manufacturer / Applicant	M/s. Manhattan Pharma. 209/3-B, Sector 5, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	MP-Nova Parenteral Solution
	Composition	Each ml contains:- Novaminsulfon……..……40mg Etilefrin as Hcl……..0.2mg Calcium Gluconate…….…..100mg

		Magnesium Gluconate……..…..10mg Sodium Salicylate…….…...7mg Nicotinamide……..…0.3mg Caffeine……...10mg Boric Acid……...10mg
	Diary No. Date of R& I & fee	Dy.No. 36693 dated 05-11-2018 Rs.20,000/- 06-11-2018
	Pharmacological Group	Analgesic, antipyretic, Energizing
	Type of Form	Form 5
	Finished product Specification	Manufacturer specifications
	Pack size & Demanded Price	Rs: 3510-/250ml
	Me-too status	NOVAFON FORTE INJECTION of M/s ZAKFAS PHARMACEUTICALS (Reg# 052325)
	GMP status	Last GMP inspection conducted on 11-05-2018 and report concludes that GMP compliance in Oral (Powder) and Oral Liquid section and Sterile injectable (General) found satisfactory. All the manufacturing activities in Sterile injectable areas (Antibiotic only) found suspended till the area is ready as per cGMP guidelines and further instruction by DRAP Islamabad.
	Remarks of the Evaluator	
	Previous Decision:	Registration Board deferred the case for expert working group consideration.
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Novaminsulfom/Dipyrone/ Metamizole for Veterinary drugs for being associated with serious adverse effects like agranulocytosis.* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	
6.	Name and address of manufacturer / Applicant	M/s. Vetz Pharmaceutical (Pvt) Ltd Plot # Q-1, S.I.T.E, Kotri, Sindh
	Brand Name +Dosage Form + Strength	Clorvetz Aerosol Spray
	Composition	Each 200 ml contains:- Chloramphenicol…..…..3.25gm Nitrofurazone ……0.15gm Gentian Violet..…..……0.15gm
	Diary No. Date of R& I & fee	Dy No. 24329 dated 19/11/2019 ; Rs. 20,000
	Pharmacological Group	Antibacterial / antiseptic
	Type of Form	Form-5
	Finished product Specification	Mfg specifications
	Pack size & Demanded Price	100 ml, 125 ml, 150 ml, 200 ml, 250 ml, 300 ml Decontrolled
	Me-too status	Clonigent Spray By M/s Star Labs, Reg. No. 023419
	GMP status	26 & 27-7-2019. Conclusion: Based on the above observation their current GMP compliance level is rated as good.
	Remarks of the Evaluator	
	Previous Decision:	Registration Board referred the case to expert working group on veterinary drugs for review of formulation (M-293).
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt chloramphenicol is not used in RRA for veterinary purpose except for its rare use in cats and dogs.* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	
7.	Name and address of manufacturer / Applicant	M/s. Hilton Pharma Pvt Ltd., Plot No. 13-14, Sector 15, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	Encohil Plus Oral Liquid

	Composition	Each 100ml contains:- Enrofloxacin……10gm Colistin sulphate…….3.5gm Amantadine Hcl…….4gm
	Diary No. Date of R& I & fee	Dy.No 7204 dated 27-05-2019 Rs.20,000/-, 24-05-2018
	Pharmacological Group	Antibacterial
	Type of Form	Form-5
	Finished product Specification	In-house
	Pack size & Demanded Price	250ml, 500ml, 100ml, 5000ml : Decontrolled
	Me-too status	Amantacol Oral Liquid Of M/S. Prix Pharmaceutica
	GMP status	Last GMP inspection conducted on 10-07-2019 and report concludes firm was considered to be operating at Good level on Compliance with GMP."
	Remarks of the Evaluator	
	Previous Decision:	Registration board deferred the case for consideration of expert Working group since applied formulation contains combination of antiviral and antibacterial.
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Amantadine in combination with antibiotic/ antibacterials in absence of any recognized scientific rational, regarding simultaneous use of antibiotic with antiviral drugs, all such combination are recommended to be withdrawn."* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	

8.	International Pharma Labs, Raiwind Road, Lahore	I-Nova-40 injection Solution IM/IV Each ml contains Novaminsulfon…40mg Etilefrine…….0.2mg Calcium Gluconate…...100mg Magnesium Gluconate…….10mg Sodium Salicylate……...7mg Nicotinamide.0.30mg Caffein…..……10mg Boric Acid…...10mg Sorbitol……...200mg Sodium Oxybenzylphosphinic acid……5mg Methyl Parahydroxy Benzoate…….0,7mg	Last inspection report conducted on 01/04/2016 The firm is in the progress of further up gradation with respect to the minor observations.	Rs 12000 fee is not in original, Rs 8000, fee is missing. 10ml 20ml 50ml 100ml 250ml 450ml 500ml 1000ml	Deferred for review of formulation by Dr. Qurban Ali, Member Registration Board
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt Novaminsulfom/Dipyrone/ Metamizole for Veterinary drugs for being associated with serious adverse effects like agranulocytosis.* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**				

9.	Name and address of manufacturer / Applicant	Kayans Pharmaceuticals Plot No. 31,32 Main Road RCCI Industrial Estate Rawat Rawalpindi
	Brand Name +Dosage Form + Strength	Fedro Spray
	Composition	Each ml contains:- Chloramphenicol …… 16.25mg Nitrofurazone ……. 0.75mg Gentian Violet …… 0.75mg

	Diary No. Date of R& I & fee	Dy No.14280: 26.05.2021 PKR. 30,000/-; 26.05.2021
	Pharmacological Group	Antibiotics, Antiseptic
	Type of Form	Form 5
	Finished product Specifications	Manufacturers Specification
	Pack size & Demanded Price	200ml/Decontrolled
	Approval status of product in Reference Regulatory Authorities	N/A
	Me-too status	Clonigent Spray (Star Labs) Reg # 023419
	GMP status	Topical Spray Section (Veterinary)-General Inspection for grant of License conducted on 12/04/2021 Panel unanimously recommended for Grant of License.
	Remarks of the Evaluator	
	Recommendation of 10th EWG:- *The Expert Working Group on Veterinary Drugs recommended the cancellation of registration of already registered drugs containing salt chloramphenicol is not used in RRA for veterinary purpose except for its rare use in cats and dogs.* **Decision: - Registration Board considered and deferred for consideration in the next Board meeting.**	

ITEM NO.II

Following cases are recommended by Expert Working Group on Veterinary Drugs.

Case No 01:- Registration of products containing Oxytocin Multi-Dose Vials for Veterinary Use.

The Registration Board in its 278th meeting held on 29-31st January, 2018 while considering their agenda item viz "Manufacture & Sale of Adulterated & Sub-Standard "Oxytocin Injection (for vet only)", *interalia*, decided as under: -

"Registration Board advised PE&R Division to present case regarding alleged use of Oxytocin multi-dose vials for enhancement of milk production in the animals."

The Board agreed to issue show cause notice of multi-dose vials on the same lines which have been adopted by India. They allow only one mL Oxytocin ampoule for human use only. Later, Registration Board in its 286th meeting was informed that show cause notices have been issued to following 25 firms having registration of Oxytocin Multi-dose vials.

S. No.	Name of Firm's
1.	M/s. Elko Organization (Pvt.) Ltd, Karachi.
2.	M/s. International Pharma Labs. Lahore.
3.	M/s. Intervac (Pvt) Ltd., Sheikhupura.
4.	M/s. Biogen Pharma, Chakbeli Road, Rawat.
5.	M/s. Epoch Pharmaceuticals, Karachi.
6.	M/s. Zakfas Pharmaceuticals Pvt Ltd., Multan.
7.	M/s. Tabros Pharma (Pvt) Ltd., Karachi.
8.	M/s. Dosaco Laboratories, Lahore.
9.	M/s. Geofman Pharmaceuticals, Karachi.
10.	M/s. Vetcon Pharmaceuticals Pvt. Ltd., Azad Kashmir.
11.	M/s. Venus Pharma, Lahore.
12.	M/s. Imran & Company, Karachi.
13.	M/s. ISIS Pharmaceuticals & Chemical Works, (Formerly M/s. Krka-Pak Pharmaceutical), Karachi.
14.	M/s. Kakasian Pharmaceuticals (Pvt) Ltd., Lahore.
15.	M/s. Amrose Pharmaceuticals, Karachi.
16.	M/s. Lawarlance Pharma, Lahore.
17.	M/s. S.J & G Fazul Ellahie (Pvt.) Ltd, Karachi.
18.	M/s. Sanna Laboratories, Faisalabad.
19.	M/s. Biorex Pharmaceuticals, Islamabad.
20.	M/s. Rex Pharmaceuticals, Karachi.
21.	M/s. Avicenna Laboratories (Pvt) Ltd., Sheikhupura.
22.	M/s. Jfrin Pharmaceutical Laboratories, Balochistan.

S. No.	Name of Firm's
23.	M/s. Manhattan Pharma, Karachi
24.	M/s. Alina Combine Pakistan (Pvt) Ltd., Karachi.
25.	M/s. Eros Pharmaceuticals (Private) Limited, Karachi.

So far replies from 11 firms have been received wherein they have responded with their point of view including request for personal hearings.

The salient points, of the responses received are summarized as under:-

i) Oxytocin Injection is not used for the enhancement of milk product in dairy animal. Oxytocin is a pituitary hormone that has very short span of effectiveness -it is absorbed immediately after natural release or injection it lasts around three minutes in the bloodstream of a healthy animal before it is completely absorbed and metabolized.

ii) Oxytocin is used as uterine contractor to precipitate and accelerate normal parturition and postpartum evacuation of uterine debris. In surgery it may be used postoperatively following cesarean section to facilitate involution and resistance to the large inflow of blood. It contracts smooth muscle cells of the mammary gland for milk letdown if the udder is in proper physiological state.

iii) Oxytocin is not intended for milk enhancement but to facilitate milking letdown process and to maximize the efficient removal of milk. Oxytocin is used to letdown the milk worldwide.

iv) A firm has requested for providing the necessary record.

v) Instead of cancelling the registration and manufacturing of this product, its misuse be stopped by regulating prescription and sales.

vi) A number of firms have requested chance to be heard in person.

Decision of 288th meeting of RB held on 14th-15th February, 2019:-

Keeping in view the above stated position, Registration Board decided to call up all the firms, having registration of multi-dose vials containing Oxytocin in veterinary, for personal hearing before Registration Board.

Expert Working Group meeting on Veterinary Drugs Held on 13th May, 2019.

The meeting was conducted on the issue of alleged misuse of Oxytocin multi-dose vials in veterinary for the purpose of milk production. The matter was deliberated extensively by the participants. Decisions/discussion is as follow;

a. Dr. Muhammad Akram informed the committee that Oxytocin is, primarily, used in veterinary for the purpose of milk letdown. He further informed that the half life of Oxytocin Injection is around 02 minutes and withdrawal period of oxytocin in milk and meat is zero hours and zero days respectively. About 1-2cc of the injection is used for milk letdown.

b. The Committee/participants decided to expand the consultation horizon to a national consultation process/level and include the following relevant/technical experts in order to probe the matter in detail and a meeting in this regard shall be convened in near future;
   i. Human and veterinary Endocrinologists.
   ii. Expert from M/o. Food Security.
   iii. Director General's of livestock departments of all provinces.

USFDA/Dailymed:

As per USFDA/Dailymed data base Oxytocin Injection of Bimeda Animal Health Limited 1B The Herbert Building the Park Carrick mines, Dublin 18, **Ireland** Application Number: 200 328 **HOW SUPPLIED:** 100mL multiple dose vials. Link accessed on dated 12-10-2020
https://animaldrugsatfda.fda.gov/adafda/views/#/home/previewsearch/200-328
https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=29aa28ea-36ef-431c-af1d-4aeec4c0e82a

As per Dailymed data base Oxytocin Injection manufactured by M/s. Bimeda-MTC Animal Health Inc. Cambridge, on Canada manufactured for M/s Aspen Veterinary Resources, ltd, USA **How supplied**:100 mL multiple dose vials. Link accessed on dated 12-10-2020
https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=97113a71-c02e-41b7-950b-6d4ebe5e7156&type=display

The case was discussed in its 49th Post Registration Variation Committee (PRVC) was held on 23-10-2020. The Committee evaluated the case and Chairman Registration Board, on the recommendations of the committee, decided to refer the case to expert committee on veterinary drugs with status of RRA and indications for evaluation and framing recommendation for consideration of Registration Board.

Manufacturer	Brand & Composition	Indication	Target species
Manufacturer: CENAVISA SL Camí Pedra Estela s / n 43205 REUS (Tarragona) **Spain**	DILA-PART 10 IU / ml solution for injection Each ml contains: **Active substance:** Oxytocin .... 10 UI	- Induction to labor. - Uterine inertia or atony. - Involution of the uterus after cesarean sections and decreased bleeding. - Expulsion of the placenta and remnants of exudates after delivery. - Initiation of lactation after childbirth. - Sow agalactia. - Pyometritis and chronic endometritis to cause the expulsion of exudates. - Adjuvant treatments to antibiotic therapy for acute and chronic mastitis, to cause the expulsion of residues and facilitate drainage	Cows, sheep, sows and mares Formats: Box with 1 vial of 100 ml Box with 1 vial of 250 ml Box with 1 vial of 500 ml Box with 10 vials of 100 ml Box with 10 vials of 250 ml Box with 12 vials of 500 ml
Animal drugs USFDA access on dated 10-03-2021 Animal Drugs @ FDA			
Zoetis Inc. 333 Portage St. Kalamazoo, Michigan 49007	**OXYTOCIN INJECTION-oxytocin liquid** Each milliliter of oxytocin injection contains 20 U.S.P. units of oxytocin	**Cattle (sows)** Milk letdown. It will contract smooth muscle cells of the mammary gland for milk letdown if the udder is in proper physiological state. **Sheep (ewes)** Obstetrical. Oxytocin may be used as a uterine contractor to precipitate and accelerate normal parturition and postpartum evacuation of uterine debris. In surgery it may be used postoperatively following cesarean section to facilitate involution and resistance to the large inflow of blood.	Cattle : Cows Equids : Horse, Mares Sheep (Domestic) : Sheep, Ewes Dogs : Dog, No Use Class Stated Or Implied Swine : Sows Cats (Domestic) : Cat, Queens

Recommendation of 10th EWG:-

The Expert Working Group on Veterinary Drugs deliberate the case and decided to allow for granting multidose vials for Oxytocin as per following details:

Oxytocin .... 10 UI upto 500ml as per Spanish authority approval or any pack size available in any other RRA.

Oxytocin .... 20 UI upto 50ml as per Australian Pesticides and Veterinary medicine Authority approval or any pack size available in any other RRA.

https://cimavet.aemps.es/cimavet/publico/detalle.html?nregistro=2357%20ESP

Public Chemical Registration Information System Search - portal.apvma.gov.au

Decision:- Registration Board considered and endorsed the decision of Expert Working Group on Veterinary Drugs decision.

Case No.02:- Request For Grant of Additional Pack Sizes For Already Registered Veterinary Drugs.

M/s. Wimits Pharmaceuticals, Lahore has applied for approval of additional packs of their registered veterinary drug as per details mentioned against each:-

S.No.	Regn. No.	Name of Drug(s)/Composition	Already Granted Pack Size(s)	Demanded Additional Pack(s)	Justification
1.	087092	Minvet Granules Each Kg contains:- Vitamin A……..…0.8gm Vitamin D3…….0.16gm Vitamin E……0.38gm Vitamin B1……...1.0gm	500g 1Kg	5 Kg 10 Kg 20 Kg	Due to market packing 5 Kg,10 Kg & 20 Kg granules

		Vitamin B2…….1.25gm Vitamin B12…….0.001gm Vitamin B3…….6.25gm Copper Sulphate…….0.25gm Magnesium Sulphate…….25gm Calcium Chloride…….....0.023gm Zinc Sulphate…….....2.17gm Manganese Sulphate…….....10gm Potassium Iodide…….....0.5gm Sodium Selenite…….....0.01gm Phosphorus…….....150mg Sodium Chloride…….....120gm VitaminB6…….....4gm (As per Innovator's Specification*)			

M/s. Wimits Pharmaceuticals, Plot No.129, Sunder Industrial Estate (P.I.E) Raiwind Road, Lahore has deposited the required fee of Rs.5,000 x 3 = Rs.15,000/- and submitted following supporting documents:-

(i) Copy of registration letter.
(ii) Affidavit.
(iii) Copy of Drug Manufacturing License.
(iv) Copy of CRF.
(v) Label.

The demanded packs are not given to other firms.

Registration Board in its 283rd meeting decided to referred the case to Expert Working Group on Veterinary drugs for further consideration. The Expert Working Group in its 5th meeting of Expert Working Group on Veterinary Drugs deferred the request of additional packs for getting additional information regarding target species and confirmation of availability of manufacturing facility for the product. Accordingly letter was issued to M/s. Wimits Pharmaceuticals, Lahore. In response the firm has provided manufacturing facility of Minvet Granules. The details are as under:-

Sr. No.	Name	Code	Capacity
1.	Ribbon Blade Mixer	BL/VET/001	500Kg
2.	Rotary Granulator	BL/VET/002	500Kg
3.	Fluidized Bed Dryer	BL/VET/003	100Kg/2hrs
4.	Fluidized Bed Dryer	BL/VET/012	500Kg/2hrs
5.	Oscillating Granulator	BL/VET/004	500Kg
6.	Double Cone Mixer	BL/VET/005	500Kg
7.	Pouch Sealer	PW/VET/017	

Target species for commercial forming is Buffalos and Cows.

Recommendation of 10th EWG:-

The Expert Working Group on Veterinary Drugs recommended to approve additional pack sizes upto 25Kg subject to provision of requisite manufacturing facility/equipment of demand pack size and stability data by the firm.

Decision:- Registration Board considered and defer the case for provision of requisite manufacturing facility/equipment of demand pack size and stability data by the firm.

Case No. 03:- Request of M/s. Hilton Pharma (Pvt) Ltd., Karachi for Grant of Additional Packs for their already Registered Veterinary Drugs.

M/s. Hilton Pharma (Pvt) Ltd., Karachi 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 with renewal	Justification
1.	026467	Beloran Disinfectant Solution Each 1000ml contains:- Benzalkonium Chloride 50%	1000ml	5 Litre 10 Litre 25 Litre	24-02-2001 02-09-2015	*Due to market needs and cost*

		Solution……800gm				*effectiveness.*

M/s. Hilton Pharma (Pvt) Ltd., Karachi has deposited the required fee of Rs.5000 x 3 = Rs. 15,000/- and submitted following supporting documents:-

(i) Copy of initial registration letter.
(ii) Renewal status.
(iii) Copy of additional packs already granted.
(iv) Justification for approval of additional packs.
(v) Undertaking.
(vi) GMP inspection conducted by DRAP conducted on 17-07-2018.

The demanded packs are not given to other firms. Registration Board in its 289th meeting deferred the case for review of the product/molecule by expert working group on veterinary drugs.

Recommendation of 10th EWG:-

The Expert Working Group on Veterinary Drugs recommended to approve additional pack sizes i.e. upto 10Litre subject to provision of requisite manufacturing facility/equipment of demand pack size and stability data by the firm.

Decision:- Registration Board considered and defer the case for provision of requisite manufacturing facility/equipment of demand pack size and stability data by the firm.

Case No. 04: Deferred cases having already available generic, referred to EWG in different meetings of Registration Board

Recommendation of 10th EWG:-

The Expert Working Group deliberated the matter for registration of generic drugs and decided that as per policy/ practice of Registration Board for approving registration of veterinary drugs having already registered generic/me-too may continue for a time being. However, EWG recommended to examine & review the possibility of drawing RRA's list for veterinary formulation standardization.

Decision:- Registration Board considered and endorsed the decision of EWG on veterinary drugs.

ITEM NO.III BIOLOGICAL CASES

Registration Board in its different meetings referred the following products of below mentioned firms to Expert Working Group on Veterinary Drugs as per following details:

Sr. No	Importer/ Applicant	Manufacturer	Brand Name & Composition	Decision
1.	M/s. Vet Line International, Lahore.	M/s. Ceva-Phylaxia Veterinary Biologicals Co. Ltd., 1107 Budapest, Szallass u.5. Hungary.	**ITA ND+IB+EDS+CORABC** Each dose contains: Newcastle disease virus, strain NDV-"SZ" La Sota……induced min. 6 log2HI with 1 dose or min. 4log2HI with 1/50 dose or min. 50PD50 Infectious bronchitis virus, strain "M-41"… induced min. 4.4 log2 HI Egg drop syndrome'76 virus, strain "B88/78"…….. induced min. 7 log2 HI Avibacterium paragallinarum serotype A…. min. 7 log 10 CFU* before inactivation Avibacterium paragallinarum serotype B…. min. 7 log 10 CFU* before inactivation Avibacterium paragallinarum serotype C…. min. 7 log 10 CFU* before inactivation	**M-284** *Registration Board decided to refer the case to expert working group on veterinary drugs regarding the non-availability of product in country of origin and advised the firm to submit accelerated stability data of 3 batches for six months.*

			*Colony Forming Unit	
2.	M/s. Vety Care (Pvt.) Ltd. Plot No. 77, Street No.6, I-10/3 Islamabad.	M/s. Intervet International B.V. Wim de Korverstraat, 5831 AN Boxmeer, The Netherlands.	**Nobivac Tricat Trio** Lyophilisate and solvent for suspension for injection **After Freeze-drying** Each dose contains: Live FCV strain F9……at least 4.6 log10 PFU Live FVR strain G2620A…….at least 5.2 log10 PFU Live FPLV strain MW-1……..at least 4.3 log10 TCID50 **Nobivac Solvent:** Each ml contains: Disodium phosphate dihydrate..0.31mg Potassium dihydrogen Phosphate……0.21mg Water for injections to……..999.16 mg	**M-292:** *Registration Board decided to refer the case to expert working group on veterinary drugs regarding the prevalence of strains and advised the firm to submit valid legalized CoPP indicating product availability in country of origin and European Union Guidelines regarding stability studies.*
3.			**Innovax ND-IBD** Each dose(ml) contains: Live Herpesvirus of turkey strain HPV 360*….at least 103.3PFU** * HPV 360 is a HVT-based recombinant encoding the NDV F protein and the IBDV VP2 protein. **Plaque Forming Units	**M-292** *Registration Board decided to refer the case to expert working group on veterinary drugs regarding the prevalence of strains and advised the firm to submit legalized evidence of product availability in reference regulatory authorities and European Union Guidelines regarding stability studies.*
4.			**Nobilis MS Live** <u>Before Freeze-drying</u> Each dose(ml) contains: Live attenuated *Mycoplasma synoviae strain* MS1……0.67ml <u>After Freeze-drying</u> Each dose contains: Live attenuated *Mycoplasma synoviae strain* MS1….≥106.5 CFU* and ≤108.0 CFU *Colony Forming Units	**M-292** *Registration Board decided to refer the case to expert working group on veterinary drugs regarding the prevalence of strains and advised the firm to submit valid legalized CoPP indicating product availability in country of origin and European Union Guidelines regarding stability studies.*
5.			**Nobilis IB Primo QX** Lyophilisate for suspension for spray Each dose of reconstituted vaccine contains:	**M-292** *Registration Board decided to refer the case to expert working group on veterinary*

			Live attenuated avian infectious bronchitis virus, strain D388…104.0-105.5 EID50* *50% egg infective dose	*drugs regarding the prevalence of strains and advised the firm to submit the European Union Guidelines regarding stability studies.*
6.	M/s. Hi-Tech Pharmaceuticals, , Lahore.	M/s. Zoetis Inc. 2000, Rockford Road, Charles City, IA 50616, USA	**Poulvac SE-ND-IB** Newcastle Bronchitis Vaccine, Mass Type, Killed Virus, Salmonella Enteritidis Bacterin Each 0.3mL dose contains: *S. Enteritidis* – Strain D1758, Phage 4 ≥ 5.0 x 10^7 CFU per dose at release *S. Enteritidis* – Strain Se.ceb.50, Phage 8 ≥ 5.0 x 10^7 CFU per dose at release *S. Enteritidis* – Strain 52-1, Phage 13a ≥ 5.0 x 10^7 CFU per dose at release Newcastle Disease Virus – Bearing Fluids ≥ $10^{7.8}$ EID_{50} per dose at release Bronchitis Virus – Bearing Fluids ≥ $10^{6.9}$ EID_{50} per dose at release	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.
7.	M/s Hipra Pakistan Pvt. Limited, Pakistan	**Product License Holder:** M/s Laboratorios HIPRA, S.A, Avda. La Selva, 135 17170 Amer (Girona) Spain. **Manufacturer:** M/s Laboratorios HIPRA, S.A, Carretera C-63, Km 48,300, Poligono Industrial EI Rieral, 17170 Amer (Girona), Spain (Also responsible for primary packaging)	**NASYM**, Lyophilisate and solvent for suspension for injection or nasal spray **25 doses vial** Each dose of 2ml contains: : Live attenuated bovine respiratory syncytial virus, strain(BRSV) strain Lym-56.....$10^{4.7}$-$10^{6.5}$ $CCID_{50}$ * *$CCID_{50}$: Cell Culture Infectious Dose, 50 % equivalent	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.
8.			**NASYM**, Lyophilisate and solvent for suspension for injection or nasal spray **5 doses vial** Each dose of 2ml contains: : Live attenuated bovine respiratory syncytial virus, strain(BRSV) strain Lym-56….$10^{4.7}$-$10^{6.5}$ $CCID_{50}$ * *CCID50 : Cell Culture Infectious Dose, 50 % equivalent	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.
9.	M/s. Vet Line International, Lahore.	M/s. Zhengzhou Bio-pharmaceutical Factory of QYH BIOTECH COMPANY LIMITED, , P.R. China.	**Newcastle Disease, Infectious Bronchitis, Egg Drop Syndrome and Avian Influenza (H9N2 Subtype) Vaccine** Each dose (0.5ml) contains: Inactivated Newcastle Disease	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.

			Virus La Sota Strain……..≥$10^{8.0}$ EID_{50} Infectious Bronchitis Virus M41 Strain……..≥$10^{6.0}$ EID_{50} Egg Drop Syndrome Virus AV-127 Strain……..≥2000HA Avian Influenza virus H9N2 subtype S2 strain…..≥$10^{7.5}$ EID_{50}	
10.	M/s. ICI Pakistan Ltd, Karachi	M/s. Choong Ang Vaccine Laboratories Co., Ltd., Korea	**PoulShot® IB-Castle** Lyophilized Solution Each dose contains: Newcastle Disease virus (NDV, NDRL0901 strain) ≥ $10^{6.0}EID_{50}$ Infectious bronchitis virus (IBV, AVR1/08 strain) : ≥ $10^{6.0}EID_{50}$	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.
11.	-do-	-do-	**PoulShot® Gumboro** Lyophilized Solution Each dose contains: Infectious bursal disease virus (IBDV, LZD 228-JAC3 strain) : ≥ $10^{2.0}TCID_{50}$	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.
12.	-do-	-do-	**PoulShot® Qx Flu-5** Injectable Solution Each dose contains: Newcastle disease virus (NDV, LaSota strain) ≥ $10^{8.0}EID_{50}$ Infectious bronchitis virus (IBV, KM91 strain) ≥ $10^{6.0}EID_{50}$ Infectious bronchitis virus (IBV, ADL05258 strain) ≥ $10^{6.0}EID_{50}$ Egg drop syndrome virus (EDSV, K11 strain) ≥ $10^{5.5}EID_{50}$ Avian influenza virus (AIV H9N2, 01310 strain) ≥ $10^{8.0}EID_{50}$	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.
13.	M/s. Huzaifa International, Sargodha	M/s. Vetal Hayvan Sagligi Urunleri A.S (Vetal Animal Health Products S.A) ,Turkey	**TEYLOVAC** Vaccine Live attenuated Freeze dried Theileria Annulata cells based vaccine with diluent Each dose of vaccine contains Theileria annulata…..1x10^{7} cells	**M-307:** Registration Board referred the case to Expert Working Group on Veterinary Drugs.

Recommendation of 10th EWG: -

(i) *The Expert Working Group on Veterinary Drugs decided to reject he product at Sr.No.1.*

(ii) *The Expert Working Group on Veterinary Drugs recommended the product at Sr. No.4 & 13 for the registration.*

(iii) *For products at Sr.No.2-3 & 5-12 deferred for expert opinion from Ministry of National Food Security & Research, Islamabad.*

Proceeding:

During the proceedings of the Board, veterinary expert Dr. Qurban Ali, Member Registration Former Director General, National Veterinary Laboratories, Islamabad apprised the Board that Theileria disease is of tropical countries and not that of countries of reference regulatory authorities so availability of Theileria vaccine will be helpful for animal health as no specific treatment is available in Pakistan.

Dr. Muhammad Akram, (Co-opted Member) Dy. Animal Husbandry Commissioner, M/o National Food Security & Research, Islam also reiterated that Theileria vaccine is highly needed for animal health for Pakistan so, it should be registered and be made available ir-respective of approval status by reference authorities.

Furthermore, the Board was also apprised that firm has also submitted following recommendations with the registration dossier:

a. A letter from Dr. Aamer Bin Zahur Director General National Veterinary Lab. Islamabad Pakistan wherein the said product was recommended to be registered for controlling Theileriosis in livestock population of Pakistan as no vaccine is available for prevention and control of said disease.
b. A letter from Dr. Riasat Waseemullah Assistant Animal Husbandry Commissioner Islamabad Pakistan wherein the said product was recommended for import to prevent Theileriosis.
c. A letter from Prof. Dr. Muhammad Fiaz Qamar Chairman Department of Pathobiology College of Veterinary & Animal Sciences Jhang Pakistan wherein the said product was recommended to be registered for controlling Theileriosis in livestock population of Pakistan as no vaccine is available for prevention and control of said disease.

Decision:- Keeping in view the recommendation of EWG and discussion during the meeting, Board decided as under:

a. Approved the product at S.No. 4 namely Nobilis MS Live vaccine as same strains are already registered.
b. Approved the product at S.No. 13 namely TEYLOVAC Vaccine as product is highly needed for veterinary use in Pakistan.
c. Rejected the product at S.No. 1 namely ITA ND+IB+EDS+CORABC vaccine as the said product is not available/ on free sale in country of origin.
d. Referred the products at S.No. 2-3 & 5-12 to Ministry of National Food Security & Research, Islamabad for comments regarding the need of vaccine, prevalence of disease and immunological relevance of the strain in Pakistan.

Case No. 05:- Registration of Drugs under the Drugs Act, 1976.

M/s. ICI Pakistan Limited, Life Sciences, 45-KM, Off. Multan Road, Lahore has requested for contract manufacturing from import to local manufacturing of their following already registered products from M/s. Selmore Pharmaceuticals (Pvt) Ltd., 36-Km, Multan Road, Lahore as per detailed below.

S. No.	Regn. No.	Name of Drug(s)/Composition	Pack Size(s)
1.	027462	Amoxi-Vet Injection Each ml contains:- Amoxycillin (as Trihydrate) equivalent to 150 Amoxycillin base	50ml
2.	027462	Amoxi-Vet Injection Each ml contains:- Amoxycillin (as Trihydrate) equivalent to 150 Amoxycillin base	100ml

Registration Board in its 307th meeting approved the request of M/s. ICI Pakistan Ltd., Karachi for change of status of above products from finished import to local contract manufacturing by M/s. Selmore Pharmaceuticals (Pvt) Ltd., 36-Km, Multan Road, Lahore at same terms and conditions.

During processing of registration letter it was observed that above mentioned imported veterinary drugs registered in finished form on the basis of Drug Sale License and transfer from import to local drug manufacturing license to contract manufacturing from M/s. Selmore Pharmaceuticals (Pvt) Ltd., 36-Km, Multan Road, Lahore at same terms and conditions. So cancellation from DSL and approval on new DML will be required.

Decision: Registration Board considered and decided as under:

a. Cancelled the registration of above-mentioned drugs from Drug Sales License of M/s. ICI Pakistan Ltd., Karachi.
b. Approved the above-mentioned drugs in the name of M/s. ICI Pakistan Limited, Life Sciences, 45-KM, Off. Multan Road, Lahore on Drug Manufacturing License and local contract manufacturing by M/s. Selmore Pharmaceuticals (Pvt) Ltd., 36-Km, Multan Road, Lahore.

Case No.01. REQUEST OF M/S PFIZER PAKISTAN LIMITED KARACHI FOR REGISTRATION OF PRODUCT FROM M/S CARE PHARMA TO THEIR NAME.

M/s Pfizer Pakistan Limited B-2, SITE, Karachi has applied for registration of following already registered products from M/s Care Pharma to their name as per details given below: -

Reg. No.	Name & Composition (as per transfer reg. letter 25-11-2008)	Existing approved Manufacturing Site (as per transfer reg. letter 25-11-2008)	New Proposed Product License Holder (as per COPP)	New Proposed Site / Manufacturer (as per COPP)
016150	DBL Leucovarin Calcium Injection 15mg/ 2ml Each 2ml contains: Folinic Acid 15mg as calcium salt	M/s Hospira Australia Pvt. Ltd	M/s Pfizer Australia Pvt. Ltd. Level 17 151 Clarence Street Sydney NSW 2000 Australia	M/s. Wasserburger Arzneimittelwerk GmbH Herderstrasse 2 Wasserburg Germany

The firm has submitted the following supporting documents: -

i. Fee of Rs.150,000 dated 30-08-2021
ii. Applications on Form-5F
iii. Copy of initial registration letter 27-11-1994 and transfer of reg. letter dated 25-11-2008. Last Renewal submission dated 20-11-2018.
iv. Original & legalized COPPs issued by TGA for above product dated 12-05-2021 showing the freely availability of product in exporting country and GMP compliant status of the product).
v. Document confirming NOC (issued within last 6 Months) from existing registration holder permitting for registration of product to another importer.
vi. Letter of Authorization from product license holder.

Decision: Keeping in view above position, Registration Board considered case and decided as follow;

a. Cancelled the registration of following product from the name of M/s Care Pharma International (Pvt) Ltd, Karachi.

S.No	Reg. No.	Name & Composition
1.	**016150**	**DBL Leucovarin Calcium Injection 15mg/ 2ml Each 2ml contains: Folinic Acid 15mg as calcium salt**

b. Approved the registration of above product in the name of M/s Pfizer Pakistan Limited, B-2, SITE, Karachi as per policy for imported finished drug registration (in accordance with details of composition and manufacturer as per CoPP).

c. A reference shall be sent to Costing & Pricing Division for their comments regarding MRP of the said product.

Case No.02. REQUEST OF M/S PFIZER PAKISTAN LIMITED, KARACHI FOR PERMISSION TO IMPORT INTERNATIONAL PACKS OF THEIR REGISTERED PRODUCTS.

M/s Pfizer Pakistan Limited, Karachi has stated to import product in a limited quantity (300 International packs) of **Xeljanz Film Coated Tablets 5mg** (Reg. No. 106849) due to Covid-19 emergency situation and dire product need highlighted by Doctors and Patients, as they are unable to provide this medicine in country specific packs any time soon.

The firm will import International packs with following components on outer box of product printed address through laser jet as per labeling and packaging rules 1986. Firm also requested to grant exemption from Urdu Text on international packs due to space constraints.

- Registration number
- Maximum retail price
- Name and address of sole agent

The firm has provided the following documents along with the application: -

a. Fee challan of Rs.7,500/- deposited dated 03 November 2021 (deposit slip no. 349242261810).
b. Copy of registration letter issued on 31 May 2021.

Decision: Registration Board considered and advised the firm to explore possibility for local printing to comply Drugs (Labelling & Packing) Rules, 1986.

A: Imported Human Biological from non-reference countries.

1.	Name, address of Applicant / Importer	M/s Bristol Mayer Biotech Pakistan 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt.
	Details of Drug Sale License of importer	License No: 05-352-0068-029407D Address: 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt Validity: 07-04-2022 Status: DSL by way of distributor
	Name and address of marketing authorization holder (abroad)	Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) – 500101, Telangana State, India
	Name, address of manufacturer(s)	Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) – 500101, Telangana State, India
	Name of exporting country	India
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: • Firm has submitted legalized CoPP certificate No. 2632/STORES/2020-1 issued by Drug Control Administration Government of Telangana. The CoPP specifies that the product is licensed to be placed for use in the exporting country. The certificate was issued on 10-08-2020. (Validity 18-10-22) Free Sale Certificate: (Legalized) L. Dis .No: 46622/TS/2020 Validity: 24/09/2021
		GMP: 1. Legalized certificate of GMP (L. Dis. No .1926/Stores/2019)
	Details of letter of authorization / sole agency agreement	Firm has submitted sole agency agreement Firm has also submitted legalized copy of letter of authorization from Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) – 500101, Telangana State, India. According to the letter, the firm Sanzyme (P) Limited authorizes Bristol Mayer Biotech Pakistan address 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt to perform the registration procedures, sales and other similar activities concerning medicinal products for territory of Pakistan. The letter is valid until 29th Dec 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. 29332-R&I(DRAP) dated 05-Nov-2020 while the original CoPP was received on 1st Feb2021.
	Details of fee submitted	PKR 100000/- dated 05-Nov-2020
	proposed proprietary name/brand name	GYNOGEN HP 75 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient and amount per unit dose: Each vial of sterile freeze dried product contains: Menotropin (HMG) BP *Equivalent to the activity of* Follicle stimulating Hormone (FSH) 75 IU Luteinizing Hormone (LH) 75IU Mannitol USP q.s Potassium Di hydrogen Phosphate BP q.s Di potassium Hydrogen Phosphate BP q.s Reconstitute with 1 ml of sodium chloride injection USP (0.9% w/v) provided in this pack
	Pharmaceutical form of applied drug	Freeze-dried powder for Injection and 0.9% w/v Sodium Chloride Injection for reconstitution
	Pharmacotherapeutic Group of (API)	Gonadotropins ATC code: G03GA02
	Reference to Finished product specifications	BP
	Proposed Pack size	1's Vial
	Proposed unit price	Rs. 2000/Pack
	The status in reference regulatory authorities	MENOPUR 75 IU powder and solvent for solution for injection (EMC)
	For generic drugs (me-too status)	Ferti M (070928) of M/s RG Pharmaceutica, 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 and drug product.
	Name, address of drug substance manufacturer	Name: Shanghai Techwell Biopharmaceutical Co., Ltd. Address : No. 4258, Jindu Road, Shanghai 201108, 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, 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	GYNOGEN HP 75 IU is supplied as one vial of freeze-dried product with GYNOGEN HP 75 IU and one ampoule of 1 ml 0.9% w/v Sodium chloride injection (for reconstitution) are packaged together in a HIP tray. This HIP tray is further packed in a carton along with package insert.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability study data of 3 batches at 5±3°C for 36 months. The accelerated stability study data is conducted at 25±2°C & 60±5% RH for 6 months. SHELF LIFE Shelf life of Menotrophin for injection is 3 years when stored at a temperature between 2°C – 8°C. STORAGE CONDITIONS Store in a refrigerator (2°C to 8°C).
	Module 4	Not Submitted. *"Our drug products Gonadotropins (Menotrophin for Injection) belongs to a "well-established medicinal use" product category by fulfilling all the requirements under Annex I(Part II : Specific marketing authorization dossiers and requirements) of* ***Directive 2001/83/EC of the European Parliament and Council*** *with supporting published literatures. Hence, we would like to state that our gonadotropins are well established in the market over decades and bibliographic references of the medicinal product would suffice the Safety and Efficacy of the product. There is no need to have Non-Clinical and Clinical trial data since innovator product & similar products are available in the market for more than decades."*
	Module 5	A prospective, Randomized, Open-Label, Controlled Study to Compare the Clinical Efficacy and Tolerability of Two Highly Purified Human Menopausal Gonadotropin Preparations Administration Subcutaneously in women undergoing in Vitro Fertilization.
Remarks of Evaluator: Initially, the firm did not submit Module-4 & 5. The firm had referred to the ***Directive 2001/83/EC of the European Parliament and Council*** wherein it is mentioned that said Modules are exempted if the product (molecule) is available in a community for 10 years. Later-on the firm submitted the clinical safety and efficacy study report of their product on 137 patients.		
Decision: Registration Board deferred the products for submission of non-clinical data (Module-4) of the product.		
2.	Name, address of Applicant / Importer	M/s Bristol Mayer Biotech Pakistan 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt
	Details of Drug Sale License of importer	License No: 05-352-0068-029407D Address: 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt Validity: 07-04-2022 Status: DSL by way of distributor

	Name and address of marketing authorization holder (abroad)	Sanzyme (P) Limited Plot No. 8, Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India
	Name, address of manufacturer(s)	Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India
	Name of exporting country	India
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: • Firm has submitted legalized CoPP certificate No. 2632/STORES/2020-2 issued by Drug Control Administration Government of Telangana. The CoPP specifies that the product is licensed to be placed for use in the exporting country. The certificate was issued on 10-08-2020. (Validity 18-10-22) Free Sale Certificate: (Legalized) L. Dis .No: 46622/TS/2020 Validity: 24/09/2021
		GMP: Legalized certificate of GMP (L. Dis. No .1926/Stores/2019)
	Details of letter of authorization / sole agency agreement	Firm has submitted sole agency agreement Firm has also submitted legalized copy of letter of authorization from Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India. According to the letter, the firm Sanzyme (P) Limited authorizes Bristol Mayer Biotech Pakistan address 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt to perform the registration procedures, sales and other similar activities concerning medicinal products for territory of Pakistan. The letter is valid until 29th Dec 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. 29331-R&I(DRAP) dated 05-Nov-2020 while the original CoPP was received on 1st Feb2021.
	Details of fee submitted	PKR 100000/- dated 05-Nov-2020.
	proposed proprietary name/brand name	GYNOGEN HP 150 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient and amount per unit dose: Each vial of sterile freeze dried product contains: Menotropin (HMG) BP *Equivalent to the activity of* Follicle stimulating Hormone (FSH) 150 IU

		Luteinizing Hormone (LH) 150IU Mannitol USP q.s Potassium Di hydrogen Phosphate BP q.s Di potassium Hydrogen Phosphate BP q.s Reconstitute with 1 ml of sodium chloride injection USP (0.9% w/v) provided in this pack
	Pharmaceutical form of applied drug	Freeze-dried powder for Injection and 0.9% w/v Sodium Chloride Injection for reconstitution
	Pharmacotherapeutic Group of (API)	Gonadotropins ATC code: G03GA02
	Reference to Finished product specifications	BP
	Proposed Pack size	1's
	Proposed unit price	Rs.2000/Pack
	The status in reference regulatory authorities	MENOPUR 150 IU powder and solvent for solution for injection (EMC)
	For generic drugs (me-too status)	Ferti M (070929) of M/s RG Pharmaceutica, 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 and drug product.
	Name, address of drug substance manufacturer	Name: Shanghai Techwell Biopharmaceutical Co., Ltd. Address : No. 4258, Jindu Road, Shanghai 201108, 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, 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	GYNOGEN HP 150 IU is supplied as one vial of freeze-dried product with GYNOGEN

		HP 150 IU and one ampoule of 1 ml 0.9% w/v Sodium chloride injection (for reconstitution) are packaged together in a HIP tray. This HIP tray is further packed in a carton along with package insert.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability study data of 3 batches at 5±3°C for 36 months. The accelerated stability study data is conducted at 25±2°C & 60±5% RH for 6 months. SHELF LIFE Shelf life of Menotrophin for injection is 3 years when stored at a temperatures between 2°C – 8°C. STORAGE CONDITIONS Store in a refrigerator (2°C to 8°C).
	Module 4	Not Submitted. *"Our drug products Gonadotropins (Menotrophin for Injection) belongs to a "well-established medicinal use" product category by fulfilling all the requirements under Annex I(Part II : Specific marketing authorization dossiers and requirements) of* ***Directive 2001/83/EC of the European Parliament and Council*** *with supporting published literatures. Hence, we would like to state that our gonadotropins are well established in the market over decades and bibliographic references of the medicinal product would suffice the Safety and Efficacy of the product. There is no need to have Non-Clinical and Clinical trial data since innovator product & similar products are available in the market for more than decades."*
	Module 5	A prospective, Randomized, Open-Label, Controlled Study to Compare the Clinical Efficacy and Tolerability of Two Highly Purified Human Menopausal Gonadotropin Preparations Administration Subcutaneously in women undergoing in Vitro Fertilization.
Remarks of Evaluator: Initially, the firm did not submit Module-4 & 5. The firm had referred to the ***Directive 2001/83/EC of the European Parliament and Council*** wherein it is mentioned that said Modules are exempted if the product (molecule) is available in a community for 10 years. Later-on the firm submitted the clinical safety and efficacy study report of their product on 137 patients.		
Decision: Registration Board deferred the products for submission of non-clinical data (Module-4) of the product.		
3.	Name, address of Applicant / Importer	M/s Bristol Mayer Biotech Pakistan 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt
	Details of Drug Sale License of importer	License No: 05-352-0068-029407D Address: 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt Validity: 07-04-2022 Status: DSL by way of distributor
	Name and address of marketing authorization holder (abroad)	Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India
	Name, address of manufacturer(s)	Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India
	Name of exporting country	India

	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: • Firm has submitted legalized CoPP certificate No. 2632/STORES/2020-3 issued by Drug Control Administration Government of Telangana . The CoPP specifies that the product is licensed to be placed for use in the exporting country. The certificate was issued on 10-08-2020. (Validity 18-10-22) Free Sale Certificate: (Legalized) L. Dis .No: 46622/TS/2020 Validity: 24/09/2021
		GMP: Legalized certificate of GMP (L. Dis. No .1926/Stores/2019)
	Details of letter of authorization / sole agency agreement	Firm has submitted sole agency agreement Firm has also submitted legalized copy of letter of authorization from Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India. According to the letter, the firm Sanzyme (P) Limited authorizes Bristol Mayer Biotech Pakistan address 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt to perform the registration procedures, sales and other similar activities concerning medicinal products for territory of Pakistan. The letter is valid until 29th Dec 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. 2933-R&I(DRAP) dated 05-Nov-2020 while the original CoPP was received on 1st Feb2021.
	Details of fee submitted	PKR 100000/- dated 05-Nov-2020
	proposed proprietary name/brand name	PUBERGEN 5000 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient and amount per unit dose: Each vial of sterile freeze dried product contains: Human Chorionic Gonadotropin USP 5000 IU Mannitol USP q.s Potassium Di hydrogen Phosphate BP q.s Di potassium Hydrogen Phosphate BP q.s Reconstitute with 1 ml of sodium chloride injection USP (0.9% w/v) provided in this pack
	Pharmaceutical form of applied drug	Freeze-dried powder for Injection and 0.9% w/v Sodium Chloride Injection for reconstitution
	Pharmacotherapeutic Group of (API)	Gonadotropins ATC code: G03GA01

	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	Rs.3500/Pack
	The status in reference regulatory authorities	Novarel (Chorionic Gonadotropin) USFDA
	For generic drugs (me-too status)	Presage (059244) of Genome, Rawalpindi
	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	Name: Shanghai Techwell Biopharmaceutical Co., Ltd. Address : No. 4258, Jindu Road, Shanghai 201108, 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, 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	PUBERGEN 5000 IU is supplied as one vial of freeze-dried product with PUBERGEN 5000 IU and one ampoule of 1 ml 0.9% w/v Sodium chloride injection (for reconstitution) are packaged together in a HIP tray. This HIP tray is further packed in a carton along with package insert.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability study data of 3 batches at 5±3°C for 36 months. The accelerated stability study data is conducted at 25±2°C & 60±5% RH for 6 months. SHELF LIFE Shelf life of Chorionic Gonadotropin for Injection is 3 years when stored at a temperatures between 2°C – 8°C. STORAGE CONDITIONS

		Store in a refrigerator (2°C to 8°C).
	Module 4	Not Submitted. *"Our drug products Gonadotropins (Menotrophin for Injection) belongs to a "well-established medicinal use" product category by fulfilling all the requirements under Annex I(Part II : Specific marketing authorization dossiers and requirements) of* ***Directive 2001/83/EC of the European Parliament and Council*** *with supporting published literatures. Hence, we would like to state that our gonadotropins are well established in the market over decades and bibliographic references of the medicinal product would suffice the Safety and Efficacy of the product. There is no need to have Non-Clinical and Clinical trial data since innovator product & similar products are available in the market for more than decades."*
	Module 5	A prospective, Randomized, Open-Label, Controlled Study to Compare the Clinical Efficacy and Tolerability of Two Highly Purified Human Menopausal Gonadotropin Preparations Administration Subcutaneously in women undergoing in Vitro Fertilization.
Remarks of Evaluator: Initially, the firm did not submit Module-4 & 5. The firm had referred to the ***Directive 2001/83/EC of the European Parliament and Council*** wherein it is mentioned that said Modules are exempted if the product (molecule) is available in a community for 10 years. Later-on the firm submitted the clinical safety and efficacy study report of their product on 137 patients.		
Decision: Registration Board deferred the products for submission of non-clinical data (Module-4) of the product.		
4.	Name, address of Applicant / Importer	M/s Bristol Mayer Biotech Pakistan 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt
	Details of Drug Sale License of importer	License No: 05-352-0068-029407D Address: 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt Validity: 07-04-2022 Status: DSL by way of distributor
	Name and address of marketing authorization holder (abroad)	Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India
	Name, address of manufacturer(s)	Sanzyme (P) Limited Plot No.8, Sy.No.542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D)-500101, Telangana State, India
	Name of exporting country	India
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: • Firm has submitted legalized CoPP certificate No. 2632/STORES/2020-4 issued by Drug Control Administration Government of Telangana . The CoPP specifies that the product is licensed to be placed for use in the exporting country. The certificate was issued on 10-08-2020. (Validity 18-10-22) Free Sale Certificate: (Legalized) L. Dis .No: 46622/TS/2020 Validity: 24/09/2021
		GMP: Legalized certificate of GMP (L. Dis. No .1926/Stores/2019)

	Details of letter of authorization / sole agency agreement	Firm has submitted sole agency agreement Firm has also submitted legalized copy of letter of authorization from Sanzyme (P) Limited Plot No. 8 , Sy.No. 542, Koltur (V), Shamirpet (M), Medchal-Malkajgiri (D) - 500101, Telangana State, India. According to the letter, the firm Sanzyme (P) Limited authorizes Bristol Mayer Biotech Pakistan address 73-B Guldasht Town, Zarrar Shaheed Road, Lahore Cantt to perform the registration procedures, sales and other similar activities concerning medicinal products for territory of Pakistan. The letter is valid until 29th Dec 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. 31381-R&I(DRAP) dated 25-Nov-2020 while the original CoPP was received on 1st Feb 2021.
	Details of fee submitted	PKR 100000/- dated 25-Nov-2020
	proposed proprietary name/brand name	PUBERGEN 10000 IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient and amount per unit dose: Each vial of sterile freeze dried product contains: Human Chorionic Gonadotropin USP 10000 IU Mannitol USP q.s Potassium Di hydrogen Phosphate BP q.s Di potassium Hydrogen Phosphate BP q.s Reconstitute with 1 ml of sodium chloride injection USP (0.9% w/v) provided in this pack
	Pharmaceutical form of applied drug	Freeze-dried powder for Injection and 0.9% w/v Sodium Chloride Injection for reconstitution
	Pharmacotherapeutic Group of (API)	Gonadotropins ATC code: G03GA01
	Reference to Finished product specification	USP
	Proposed Pack size	1's
	Proposed unit price	Rs.3500/Pack
	status in reference regulatory authorities	Novarel (Chorionoc Gonadotropin) USFDA
	For generic drugs (me-too status)	Profasi 10000IU (016759) of M/s Hilton Pharma, 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 and drug product.
	Name, address of drug substance manufacturer	Name: Shanghai Techwell Biopharmaceutical Co., Ltd. Address : No. 4258, Jindu Road, Shanghai 201108, 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, 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	PUBERGEN 10000 IU is supplied as one vial of freeze-dried product with PUBERGEN 10000 IU and one ampoule of 1 ml 0.9% w/v Sodium chloride injection (for reconstitution) are packaged together in a HIP tray. This HIP tray is further packed in a carton along with package insert.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted long term stability study data of 3 batches at 5±3°C for 36 months. The accelerated stability study data is conducted at 25±2°C & 60±5% RH for 6 months. SHELF LIFE Shelf life of Chorionic Gonadotropin for Injection is 3 years when stored at temperatures between 2°C – 8°C. STORAGE CONDITIONS Store in a refrigerator (2°C to 8°C).
	Module 4	Not Submitted. *"Our drug products Gonadotropins (Menotrophin for Injection) belongs to a "well-established medicinal use" product category by fulfilling all the requirements under Annex I(Part II : Specific marketing authorization dossiers and requirements) of Directive 2001/83/EC of the European Parliament and Council with supporting published literatures. Hence, we would like to state that our gonadotropins are well established in the market over decades and bibliographic references of the medicinal product would suffice the Safety and Efficacy of the product. There is no need to have Non-Clinical and Clinical trial data since innovator product & similar products are available in the market for more than decades."*

	Module 5	A prospective, Randomized, Open-Label, Controlled Study to Compare the Clinical Efficacy and Tolerability of Two Highly Purified Human Menopausal Gonadotropin Preparations Administration Subcutaneously in women undergoing in Vitro Fertilization.

Remarks of Evaluator:

Initially, the firm did not submit Module-4 & 5. The firm had referred to the ***Directive 2001/83/EC of the European Parliament and Council*** wherein it is mentioned that said Modules are exempted if the product (molecule) is available in a community for 10 years. Later-on the firm submitted the clinical safety and efficacy study report of their product on 137 patients.

Decision: Registration Board deferred the products for submission of non-clinical data (Module-4) of the product.

B: Miscellaneous/ Deferred Cases

1. Imported Human Biological applied by M/s Bristol Mayer Biotech approved in 297th meeting of Registration Board.

M/s Bristol Mayer Biotech, Lahore applied for registration of human biological drug which was approved in 297th meeting of Reg. Board as under: (Minutes**: P. 138-139/Corr.)**

Name of manufacturer	Brand Name & Composition	Registration Board Decision
VEM ÌLAÇ San. Ve Tic. A.S. Sogutozu Mahallesi 2177. Cad. No:10 B/49 Cankaya / ANKARA / TURKEY. **Factory Address:** Cerkezkoy Organize Sanayi Bolgesi Karaagac Mahallesi Fatih Bulvari No:38 Kapakli/TEKIRDAG/TURKEY.	**Vasparin 25000 IU/5mL I.V.** Solution for Injection Vial. Each 5ml (1 vial) contains: Heparin sodium …….25000IU	*Keeping in view the opinion of Council of Islamic Ideology and legalized CoPP indicating product availability in country of origin; Registration Board approved the product subject to compliance of current Import Policy for finished drugs. The firm will submit valid legalized CoPP before issuance of Registration letter. Chairman Registration Board is authorized for issuance of letter after submission of said document.*

It is submitted that the Reg. Board approved the product subject to submission of valid legalized CoPP before issuance of Registration letter because the previous CoPP and GMP were expired at the time of approval. The firm submitted the CoPP and GMP which however, has following differences in address;

Address of PLH mentioned in Previous documents and approved minutes	Address of PLH and manufacturer mentioned in latest documents
VEM ÌLAÇ San. Ve Tic. A.S. Sogutozu Mahallesi 2177. Cad. No:10 B/49 Cankaya / ANKARA / TURKEY	VEM ÌLAÇ San. Ve Tic. A.S**. Maslak Mahallesi AOS 55. Sokak 42 Maslak A Block Sit. No: 2/134 Sariyer/ ISTANBUL / TURKEY**

Now, the firm has applied for change in address of product license holder and submitted the following:

a. Fee Challan of Rs. 7500/-
b. Valid legalized CoPP indicating new address.
c. Copy of letter from their product license holder regarding change in address.
d. Copy of letter of authorization with new address.
e. An under taking that the given information is true and correct.

Decision: Keeping in view legalized CoPP indicating new Product License Holder; Registration Board approved the change in product license holder from M/s VEM ÌLAÇ San. Ve Tic. A.S. Sogutozu Mahallesi 2177. Cad. No:10 B/49 Cankaya / ANKARA / TURKEY to M/s VEM ÌLAÇ San. Ve Tic. A.S. Maslak Mahallesi AOS 55. Sokak 42 Maslak A Block Sit. No: 2/134 Sariyer/ ISTANBUL / TURKEY for Vasparin 25000IU/5mL.

The meeting ended with the vote of thanks to and from the Chair

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