MINUTES OF 332ND MEETING OF REGISTRATION BOARD HELD ON 05TH DECEMBER, 2023

DRUG REGULATORY AUTHORITY OF PAKISTAN
T.F. COMPLEX, MAUVE AREA, G-9/4
ISLAMABAD.

332nd meeting of Registration Board was held on 05th December, 2023 in the Committee Room, Drug Regulatory Authority of Pakistan, G-9/4, Islamabad.

The meeting was chaired by Dr. Muhammad Fakhruddin Aamir, Chairman, Registration Board, DRAP. The meeting started with recitation of the Holy Verses.

Following members attended the meeting:

1.	Lt. Gen.(R) Prof. Dr. Karamat A. Karmat, (HI-M, SI-M), Former Surgeon General Pakistan, Rawalpindi (On line)	Co-opted Member
2.	Mr. Muhammad Aslam, Additional Draftsman, M/o Law & Justice, Islamabad.	Member
3.	Mr. Sartaj Khan, Drug Analyst. Rep of Director DTL, Govt. of KP	Member
4.	Dr. Ali Jan, Director, DTL, Govt. of Baluchistan Quetta	Member
5.	Mr. Iftikhar A. Chaudhary, Hospital Pharmacist, Lahore (Online)	Co-opted Member
6.	Syed Adnan Rizvi, Director DTL. Govt. of Sindh. Karachi (online)	Member
7.	Mr. Ajmal Sohail Asif, Director, Director, QA&LT, DRAP, Islamabad.	Member
8.	Mr. Abdul Ghaffar, Additional Director, Rep. of Director, Division of BE&R	Member
9.	Ch. Zeeshan Nazir Bajar, Additional Director	Secretary
10.	Mr. Saadat Ali Khan, Deputy Director, Rep. of Director, MD&MC Division	Member
11.	Dr. Qurban Ali, Ex-Director General, NVL, Veterinary Expert (Online)	Co-opted Member

Mr. Nadeem Alamgir (Pharma Bureau), Mr. Jalal-ud-Din Zafar (online), PPMA and Mr. Ziaulhaq (PCDA) attended the meeting as observers.

Item No. I. Confirmation of Minutes of 331st meeting of Registration Board

331st meeting of Registration Board was held on 31st October, 2023 to 2nd November, 2023. Accordingly, draft minutes of the meeting were prepared and circulated among the members through email and Whatsapp group of Registration Board on 19th November, 2023 for their perusal / approval / comments (if any) at the earliest except draft minutes of Biological Division. No comments received and fair minutes were circulated on 20.11.2023. Hence minutes of 331st meeting of RB stand approved. Draft minutes of Biological Division were circulated among the members through email and Whatsapp group of Registration Board on 24th November, 2023 for their perusal / approval / comments (if any) at the earliest. No comments received and fair minutes were circulated on 30.11.2023.

After approval of Chairman, Registration Board, approved minutes of 331st meeting of Registration Board has been circulated among relevant Divisions / Sections for implementation / compliance of decisions.

Decision: Registration Board noted the information and unanimously confirmed the minutes of 331st meeting of Registration Board.

Item No. II Division of Pharmaceutical Evaluation & Registration

Case No.01 Suspension of Registration of Drugs in compliance with Directions of Drug Court Rawalpindi.

Mr. Nadeem Babar Khan, Chairman /Judge Drug Court, Rawalpindi Division, Rawalpindi vide letter No. 194-95/DC dated 07-08-2023 has referred the case No. 3995/Judl/DC/RWP/2019 with title *"the state versus M/s. Flow Pharmaceuticals(Pvt) Ltd., 17-Km, Sheikhupura Road, Lahore and others Case No. 3995/Judl/DC/RWP/2019"* and states as under:

> ***'The above mentioned case has been filed against FLOW Pharmaceuticals (Pvt) Ltd, and others on the charge of manufacturing and sale of substandard drug and for issuing false warranty. The accused (C.E.O, Production Manager, QC Manager and Warrantor) being the alleged responsible officers of the accused company at the relevant time are being summoned by this court but their service has not yet been affected as they are intentionally hiding from the process of law. Since the firm is manufacturer of drugs which require registration by DRAP. Therefore, you are directed to suspend the registration of the all drugs being manufactured by the firm with immediate effect and restoration of registration of drugs shall be subject to appearance of accused before the court and issuance formal order of restoration by this court.'***

The case was presented before the 331st meeting of Regsistration Board, wherein the Board decided as under:

Decision of 331st Meeting of the Board:-

"Registration Board referred the case to Licensing Division."

Mr. Nadeem Babar Khan, Chairman Drug Court, Rawalpindi vide letter No. 276-77/DC, Rawalpindi dated 07th November, 2023 has directed to Chairman, Registration Board to appear before the Court on 28th November, 2023.

No. 276-77 /DC, Rawalpindi the 07 November, 2023.

To,

Dr. Fakhar-ud-din Amir,
The Director, Licensing Division, DRAP,
Islamabad.

Subject: **SUSPENSION OF DRUGS MANUFACTURING LICENSE.**

In Re; the state versus M/S Flow Pharmaceuticals (Pvt) Ltd 17-Km Sheikhupura Road, Lahore and others Case No. 3995/Judl/DC/RWP/2019.

You were directed vide this court's office letter No. 194-95/DC/RWP dated 07.08.2023 to suspend the registration of the all drugs being manufactured by the firm with immediate effect and restoration of registration of drugs shall be subject to the appearance of accused before court and issuance of formal order for restoration by this court.

No report has been submitted in this regard before this court to date. This tantamount to disrespect the court's order and process of law. You are therefore, directed to appear in person along with the compliance report on 28.11.2023.

(Nadeem Babar Khan)
Judge/Chairman
Drug Court Rawalpindi Division
Rawalpindi

C.C:
The CEO, Drug Regulatory Authority of Pakistan, Islamabad.

In compliance Dr. Muhammad Fakhruddin Aamir, Chairman Registration Board appeared before the Court on 28th November, 2023. The Chairman Drug Court, Rawalpindi has directed to comply direction of court and submit compliance report on or before 11th November, 2023.

The case is presented before the Board in the light of directions of Mr. Nadeem Babar Khan, Chairman Drug Court, Rawalpindi, please.

Decision: Registration Board deliberated on the matter in the presence of Mr. Muhammad Aslam, Additional Draftsman, Ministry of Law & Justice, Islamabad in compliance with the directions of Drug Court, Rawalpindi decided to suspend all the drug products registered in the name of M/s. Flow Pharma (Pvt) Ltd. 17-Km Sheikhupura Road Lahore with immediate effect. The court further directed that the registrations will remain suspend till appearance of accused persons before the Drug Court, Rawalpindi and issuance of formal order for restoration of registrations of products by the Drug Court, Rawalpindi. The Board further decided that in order to comply directions of Drug Court, Rawalpindi partial minutes of the meeting of this case shall be issued today, positively.

Furthermore, letter of Drug Court, Rawalpindi regarding details of CNICs and whereabouts of the technical staff of M/s. Eros Pharmaceuticals (Pvt) Ltd., Karachi has already been referred to Licensing Division vide E-office Diary No. 898-Dir (PE&R) dated 22.11.2023.

Item No. II. Division of Biological Evaluation & Research

CASES OF DD-I (MR. MUHAMMAD KASHIF)

CHANGE IN MANUFACTURING SITE (Humulin R 100IU/mL vial**)**.

M/s. Eli Lilly Pakistan (Pvt) Limited, Karachi has applied for the change in manufacturing site of their already registered biological product as per following details:

Sr.	Reg. No. and date	Brand Name	Existing Marketing Authorization Holder & Manufacturer	Demanded New Manufacturing Site:
1.	008302 Dated 24-09-1985	Humulin R, 100IU/mL Vial Each vial contains: Human insulin Regular (rDNA Origin)	Manufacturer: M/s Eli Lilly and Company Indianapolis, IN 46285, USA Product License Holder: Not Mentioned	Manufacturer & Product License Holder (As per CoPP): M/s. Gland Pharma Limited, Sy No. 143 to 148, 150 & 151, Near Gandimaisamma Cross Roads, D.P. Pally, Dundigal Post, Dundigal - Gandimaisamma Mandal, Medchal-Malkajgiri District, Hyderabad - 500 043, Telangana, INDIA. Product License Holder (As per Agreement between M/s Eli Lilly & M/s. Gland Pharma Limited & as per Authorization letter and copy of New submitted CoPP): M/s Eli Lilly and Company Indianapolis, IN 46285, USA.

The applications have been evaluated as per approved SOPs and tabulated below:

Documents required as per SOP	Documents submitted by the firm
Application	Submitted
Required fee.	Fee of Rs. 150,000/- Online Slip Number: 82260366338
Copy of registration letter and last renewal status	Submitted Copy of Registration letter to Ali Gohar and Company, dated 24-09-1985. Copy of transfer of Registration letter from Ali Gohar and Company to M/s. Eli Lilly Pakistan (Pvt) Limited, dated 07-06-2000. Copy of all renewals dated 04-05-2005, 26-04-2010, 05-09-2014, 24-04-2015. Copy of last renewal submission dated 11-05-2020 has been submitted
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.	• Firm has submitted Original Legalized Indian CoPP for Humulin R, 100IU/mL Vial – 10ml (Certificate# 3920591/TS/2023) with issue date: 28.02.2023 valid until 15.01.2026 issued by Drug Control Administration, India. • The CoPP specifies free sale status of applied product in exporting country. • The CoPP also confirms GMP compliant status of the manufacturer.
Site Master file	Submitted

Revised Sole Agency Agreement and any proof/evidence of the contract between Product License Holder & manufacturer (with changed/new name), where the manufacturer and product license holder are different entities	Submitted
Comparative manufacturing process at two sites	Submitted
Manufacturing Process and Batch Analysis Data of both Manufacturing Sites	Submitted
Undertaking that provided information/ documents are true & correct.	Submitted

Copy of Approval is submitted by the firm that M/s. Gland Pharma Limited is approved by Korea Ministry of Food and Drug Safety (MFDS) to Manufacture Humulin R and Korea is the member of PIC/S.
Copy of Contract is submitted between Eli Lilly and Company and M/s. Gland Pharma Limited to manufacture Humulin R, 100IU/ml Vial.
In the submitted copy of contract, it is clarified that MAH Holder of the above stated product will be M/s Eli Lilly.
Original Letter of Authorization submitted from Eli Lilly and Company USA for Eli Lilly Pakistan and mentioning Gland Pharma their source of supply for Humulin 70/30 Vial.
The firm has submitted technology transfer report from M/s Eli Lilly to M/s. Gland Pharma Limited.
The pharmaceutical concerns has submitted copy of revised CoPP in which the Marketing Authorization Holder is M/s Eli Lilly and Company Indianapolis, IN 46285, USA.

CHANGE IN MANUFACTURING SITE (Humulin N, 100IU/mL Vial**)**

M/s. Eli Lilly Pakistan (Pvt) Limited, Karachi has applied for the change in manufacturing site of their already registered biological product as per following details:

2.	**Reg. No. and date**	**Brand Name**	**Existing Marketing Authorization Holder & Manufacturer**	**Demanded New Manufacturing Site:**
	008300 Dated 24-09-1985	**Humulin N, 100IU/mL Vial** Each vial contains: Human insulin NPH Isophane Suspension (rDNA Origin)	Manufacturer: M/s Eli Lilly and Company Indianapolis, IN 46285, USA Product License Holder: Not Mentioned	Manufacturer & Product License Holder (As per CoPP): M/s. Gland Pharma Limited, Sy No. 143 to 148, 150 & 151, Near Gandimaisamma Cross Roads, D.P. Pally, Dundigal Post, Dundigal - Gandimaisamma Mandal, Medchal-Malkajgiri District, Hyderabad - 500 043, Telangana, INDIA. Product License Holder (As per Agreement between M/s Eli Lilly & M/s. Gland Pharma Limited & as per Authorization letter and copy of New submitted CoPP): M/s Eli Lilly and Company Indianapolis, IN 46285, USA.

The applications have been evaluated as per approved SOPs and tabulated below:

Documents required as per SOP	Documents submitted by the firm
Application	Submitted
Required fee.	Fee of Rs. 150,000/- Online Slip Number: 971519155338
Copy of registration letter and last renewal status	Submitted Copy of Registration letter to Ali Gohar and Company, dated 24-09-1985. Copy of transfer of Registration letter from Ali Gohar and Company to M/s. Eli Lilly Pakistan (Pvt) Limited, dated 07-06-2000.

	Copy of all renewals dated 04-05-2005, 26-04-2010, 24-04-2015. Copy of last renewal submission dated 11-05-2020 has been submitted
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.	• Firm has submitted Original Legalized Indian CoPP for Humulin N, 100IU/mL Vial – 10ml (Certificate# 3941082/TS/2023) with issue date: 25.02.2023 valid until 15.01.2026 issued by Drug Control Administration, India. • The CoPP specifies free sale status of applied product in exporting country. • The CoPP also confirms GMP compliant status of the manufacturer.
Site Master file	Submitted
Revised Sole Agency Agreement and any proof/evidence of the contract between Product License Holder & manufacturer (with changed/new name), where the manufacturer and product license holder are different entities	Submitted
Comparative manufacturing process at two sites	Submitted
Manufacturing Process and Batch Analysis Data of both Manufacturing Sites	Submitted
Undertaking that provided information/ documents are true & correct.	Submitted

Copy of Approval is submitted by the firm that M/s. Gland Pharma Limited is approved by Korea Ministry of Food and Drug Safety (MFDS) to Manufacture Humulin R and Korea is the member of PIC/S.
Copy of Contract is submitted between Eli Lilly and Company and M/s. Gland Pharma Limited to manufacture Humulin N, 100IU/ml Vial.
In the submitted copy of contract, it is clarified that MAH Holder of the above stated product will be M/s Eli Lilly.
Original Letter of Authorization submitted from Eli Lilly and Company USA for Eli Lilly Pakistan and mentioning Gland Pharma their source of supply for Humulin 70/30 Vial.
The firm has submitted technology transfer report from M/s Eli Lilly to M/s. Gland Pharma Limited.

The pharmaceutical concerns have submitted copy of revised CoPP in which the the Marketing Authorization Holder is M/s Eli Lilly and Company Indianapolis, IN 46285, USA.

Deferred cases in 331st Registration Board Meeting.

CHANGE IN MANUFACTURING SITE (Humulin 70/30, 100IU/mL Vial**)**

M/s. Eli Lilly Pakistan (Pvt) Limited, Karachi has applied for the change in manufacturing site of their already registered biological product as per following details:

3.	**Reg. No. and date**	**Brand Name**	**Existing Marketing Authorization Holder & Manufacturer**	**Demanded New Manufacturing Site and Product License Holder:**

	011149 Dated 28-07-1990	Humulin 70/30, 100IU/mL Vial Each vial contains: 70% human insulin isophane suspension, 30% human insulin (rDNA Origin)	Manufacturer: M/s Eli Lilly and Company Indianapolis, IN 46285, USA Product License Holder: Not Mentioned	Manufacturer & Product License Holder (As per CoPP): M/s. Gland Pharma Limited, Sy No. 143 to 148, 150 & 151, Near Gandimaisamma Cross Roads, D.P. Pally, Dundigal Post, Dundigal - Gandimaisamma Mandal, Medchal-Malkajgiri District, Hyderabad - 500 043, Telangana, INDIA. Product License Holder (As per Agreement between M/s Eli Lilly & M/s. Gland Pharma Limited & as per Authorization letter): M/s Eli Lilly and Company Indianapolis, IN 46285, USA.

The case has been evaluated as per approved Guidelines: Post Registration Variation Guidelines and tabulated below:

Documents required as per Guidelines	Documents submitted by the firm
Application	Submitted
Required fee as per relevant SRO.	Humulin 70/30, 100IU/mL Vial Fee Challan of Rs. 150,000/- Online Slip Number: 11740145 dated 09-05-2023 has been submitted
Copy of registration letter and last renewal status	Submitted Copy of Registration letter to Ali Gohar and Company, dated 28-07-1990. Copy of transfer of Registration letter from Ali Gohar and Company to M/s. Eli Lilly Pakistan (Pvt) Limited, dated 07-06-2000. Copy of all renewals dated 04-05-2005, 26-04-2010, 05-09-2014, 24-04-2015. Copy of last renewal submission dated 11-05-2020 has been submitted
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.	• Firm has submitted Original Legalized Indian CoPP for Humulin 70/30, 100IU/mL Vial – 10ml (Certificate# 4126448/TS/2023) with issue date: 06.04.2023 valid until 06.02.2026 issued by Drug Control Administration, India. • The CoPP specifies free sale status of applied product in exporting country. • The CoPP also confirms GMP compliant status of the manufacturer.
Site Master file	Submitted
Revised Sole Agency Agreement and any proof/evidence of the contract between Product License Holder & manufacturer (with changed/new name), where the manufacturer and product license holder are different entities	Submitted
Comparative manufacturing process at two sites	Submitted
Manufacturing Process and Batch Analysis Data of both Manufacturing Sites	Submitted
Undertaking that provided information/ documents are true & correct.	Submitted

Copy of Approval is submitted by the firm that M/s. Gland Pharma Limited is approved by Korea Ministry of Food and Drug Safety (MFDS) to Manufacture Humulin 70/30 and Korea is the member of PIC/S. Copy of Contract is submitted between Eli Lilly and Company and M/s. Gland Pharma Limited Limited to manufacture Humulin 70/30, 100IU/ml Vial.

In the submitted copy of contract, it is clarified that MAH Holder of the above stated product will be M/s Eli Lilly.

Original Letter of Authorization submitted from Eli Lilly and Company for Eli Lilly Pakistan and mentioning Gland Pharma their source of supply for Humulin 70/30 Vial.
The firm has submitted technology transfer report from M/s Eli Lilly to M/s. Gland Pharma Limited.

Registration Board in its 307th meeting delegated its power/functions for Change of contract manufacturer/ manufacturing site of already registered products to the Chairman Registration Board.

The case was placed in 331st Registration Board Meeting and the Registration Board decided as under.

Decision of 331st DRB: Registration Board deferred the case for following:

1) *Submission of valid legalized CoPP indicating that M/s Eli Lilly USA is Market Authorization Holder of Humulin 70/30, 100IU/mL Vial manufactured by M/s. Gland Pharma Limited, Sy No. 143 to 148, 150 & 151, Near Gandimaisamma Cross Roads, D.P. Pally, Dundigal Post, Dundigal - Gandimaisamma Mandal, Medchal-Malkajgiri District, Hyderabad - 500 043, Telangana, INDIA.*
2) *Approval of product manufactured by M/s. Gland Pharma Limited, Sy No. 143 to 148, 150 & 151, Near Gandimaisamma Cross Roads, D.P. Pal)ly, Dundigal Post, Dundigal -Gandimaisamma Mandal, Medchal-Malkajgiri District, Hyderabad - 500 043, Telangana, INDIA in reference regulatory authorities.*
3) *Data as per DRAP notified post registration variation guideline for change of manufacturing site.*

The pharmaceutical concerns submitted Original and Legalized CoPP in which the Marketing Authorization Holder is M/s Eli Lilly and Company Indianapolis, IN 46285, USA.

Decision*: The Board was apprized that Special Investment and facilitation council, Prime Minister's Office vide letter No.F-5 (30) 09 / SIFC Islamabad dated 23rd November, 2023 has also forwarded request of the company for support needed in the interest of diabetes patients.*
***Keeping in view data / documents / information alongwith original legalized CoPP clearly indicating Marketing Authorization Holder as M/s Eli Lilly and Company Indianapolis, IN 46285, US, the Board acceded to request of the pharmaceutical concern for change of manufacturing site from M/s Eli Lilly and Company Indianapolis, IN 46285, USA to M/s. Gland Pharma Limited, Sy No. 143 to 148, 150 & 151, Near Gandimaisamma Cross Roads, D.P. Pally, Dundigal Post, Dundigal - Gandimaisamma Mandal, Medchal-Malkajgiri District, Hyderabad - 500 043, Telangana, INDIA for already registered products namely; Humulin R 100IU/ml vial, Humulin N 100IU/ml vial and Humulin 70/30 100IU/ml vial subject to submission of legalized GMP certificate issued by Korea Ministry of Food & Drug Safety and compliance to current import policy for finished drugs. R*eference shall be sent to Cost & Pricing division for price confirmation.**

ADDITION OF MANUFACTURING SITE (Insulatard HM 100IU/mL, 10 mL Vial)

M/s Novo Nordisk Pharma (Pvt.) Limited, Karachi has applied for the addition of a manufacturing site for their already registered biological products as per the following details:

4.	**Reg. No. and date**	**Brand Name and Composition**	**Existing Registered Manufacturing Site**	**Demanded Additional Manufacturing Site**
	010205 Dated 11-11-2005	Insulatard HM 100IU/ml, 10 ml Vial. Suspension for injection in 10ml Vial.	M/s Novo Nordisk Production SAS, 45 Avenue d' Orleans, F-28000 Chartres, France.	Eskayef Pharmaceuticals Limited, 400 Squibb Road, Tongi Industrial Area, Tongi, Ghazipur 1711, Bangladesh.

The applications have been evaluated as per approved SOPs and tabulated below:

Documents required as per SOP	Documents submitted by the firm
Application on Form-5F	Submitted
Required fee as per relevant SRO.	PKR 150,000/-: dated 03/02/2023 Deposit Slip No. 02835880

Copy of registration letter and last renewal status	Registration letter: dated 11-11-2005 Renewal application 13-05-2010 Renewal application 16-04-2015 Site change 16-03-2017. Copy of last renewal submission dated 04-05-2020
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.	Firm has submitted legalized copy of CoPP (No. DA/6-39/05/2408) dated 19-01-2023 issued by Directorate General of Drug Administration. The CoPP specifies free sale of the product in exporting country. The CoPP also confirms the GMP status of the firm
Site master file of new manufacturing site in case of change of manufacturing site/ source	Submitted
Revised Sole Agency Agreement when there is change in MAH	Submitted
Undertaking that provided information/ documents are true & correct.	Submitted

Form 5F Assessment report is as follows:

FORM 5-F ASSESSMENT REPORT
Insulatard® HM Vial 100IU/mL, 10 mL Vial.

Documents required as per SOP	Documents submitted by the firm
Name, address of Applicant / Marketing Authorization Holder	M/s Novo Nordisk Pharma (Private) Limited, 113, Shahrah-e-Iran, Clifton, Karachi-75600., Pakistan
Details of Drug Sale License of importer	Novo Nordisk Pharma (Pvt.) Limited Address: 113, Shahrah-e-Iran, Clifton, Karachi, Pakistan. Address of go-down: 208/1, Sector 23, KIA, Karachi Validity: 09-04-2023 Status: License to sell drugs by way of Wholesale.
Name and address of marketing authorization holder/ Product License Holder (abroad)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
Name, address of manufacturer(s)	Eskayef Pharmaceuticals Limited 400 Squibb Road, Tongi Industrial Area, Tongi, Gazipur 1711, Bangladesh
Name of exporting country	Bangladesh
Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted legalized copy of CoPP (No. DA/6-39/05/2408) dated 19-01-2023 issued by Directorate General of Drug Administration Bangladesh. The CoPP specifies free sale of the product in exporting country. The CoPP also confirms the GMP status of the firm.
Details of letter of authorization / sole agency agreement	Firm has submitted an attested and legalized letter of product-specific authorization from Senior Vice President (Submissions and Life Cycle Management) of Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark has a contract manufacturing site in Bangladesh in name of Eskayef Pharmaceuticals. Further, Novo Nordisk A/S has provided sole authorization to Novo Nordisk Pharma (Private) Limited" to import, Distribute, and sale the registered product Insulatard® HM Vial 100IU/ml 10 ml Vial. The letter was issued on 07-February-2023.

Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
Dy. No. and date of submission	Dy. No. 8142 dated 22-03-2023
Details of fee submitted	PKR 150,000/-: dated 03/02/2023 Deposit Slip No. 02835880
The proposed proprietary name / brand name	INSULATARD® HM 100 IU/ml, 10 ml Vial Suspension for injection
Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient(s) Insulin Human (rDNA) Ph.Eur. [Suspension of isophane (NPH) insulin] Quantity/100ml 383.142 mg (Eq. to 350.000 mg as 100% potency eq. to 10000 IU of Human insulin) **Human insulin is produced in Saccharomyces cerevisiae by recombinant DNA technology*
Dosage form of applied drug	Suspension for injection
Pharmacotherapeutic Group of (API)	Drugs used in diabetes. Insulins and analogues for injection, Intermediate-acting, insulin (human). ATC code: A10AC01
Reference to Finished product specifications	Ph. Eur Specs
Proposed Pack size	Each Pack contains: 1 x 10ml Vial®
Proposed unit price	MRP already available Insulatard® HM Vial Reg.No.010205
Shelf Life	30 Months
Storage Conditions	Store in refrigerator (2°C – 8°C).
The status in reference regulatory authorities	Novo Nordisk A/S holds registration in Reference Authorities. Eg: EMA & FDA Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark has a contract manufacturing site in Bangladesh in name of Eskayef Pharmaceuticals. Further, Novo Nordisk A/S has provided sole authorization to Novo Nordisk Pharma (Private) Limited" to import, Distribute and sale the registered product Insulatard®. The letter was issued on 07-February-2023
For generic drugs (me-too status)	Not Applicable

Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to nomenclature, structure, general properties, manufacturer, description of the manufacturing process and process controls, control of materials, control of critical steps and intermediates, process validation and/or evaluation, manufacturing process development, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard or material, container closure system and stability studies of drug substance and drug product. The firm has also submitted non-clinical and clinical overviews and summaries	
Name, address of drug substance manufacturer	Address	Activity
	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.	Production of Master cell bank and working cell bank. Storage of Master Cell Bank and Working Cell Bank.
	Novo Nordisk A/S Hallas Allé 4400 Kalundborg Denmark	Storage and stability testing of Master Cell Bank and Working Cell Bank. Recovery from fermentation broth. Purification of insulin human Quality control of in-process samples and drug substance.
Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical state, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard or material, 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 and accelerated time conditions. The long-term stability data is conducted at -18°C±2°C for 60 months with 3 batches as per claim shelf life of 60 months. The accelerated study conducted at +5 °C±3°C for 12 months.	
Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.	
Analytical method validation/verification of product	The firm has submitted analytical methods as per specifications/Ph. Eur. The methods are validated as per SOPs. The Analytical methods are listed below Macroscopy (Ph. Eur.) Microscopy (Ph. Eur.) Identity of Human insulin (Ph. Eur.) Assay of insulin (Ph. Eur.) pH (Ph. Eur. / USP / JP) Insulin in the supernatant (Ph. Eur.)	

	High molecular weight proteins (Ph. Eur. / USP) A21 Desamido insulin (Ph. Eur.) Other related impurities (Ph. Eur.) Zinc total (Ph. Eur. / USP / JP) Bacterial endotoxins (Ph. Eur. Method D) Sterility (Ph. Eur. / USP / JP) Total dissolved insulin (A2619a) Isophane confirmation (A2361a) Identity of preservatives (A2461a) Phenol (A2461a) Metacresol (A2461a) Particulate matter (Ph. Eur. / USP / JP)
Container closure system of the drug product	The vial is made of colorless glass with a hydrolytic resistance as defined in Ph Eur and USP (type I glass). The plunger is made of bromobutyl rubber.
Stability study data of drug product, shelf life and storage conditions	Firm has submitted comparability report for 3 PPQ batches of stability manufactured at site Chartres and at Contract Manufacturing Site Eskayef stored for 30 months at long term conditions at 5°C±3°C.
Module 4 & Module 5 (Non-Clinical & Clinical Documentation)	No change Statement concerning to Module 4 and Module 5.

1. The firm has not submitted any evidence that the applied product is registered in any reference country.
2. The application has been sent to Legal Affairs Division, DRAP and their opinion regarding grant of additional manufacturing site is still awaited.

Decision of 331st DRB: The Board noted that opinion of the legal division for grant of additional manufacturing site is yet to come and therefore decided to defer the case and to place the matter before the Board after seeking opinion from Legal Affairs Division of the DRAP.

The comments of Legal Affairs Division are as under:

"Reference para 289/N. The Registration Board, in its 330th meeting held on 24th to 26th July, 2023, referred the matter of M/s Novo Nordisk Pharma (Pvt.) Limited, Karachi for the addition of a manufacturing site for its already registered biological products. The existing manufacturing site is M/s Novo Nordisk Production SAS, 45 Avenue d' Orleans, F-28000 Chartres, France and the demanded additional manufacturing site is M/s Eskayef Pharmaceuticals Limited, 400 Squibb Road, Tongi Industrial Area, Tongi, Ghazipur 1711, Bangladesh.

The case has been examined and it is found that the law is silent on the issue of allowing an additional manufacturing site for a registered product. Previously, during the pandemic of Covid-19, M/s Roche Pakistan Limited, Karachi made a similar request which was considered in 295th meeting of the Registration Board held on 8th to 11th June, 2020 and the Board approved the addition of M/s Genetech Inc., 4625 NE Brookwood Parkway, Hillsboro, OR 97124, USA as manufacturing site for Actemra 400mg/20ml (Reg. No. 083136) as an interim measure subject to certain conditions due to the fact that the firm's global supply chain is unable to fulfill the demand of many international markets from the existing manufacturing facility (M/s Utsunomiya Plant of Chugai Pharma Manufacturing Co., Limited, 16-3, Kiyohara Kogyodanchi, Utsunomiya-city, Tochigi, Japan).

The instant case may be considered in light of the aforesaid decision of the Registration Board as insulins are included in the Model List of Essential Medicines – 23rd List (2023) published by the World Health Organization (WHO) and notified by the Ministry of National Health Services, Regulations and Coordination vide Notification No. F.8-43/2021-DD(PS) dated 2nd October, 2023 under paragraph 2(1)(xi) of the Drug Pricing Policy, 2018.

The Registration Board may develop guidelines for allowing additional manufacturing sites keeping in view the safety, efficacy and quality parameters of a product."

ADDITION OF MANUFACTURING SITE (Actrapid HM 100 IU/mL, 10 mL Vial**)**

Case: M/s Novo Nordisk Pharma (Pvt.) Limited, Karachi has applied for the addition of a manufacturing site for their already registered biological products as per the following details:

5.	Reg. No. and date	Brand Name and Composition	Existing Registered Manufacturing Site	Demanded Additional Manufacturing Site
	010204 Dated 11-11-2005	Actrapid HM 100 IU/mL, 10 mL Vial Suspension for injection in 10mL Vial.	M/s Novo Nordisk Production SAS, 45 Avenue d' Orleans, F-28000 Chartres, France.	M/s Eskayef Pharmaceuticals Limited, 400 Squibb Road, Tongi Industrial Area, Tongi, Ghazipur 1711, Bangladesh.

The application has been evaluated as per approved SOPs and tabulated below:

Documents required as per SOP	Documents submitted by the firm
Application on Form-5F	Submitted
Required fee as per relevant SRO.	PKR 150,000/-: dated 03/02/2023 Deposit Slip No. 25106201728
Copy of registration letter and last renewal status	Registration letter: dated 11-11-2005 Renewal application 13-05-2010 Renewal application 16-04-2015 Site change letter dated 06-03-2017 Copy of last renewal submission dated 04-05-2020
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.	The firm has submitted legalized of CoPP (No. DA/6-39/05/2410) dated 19-01-2023 issued by the Directorate General of Drug Administration Mohakhali, Dhaka-1212. The CoPP specifies free sale status of the product in the exporting country. The CoPP also confirms the GMP status of the firm.
Site master file of new manufacturing site in case of change of manufacturing site/ source	Submitted
Revised Sole Agency Agreement when there is change in MAH	Submitted
Undertaking that provided information/ documents are true & correct.	Submitted

FORM 5-F ASSESSMENT REPORT

Actrapid® HM 100 IU/mL, 10 mL Vial

Documents required as per SOP	Documents submitted by the firm
Name, address of Applicant / Marketing Authorization Holder	M/s Novo Nordisk Pharma (Private) Limited, 113, Shahrah-e-Iran, Clifton, Karachi-75600 Pakistan
Details of Drug Sale License of Importer	Novo Nordisk Pharma (Pvt.) Limited Address: 113, Shahrah-e-Iran, Clifton, Karachi, Pakistan. Address of go-down: 208/1, Sector 23, KIA, Karachi Validity: 09-04-2023 Status: License to sell drugs by way of Wholesale.
Name and address of marketing authorization holder/ Product License Holder (abroad)	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.
Name, address of manufacturer(s)	Eskayef Pharmaceuticals Limited 400 Squibb Road, Tongi Industrial Area, Tongi, Gazipur 1711, Bangladesh
Name of exporting country	Bangladesh
Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted legalized copy of CoPP (No. DA/6-39/05/2410) dated 19-01-2023 issued by Directorate General of Drug Administration Mohakhali, Dhaka-1212. The CoPP

	specifies free sale status of the product in the exporting country. The CoPP also confirms the GMP status of the firm.
Details of letter of authorization / sole agency agreement	Firm has submitted attested and legalized letter of product specific authorization from Senior Vice President (Submissions and Life Cycle Management) of Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark has a contract manufacturing site in Bangladesh in name of Eskayef Pharmaceuticals. Further, Novo Nordisk A/S has provided sole authorization to Novo Nordisk Pharma (Private) Limited" to import, Distribute and sale the registered product Actrapid® HM Vial 100IU/ml 10 ml Vial. The letter was issued on 07-February-2023.
Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
Dy. No. and date of submission	Dy. No. 8141 dated 24-03-2023
Details of fee submitted	PKR 150,000/-: dated 03/02/2023 Deposit Slip No. 25106201728
The proposed proprietary name / brand name	ACTRAPID® HM 100 IU/mL, 10 mL Vial Solution for injection
Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient(s) Insulin Human (rDNA) Ph.Eur. Quantity /100Ml 383.142 mg (Eq. to 350.000 mg as 100 % potency eq. to 10000 IU of Human insulin) **Human insulin is produced in Saccharomyces cerevisiae by recombinant DNA technology*
Dosage form of applied drug	Solution for injection
Pharmacotherapeutic Group of (API)	Drugs used in diabetes. Insulins and analogues for injection, fast-acting, insulin (human). ATC code: A10AB01.
Reference to Finished product specifications	Ph. Eur Specs
Proposed Pack size	Each Pack contains: 1 x 10mL Vial®
Proposed unit price	MRP already available Actrapid® HM Vial Reg.No.010204
Shelf Life	30 Months
Storage Conditions	Store in refrigerator (2°C – 8°C).
The status in reference regulatory authorities	Novo Nordisk A/S holds registration in Reference Regulatory Authorities. Eg: EMA & FDA

	Novo Nordisk A/S, Denmark. According to the letter, the firm Novo Nordisk A/S, Denmark has a contract manufacturing site in Bangladesh in name of Eskayef Pharmaceuticals. Further, Novo Nordisk A/S has provided sole authorization to Novo Nordisk Pharma (Private) Limited" to import, Distribute and sale the registered product Insulatard®. The letter was issued on 07-February-2023	
For generic drugs (me-too status)	Not Applicable	
Module-II (Quality Overall Summary)	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to nomenclature, structure, general properties, manufacturer, description of manufacturing process and process controls, control of materials, control of critical steps and intermediates, process validation and/or evaluation, manufacturing process development, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard or material ,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	Address	Activity
	M/s Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark	Production of Master cell bank and working cell bank. Storage of Master Cell Bank and Working Cell Bank.
	M/s Novo Nordisk A/S, Novo Allé, 4400 Kalundborg, Denmark.	Storage and stability testing of Master Cell Bank and Working Cell Bank. Recovery from fermentation broth. Purification of insulin human Quality control of in-process samples and drug substance.
Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical state, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard or material, 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 and accelerated time conditions. The long term stability data is conducted at -18°C±2°C for 60 months with 3 batches as per claim shelf life of 60 months. The accelerated study conducted at +5 °C±3°C for 12 months.	
Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, no change statement concerning to Actrapid® 100IU/ml,10 ml, 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 firm has submitted analytical methods as per specifications/Ph. Eur. The methods are validated as per SOPs. The Analytical methods are listed below Macroscopy (Ph. Eur.) Microscopy (Ph. Eur.) Identity of Human insulin (Ph. Eur.) Assay of insulin (Ph. Eur.) pH (Ph. Eur. / USP / JP) Insulin in the supernatant (Ph. Eur.) High molecular weight proteins (Ph. Eur. / USP) A21 Desamido insulin (Ph. Eur.) Other related impurities (Ph. Eur.) Zinc total (Ph. Eur. / USP / JP) Bacterial endotoxins (Ph. Eur. Method D) Sterility (Ph. Eur. / USP / JP) Total dissolved insulin (A2619a) Isophane confirmation (A2361a) Identity of preservatives (A2461a) Phenol (A2461a) Metacresol (A2461a) Particulate matter (Ph. Eur. / USP / JP)
Container closure system of the drug product	The vial is made of colorless glass with a hydrolytic resistance as defined in Ph Eur and USP (type I glass). The plunger is made of bromobutyl rubber.
Stability study data of drug product, shelf life and storage conditions	Firm has submitted comparability report for 3 PPQ batches of stability manufactured at site Chartres and at Contract Manufacturing Site Eskayef stored for 30 months at long term conditions at 5°C±3°C.
Module 4 & Module 5 (Non-Clinical & Clinical Documentation)	No change Statement concerning to Module 4 and Module 5.

1. The firm has not submitted any evidence that the applied product is registered in any reference country.
2. The application has been sent to Legal Affairs Division, DRAP and their opinion regarding grant of additional manufacturing site is still awaited.

Decision of 331st DRB: The Board noted that opinion of the legal division for grant of additional manufacturing site is yet to come and therefore decided to defer the case and to place the matter before the Board after seeking opinion from LegalAffairs Division of the DRAP.

The comments of Legal Affairs Division are as under:

Reference para 289/N. The Registration Board, in its 330th meeting held on 24th to 26th July, 2023, referred the matter of M/s Novo Nordisk Pharma (Pvt.) Limited, Karachi for the addition of a manufacturing site for its already registered biological products. The existing manufacturing site is M/s Novo Nordisk Production SAS, 45 Avenue d' Orleans, F-28000 Chartres, France and the demanded additional manufacturing site is M/s Eskayef Pharmaceuticals Limited, 400 Squibb Road, Tongi Industrial Area, Tongi, Ghazipur 1711, Bangladesh.

The case has been examined and it is found that the law is silent on the issue of allowing an additional manufacturing site for a registered product. Previously, during the pandemic of Covid-19, M/s Roche Pakistan Limited, Karachi made a similar request which was considered in 295th meeting of the Registration Board held on 8th to 11th June, 2020 and the Board approved the addition of M/s Genetech Inc., 4625 NE Brookwood Parkway, Hillsboro, OR 97124, USA as manufacturing site for Actemra 400mg/20ml (Reg. No. 083136) as an interim measure subject to certain conditions due to the fact that the firm's global supply chain is unable to fulfill the demand of many international markets from the existing manufacturing facility (M/s Utsunomiya Plant of Chugai Pharma Manufacturing Co., Limited, 16-3, Kiyohara Kogyodanchi, Utsunomiya-city, Tochigi, Japan).

The instant case may be considered in light of the aforesaid decision of the Registration Board as insulins are included in the Model List of Essential Medicines – 23rd List (2023) published by the World Health Organization (WHO) and notified by the Ministry of National Health Services, Regulations and Coordination vide Notification No. F.8-43/2021-DD(PS) dated 2nd October, 2023 under paragraph 2(1)(xi) of the Drug Pricing Policy, 2018.

The Registration Board may develop guidelines for allowing additional manufacturing sites keeping in view the safety, efficacy and quality parameters of a product.

Decision: Registration Board deliberated the matter in detail. Representative from M/o Law and Justice, Islamabad opined that there is no provision under law to grant additional manufacturing site. Accordingly keeping in view legalized CoPP, availability of product in country of origin i.e. Bangladesh & MA Holder on CoPP i.e M/s Novo Nordisk, Denmark and release of batch from manufacturer, after approval from MA Holder i.e M/s Novo Nordisk, Denmark, Registration Board, decided to approve new manufacturing site i.e., M/s Eskayef Pharmaceuticals Limited, 400 Squibb Road, Tongi Industrial Area, Tongi, Ghazipur 1711, Bangladesh for Insulatard HM 100IU/mL, 10 mL Vial and Actrapid HM 100 IU/mL, 10 mL Vial, subject to compliance of current import policy for finished drugs. Moreover, reference shall be sent to cost & pricing division for confirmation of price. The Board further decided to call the management for personal hearing to initiate the process of cancellation of said products from existing site i.e. M/s Novo Nordisk, France.

Priority / Out of Queue consideration of Heparin & Enoxaparin Injections

DRAP Authority in its 144th meeting held on 26-08-2022 while considering the shortage of Heparin & Enoxaparin injections decided as follows:

"The Authority, as a one-time exercise, approved out of queue consideration of submitted registration applications of following drugs in order to ensure their smooth and continuous supply in the market:

Paracetamol (Tablets, lnfusion and Syrup / Suspension)
Albumin bound Paclitaxel lnjection
Heparin and Enoxaprin lnjection

PE&R and BE&R Divisions are advised to process the cases of abovementioned drugs without waiting for formal approval of minutes."

Imported Heparin Injection from non-Reference countries:

6.	Name, address of Applicant / Marketing Authorization Holder	**M/s Hakimsons (Impex) (Pvt.) Ltd.,** Address: Hakimsons Building, 19 T-30 West Wharf Road Karachi 74000 Pakistan
	Product license holder	LABORATORIOS FARMACEUTICOS ROVI, S.A. Julián Camarillo, 35 28037 Madrid – Spain
	Name, address of Manufacturing site.	Manufacturing and primary and secondary packaging site of the finished product; ROVI PHARMA INDUSTRIAL SERVICES, S.A. Paseo de Europa, 50, San Sebastian de los Reyes 28703 Madrid-Spain Batch control and batch Release site; ROVI PHARMA INDUSTRIAL SERVICES, S.A./ Julián Camarillo, 35 28037 Madrid – Spain Marketed by; Merilios Global Private Ltd. 16th Floor, Hoechst House, Nariman Point, Mumbai- 400-021, Maharashtra, India.

	Name of exporting country	Spain
	Status of the applicant	☒ Importer ☐ Manufacturer ☐ Is involved in none of the above (contract)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Diary No. 982 dated 18th October 2023.
	Details of fee submitted	PKR 150000.0/- Dated 27/09/2023
	The proposed proprietary name / brand name	Heparin Rovi 1000 IU/ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml vial contains: Heparin Sodium…….5000 IU
	Pharmaceutical form of applied drug	Solution for injection
	Pharmacotherapeutic Group of (API)	Injectable anticoagulants drugs (B01A2), ATC Code: B01AB, antithrombotic
	Reference to Finished product specifications	Ph.Eur Specifications
	Proposed Pack size	Box of 100 Vial of 5ml
	Proposed unit price	4.20 € /vial
	The status in reference regulatory authorities	Heparin Sodium Solution for injection 1000IU/ml is Registered in the country of the origin Spain. Drug Name: HEPARIN SODIUM, API: HEPARIN SODIUM, Strength: 10,000 IU/ml. Dosage Form: INJECTABLE;INJECTION, Company Name: FRESENIUS KABI USA
	For generic drugs (me-too status)	Gratin Inj, 1000IU/ml, Reg. No. 085774
	GMP status of the Finished product manufacturer	Firm has submitted Legalized GMP certificate (ES//110HVI/2Ib) valid till dated 03-06-2024
	Name and address of API manufacturer.	Yantai Dongcheng Biochemical Co., Ltd. No.07, Changbaishan Road, Yantai Development Zone, Shandong 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, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, 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: 25°C ± 2°C / 60 ± 5%RH Accelerated: 40°C ± 2°C / 75 ± 5%RH Batches: (Real time: 25 ± 2 °C / 60 ± 5%RH Accelerated: 40°C ± 2°C / 75 ± 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.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system	Vial: Type I glass (European Ph. <3.2.1.>). Stopper: Bromobutyl rubber elastomer Type I (European Ph. <3.2.9.>). Coloured aluminium protective cap.
	Stability data of Drug Product	The firm has submitted stability study data of 3 batches under following conditions: Accelerated, 6 months, 40°C ± 2°C/ 75%±5%RH Intermediate, 36 months, 30°C ± 2°C/ 65%±5%RH Batch no. | Batch size | Mfg. date 110501 | 42 L (Pilot batch) | Dec. 2011 110502 | 350 L (Ind. Batch) | Dec. 2011 110503 | 350 L (Ind. Batch) | Dec. 2011
	Remarks	• *The firm has claimed Ph. Eur. Specifications while the product is available in British Pharmacopoeia.*
Decision: The case was discussed in 331st meeting and deferred for clarification regarding finish product specification. No response received from the firm. Registration Board again deferred the case for clarification of finished product specifications (as the product is available in British Pharmacopoeia, while the firm requested for Ph. Eur. Specification) and role of marketed by. As it is mentioned on Form-5 that the product is marketed by Merilios Global Private Ltd. 16th Floor, Hoechst House, Nariman Point, Mumbai- 400-021, Maharashtra, India.		
7.	Name, address of Applicant / Importer	**M/s Himmel Pharmaceuticals (Pvt.) Ltd**. Ground Floor,6- Judicial Colony Phase-I (Ext.) Shahrah Nazaria e Pakistan, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0065-016174-D Address: Ground Floor,6- Judicial Colony Phase-I (Ext.) Shahrah Nazaria e Pakistan, Lahore Address of Godown: NA Validity: 06. Feb. 2024 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.
	Name, address of manufacturer(s)	M/s BEACON Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh.
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: Original legalized CoPP (No. DA/ 6-110/ 2016/ 13526) dated 19-07-2023 valid upto 19-07-2025 issued by Government of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration,

		Oushad Bhaban, Mohkhali Dhaka-1212, and Bangladesh. The certificate confirms free sale status of the product in the country of origin as well as GMP status. GMP: Copy of GMP certificate No. DA/ 6-110/ 06/ 6751 dated; 23.03.2023 issued by M/s Beacon Pharmaceuticals Limited.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of authorization certificate from Beacon Pharmaceuticals limited. The letter specifies that the manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 325 ; Dated: 06-09-2023
	Details of fee submitted	PKR. 150,000/- Dated: 16-08-2023
	The proposed proprietary name / brand name	Heparon Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Heparin Sodium…….25000 IU
	Pharmaceutical form of applied drug	Liquid Injection
	Pharmacotherapeutic Group of (API)	Anti-coagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Heparin sodium 25,000 I.U./ml solution for injection (Wockhardt UK Ltd, UK)
	For generic drugs (me-too status)	PINE 5000 IU/5ml injection (Heparin sodium) by; HSC
	Module-II (Quality Overall Summary)	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	Suzhou Erye Pharma Co., Ltd. No. 2 Anmin Road Dongqiao Huangtai Town, Xiangcheng District, Suzhou City, Jiangsu, P.R. 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.

	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches at long term conditions at 25℃ ± 2℃ / 60% RH ± 5% RH for 18 months. The accelerated stability data is conducted at 40°C±2℃ / 60%±5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	5 ml clear glass Vial, 20 mm Rubber Stopper, 20 mm Flip off seal with ash color top.
	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 75% ± 5% for 36 months. 2460054 2460055 2460056
	Remarks of Evaluator	Non- clinical and Clinical trial data are not submitted by the firm. Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin. *The firm has claimed BP specifications however, the test of Zone electrophoresis has not been performed for Identification*.
Previous Decision: Deferred for submission of analytical procedure indicating test of Zone electrophoresis for identification of the product as per British Pharmacopoeia (M-331). **Evaluation by BE&R:** The firm has submitted analytical method validation protocol and report for identification of Heparin sodium in Heparon 25000 IU/5ml injection by Zone Electrophoresis.		
Decision: On the basis of documents/information/data along with legalized CoPP indicating product availability in the country of origin, Registration Board after detailed deliberation approved the product subject to compliance to current Import Policy for finished drugs and provision of legalized GMP certificate from drug substance manufacturer.		
8.	Name, address of Applicant / Importer	**M/s Safemed Technologies**, APT, 3, 2nd Floor, Retoon Plaza, Mini Market, Sector G-15/1, Islamabad.
	Details of Drug Sale License of importer	License No: DHO-ISB-333 Address: APT, 3, 2nd Floor, Retoon Plaza, Mini Market, Sector G-15/1, Islamabad. Validity: 24-08-2024 Status: Distribution License
	Name and address of marketing authorization holder (abroad)	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd., No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Name, address of manufacturer(s)	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd.,

		No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	Firm has submitted legalized CoPP (No. Hebei 20210440) dated 15-10-2021 valid till 14-10-2023 issued by Hebei Province Drug Administration. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of the product in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted product specific Letter of Authorization from Enterprise Legal Person of M/s Hebei Changshan Biochemical Pharmaceutical Co., Ltd., According to the letter, the firm *M/s Hebei Changshan* exclusively authorizes "Safemed Technologies" to register, sale and quote the product. The letter was issued on 06-04-2022 and valid till 30-03-2025.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 14234 (R&I) Dated 13-06-2022
	Details of fee submitted	Rs. 150,000/- dated 02-06-2022
	The proposed proprietary name / brand name	Metaparin Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial (5ml) contains: Heparin Sodium……25000IU
	Dosage form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	5's Vials
	Proposed unit price	Rs. 1600/Vial
	Shelf Life	03 Years
	Storage Conditions	25±2°C/60±5% RH
	The status in reference regulatory authorities	Heparin Panpharma of M/s Panpharma, France.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and

		justification of specification, reference standard, container closure system and stability studies of drug substance and drug product. The firm has also submitted the non-clinical and clinical overviews and summaries.
	Name, address of drug substance manufacturer	M/s Hebei Changshan Biochemical Pharmaceutical Co. Ltd., No. 71 Menglong Street, South District of Zhengding High-tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone (050800), China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of Drug Substance at real time conditions for 36 months and accelerated conditions for 06 months. The real time stability data conducted at $25^0C \pm 2^0C/60 \pm 5\%RH$.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods of Anti-factor IIa Activity, Anti-factor Xa activity, Benzyl Alcohol determination & Sterility test. Firm has submitted verification of Analytical methods of Related substances & Bacterial Endotoxin test.
	Container closure system of the drug product	EP Type I Colorless Glass vial, Grey Halogenated Butyl Rubber stopper, Aluminum & Plastic combined caps.
	Stability study data of drug product	Firm has submitted stability study data of 03 batches. The accelerated stability study data is conducted at 40±2°C/75%RH±5% for 6 months. The real time stability study data is conducted at 25±2°C/60%±5RH for 36 months.
	Remarks of Evaluator	Non- clinical and Clinical trial data are not submitted by the firm. Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product, hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin.

Previous Decision: Keeping in view the availability of product in country of origin as per submitted CoPP and Heparin Injection being non-rDNA pharmacopoeial product; Registration Board approved the product as per current Import Policy for finished drugs (M-320).

Evaluation by BE&R: Initially, the applied product was considered and approved in 320th meeting of Registration Board. After that, the panel comprising of Mr. Muhammad Kashif and Mr. Faisal Shehzad conducted virtual GMP inspection on 10-04-2023 & 11-04-2023 and concluded as following:

> "*Based on the proceedings of virtual inspection, documents reviewed and videos of the unit seen, and considering the fact that Heparin sodium is a polysaccharide (no killed/attenuated organism in final product), the panel has concluded that the firm has adequate systems to manufacture heparin sodium and appeared to comply with the cGMP requirements.* ***However, the panel also observed during virtual inspection documentary review that the manufacturer***

does not hold CoPP for applied strength of 25000 IU in China. Hence, the panel recommended that the provisions under DRAP Act, 2012 and relevant rules must be checked for grant of registration for such biological drugs. *The importing firm may also be directed to update DRAP for inclusion of manufacturing of any other biological drug in bulk production and / or filling area by the manufacturer along with their NRA approval, QRM report and re-validation of cleaning, if added in future.*"

During further processing of the case, it was observed that the product is not licensed to be placed on the market for use in China. Recently, the firm has submitted that our product is manufactured under license of Ministry of Health of China. The product is also being exported and registered with health authorities of Republic of the Philippines, Uzbekistan and Bolivia. Copies of registration certificates for these countries have been provided.

Decision: Registration Board deferred the case for evidence of availability of product in the country of origin or in RRA or in any three eastern European countries from same manufacturer.

9.	Name, address of Applicant / Importer	**M/s PAK CHINA INTERNATIONAL,** 498-C Feroz Shah Mehta Road, Karachi.
	Details of Drug Sale License of importer	License No: 0117 Address: 498-D Hume Road, Quaideen Colony, Near 3 Star Hall, Jamshed Road, Karachi Validity: 18-04-2023.
	Name and address of marketing authorization holder (abroad)	M/s Cisen Pharmaceutical Co. Ltd., Tongji Tech Industry Garden, Jining High and New Technology Industries Development Zone, Jining, Shandong Province, P.R. China.
	Name, address of manufacturer(s)	M/s Cisen Pharmaceutical Co. Ltd., Tongji Tech Industry Garden, Jining High and New Technology Industries Development Zone, Jining, Shandong Province, P.R. China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	CoPP: The firm has submitted original, legalized CoPP (Shandong2036072) issued by Shandong Provincial Medical Products Administration. The certificate confirm that the product is actually on the market in the exporting country and facilities and operations conform to GMP as recommended by WHO. The certificate is valid till 03-12-2024.
	Details of letter of authorization / sole agency agreement	Copy of product specific sole agency agreement from manufacturer abroad hereby authorizes M/s Pak China International, Karachi to act as authorized representative to conduct all the formalities related to import, sell, distribute in the territory of Pakistan.
	Status of the applicant	☐Manufacturer ☒Importer ☐Is involved in none of the above (contract giver)
	Status of application	☐New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging

		☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Diary No. 804, Dated: 06-10-2023
	Details of fee submitted	Rs: 150,000/- Dated: 04-10-2023 Deposit Slip No. 640275156
	The proposed proprietary name / brand name	HEPARIN INJECTION 5ml/25000IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml vial contains: Heparin Sodium……..25000 IU
	Dosage form of applied drug	Liquid Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Finished product specifications	BP specifications
	Proposed Pack size	1 × 5 ml vial
	Proposed unit price	As per SRO
	Shelf Life	24 months
	Storage Conditions	Store at 20°C – 25°C
	Reference Regulatory Authorities	Heparin sodium Injection, USFDA Approved.
	For generic drugs (me-too status)	PINE 5000 IU/5ml injection (Heparin sodium) by; HSC
	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 Dongying Tiandong Pharmaceutical Co Ltd. Address: No. 1236, Nan-er Road, Dongying City, Shandong, P.R. 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	Firm has submitted stability study data of 3 batches at long term conditions at 25°C ± 2°C / 60% RH ± 5% RH for 18 months. The accelerated stability data is conducted at 40°C±2°C / 60%±5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Analytical method Validation / verification of the product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	5ml vial low borosilicate glass tubing
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of Heparin Injection at accelerated and real time conditions. The real time stability data conducted at 30°C ± 2°C / 65% RH ± 5%RH for 36 months and accelerated stability data conducted at 40°C ± 2°C/75% RH ± 5%RH for 06 months for 3 batches. 170426 170427 170428
	Remarks of Evaluator	• Non- clinical and Clinical trial data are not submitted by the firm. The same is not required as Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin. • The product was already registered with Pak china International (Reg # 013266) dated 5th July 1992 with same exporter as applied in the instant case i.e.Ningbo Nuobai Pharmaceutical Co.,Ltd, China, However, the firm did not submit the renewal application after 2007. As per SRO when the renewal is submitted after the lapse of one year of due date of submission of renewal application, the product is automatically deregistered. Therefore, the firm has submitted new application.
Previous Decision: Deferred for the clarification regarding the availability in the country of origin (M-331).		
Decision: Registration Board deferred the case for evidence of availability of product in the country of origin or in RRA or in three eastern European countries from same manufacturer.		
10.	Name, address of Applicant / Importer	**M/s AMB HK Enterprises (Pvt) Ltd.,** 2nd Floor, Plaza 60, Commercial Block K, Phase-1 DHA, Lahore. Godown address: House 27, Street 4-A Sanda Bhatian Wala Gulshan Ravi, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0058-104514D Validity: 08-05-2028 Address of Godown: House 27, Street 4-A Sanda Bhatian Wala Gulshan Ravi, Lahore Status: License to sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	**M/s Skymap Pharmaceuticals Pvt. Ltd.,** B-2 Dev Bhoomi Industrial Estate, Puhana Iqbalpur Road, Roorkee-247667 Distt. Haridwar Uttarakhand India.
	Name, address of manufacturer(s)	**M/s Skymap Pharmaceuticals Pvt. Ltd.,** B-2 Dev Bhoomi Industrial Estate, Puhana Iqbalpur Road, Roorkee-247667 Distt. Haridwar Uttarakhand India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	CoPP: The firm has submitted copy of CoPP (26/1/Drug/92/2019/19184) issued by Food Safety and Drug Administration Authority, Directorate General of

		Medical health & Family Welfare Uttarakhand, India. The certificate confirm that the product is actually on the market in the exporting country and facilities and operations conform to GMP as recommended by WHO. The certificate is valid till 07-06-2025.
	Details of letter of authorization / sole agency agreement	Copy of sole agency agreement from manufacturer abroad hereby authorizes M/s AMB HK Enterprises Pvt Ltd, Lahore to act as authorized representative to conduct all the formalities related to import, sell, distribute in the territory of Pakistan.
	Status of the applicant	☐Manufacturer ☒Importer ☐Is involved in none of the above (contract giver)
	Status of application	☐New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Diary No. 17338, Dated: 11-07-2023
	Details of fee submitted	Rs: 150,000/- Dated: 10-07-2023 Deposit Slip No. 852401390
	The proposed proprietary name / brand name	Heparin Injection 5ml / 5000IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml vial contains: Heparin Sodium……..5000 IU
	Dosage form of applied drug	Liquid Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Finished product specifications	BP specifications
	Proposed Pack size	1 × 5 ml vial
	Proposed unit price	As per SRO
	Shelf Life	24 months
	Storage Conditions	Store at a temperature not exceeding 30 °C.
	Reference Regulatory Authorities	Heparin sodium Injection, MHRA Approved.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted QOS 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 Hebei Changshan Biochemical Pharmaceutical Co., Ltd. No. 71, Menglong street, South District of

		Zhengding High-Tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone P.R. 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	Firm has submitted stability study data of 3 batches at long term conditions at 25°C ± 2°C / 60% RH ± 5% RH for 48 months. The accelerated stability data is conducted at 40°C±2°C / 60%±5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method Validation / verification of the product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	A colourless or straw coloured liquid free from turbidity filled from turbidity filled in 5ml light amber colour, tubular glass vials, plugged with 13mm bromo butyl rubber stopper and sealed with 13 mm white flip off.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of Heparin Injection at accelerated and real time conditions. The real time stability data conducted at 30°C ± 2°C / 65% RH ± 5%RH for 24 months and accelerated stability data conducted at 40°C ± 2°C/75% RH ± 5%RH for 06 months for 3 batches. A20LV129 A20LV130 A20LV138
	Remarks of Evaluator	• Non- clinical and Clinical trial data are not submitted by the firm. The same is not required as Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin. • *Original, legalized CoPP issued by concerned authority of country of origin is required to be submitted.* • *Original / notarized copy of sole agency agreement are required to be submitted.*
Decision: Deferred for submission of following: • **Legalized CoPP issued by concerned authority of country of origin.** • **Original product specific sole agency agreement / Letter of Authorization.**		

• **Legalized GMP certificate of drug substance manufacturer.**		
11.	Name, address of Applicant / Importer	**M/s AMB HK Enterprises (Pvt) Ltd.,** 2nd Floor, Plaza 60, Commercial Block K, Phase-1 DHA, Lahore. Godown address: House 27, Street 4-A Sanda Bhatian Wala Gulshan Ravi, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0058-104514D Validity: 08-05-2028 Address of Godown: House 27, Street 4-A Sanda Bhatian Wala Gulshan Ravi, Lahore Status: License to sell drugs by way of whole sale.
	Name and address of marketing authorization holder (abroad)	**M/s Skymap Pharmaceuticals Pvt. Ltd.,** B-2 Dev Bhoomi Industrial Estate, Puhana Iqbalpur Road, Roorkee-247667 Distt. Haridwar Uttarakhand India.
	Name, address of manufacturer(s)	**M/s Skymap Pharmaceuticals Pvt. Ltd.,** B-2 Dev Bhoomi Industrial Estate, Puhana Iqbalpur Road, Roorkee-247667 Distt. Haridwar Uttarakhand India.
	Name of exporting country	India
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	**CoPP:** The firm has submitted copy of CoPP (26/1/Drug/92/2019/19184) issued by Food Safety and Drug Administration Authority, Directorate General of Medical health & Family Welfare Uttarakhand, India. The certificate confirm that the product is actually on the market in the exporting country and facilities and operations conform to GMP as recommended by WHO. The certificate is valid till 07-06-2025.
	Details of letter of authorization / sole agency agreement	Copy of sole agency agreement from manufacturer abroad hereby authorizes M/s AMB HK Enterprises Pvt Ltd, Lahore to act as authorized representative to conduct all the formalities related to import, sell, distribute in the territory of Pakistan.
	Status of the applicant	☐Manufacturer ☒Importer ☐Is involved in none of the above (contract giver)
	Status of application	☐New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Diary No. 17339, Dated: 11-07-2023
	Details of fee submitted	Rs: 150,000/- Dated: 10-07-2023 Deposit Slip No. 8120832213
	The proposed proprietary name / brand name	Heparin Plus Injection 5ml / 25,000IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml vial contains: Heparin Sodium……..25000 IU

	Dosage form of applied drug	Liquid Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Finished product specifications	BP specifications
	Proposed Pack size	1 × 5 ml vial
	Proposed unit price	As per SRO
	Shelf Life	24 months
	Storage Conditions	Store at a temperature not exceeding 30 °C.
	Reference Regulatory Authorities	Heparin sodium Injection, USFDA Approved.
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted QOS 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 Hebei Changshan Biochemical Pharmaceutical Co., Ltd. No. 71, Menglong street, South District of Zhengding High-Tech Industrial Development Zone, Zhengding Area of China (Hebei) Pilot Free Trade Zone P.R. 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	Firm has submitted stability study data of 3 batches at long term conditions at 25℃ ± 2℃ / 60% RH ± 5% RH for 48 months. The accelerated stability data is conducted at 40°C±2℃ / 60%±5%RH for 06 months for accelerated conditions.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Analytical method Validation / verification of the product	Firm has submitted the details of analytical method validation.
	Container closure system of the drug product	A colourless or straw coloured liquid free from turbidity filled from turbidity filled in 5ml light amber colour, tubular glass vials, plugged with 13mm bromo butyl rubber stopper and sealed with 13 mm white flip off.

	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of Heparin Injection at accelerated and real time conditions. The real time stability data conducted at 30°C ± 2°C / 65% RH ± 5%RH for 24 months and accelerated stability data conducted at 40°C ± 2°C/75% RH ± 5%RH for 06 months for 3 batches. A20LV141 A20LV142 A21LV032
	Remarks of Evaluator	• Non- clinical and Clinical trial data are not submitted by the firm. The same is not required as Registration Board in its 271st meeting considered that Heparin Sodium Injection is non-rDNA pharmacopoeial product hence, revised its decision of 260th meeting and granted the approvals on the basis of valid legalized CoPP & availability in country of origin. • *Original, legalized CoPP issued by concerned authority of country of origin is required to be submitted.* • *Original / notarized copy of sole agency agreement are required to be submitted.*
Decision: Deferred for submission of following: • **Legalized CoPP issued by concerned authority of country of origin.** • **Original product specific sole agency agreement / Letter of Authorization.** • **Legalized GMP certificate of drug substance manufacturer.**		
12.	Name, address of Applicant / Importer	**M/s We Care** **Address:** Flat B-6 Block 12 D 2nd Floor G-8 Markaz Islamabad Pakistan.
	Details of Drug Sale License of importer	License No: DHO-ISB-930 Address: Flat B-6 Block 12 D 2nd Floor G-8 Markaz Islamabad Pakistan Validity: 19-06-2025 Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s PT PRATAPA NIRMALA JL. INDUSTRI VI TANGERANG 15135-INDONESIA
	Name, address of manufacturer(s)	M/s PT PRATAPA NIRMALA JL. INDUSTRI VI TANGERANG 15135-INDONESIA
	Name of exporting country	Indonesia
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	Firm has submitted legalized CoPP (No.RG.01.05.32.321.05.22.3865) dated 17-05-2022 valid till 17-05-2024 issued by National Agency of Drug and Food control Jl. Percetakan Negara No. 23, JAKARTA- INDONESIA. The certificate specifies the GMP status of the manufacturer. The certificate specifies the Free Sale status of 5's x 5ml vial in country of origin.
	Details of letter of authorization / sole agency agreement	Firm has submitted legalized LOA dated 26-04-2022 and legalized distribution agreement dated 21-04-2022 (signed by both firms) valid for five years.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale

		☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Bulk import and local repackaging ☐ Bulk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 5109 (R&I) dated 21-02-2023
	Details of fee submitted	Deposit Slip # 8167115543 of PKR. 150,000/- dated 22-02-2023
	The proposed proprietary name / brand name	**Inviclot Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Heparin Sodium……5000IU
	Dosage form of applied drug	Liquid Injection
	Pharmacotherapeutic Group of (API)	Anticoagulant
	Reference to Finished product specifications	-
	Proposed Pack size	5's x 5ml vial
	Proposed unit price	Not Provided
	Shelf Life	24 months
	Storage Conditions	Store Below 30℃
	The status in reference regulatory authorities	Not provided
	For generic drugs (me-too status)	Vaxcel Heparin Sodium Injection of M/s Ghazali Brothers (Reg. No. 088528).
	Module-II (Quality Overall Summary)	Firm has submitted QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, flow of manufacturing process, analytical procedures, justification of specification.
	Name, address of drug substance manufacturer	**Company:** Adeste Indústria de Produtos Animais LTD **Address:**Rua Paes Leme, 524, 6º andar Grupo 63 - CEP 054 24 904 Pinheiros – São Paulo – Brazil Phone: 55 11 30975544 Fax: 55 11 30975545
	Module-III Drug Substance:	Firm has submitted drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, specifications, analytical procedures, batch analysis and justification of specifications.
	Stability Studies of Drug Substance	Firm has provided stability studies of 3 batches of drug substance.
	Module-III Drug Product:	Firm has summarized data of drug product including its composition, manufacturing process, control of drug product, process verification, specifications, batch analysis, container closure system and stability.
	Analytical method validation/verification of product	Firm has submitted validation of Analytical methods
	Container closure system of the drug product	Heparin Sodium 5000 units/mL is supplied as 5-mL volume injection, in a vial made of type I glass and packed in a box. Each container bears printed information concerning product characteristics (name, active ingredient, pharmaceutical form, strength) and batch characteristics (batch number and expiration date). The suitability of the primary packaging is confirmed by the Certificate of Quality from the vial manufacturer. Incompatibilities with primary packaging or excipients used were not observed; however, during the stability

		study there were not any particles leaked and the parameters tested remained within the requirements.
	Stability study data of drug product	Firm has submitted stability study data of 03 batches. The accelerated stability studies are conducted at 40±2°C/75%RH±5% for 6 months. The real time stability studies are conducted at 30±2°C/75%±5RH for 36 months for one batch. While at 30±2°C/60%±5RH for other two batches. Bacterial Endotoxin test and sterility test are performed at 0,6,24 and 36 months in real time stability studies while at 0 and 6 months in accelerated stability studies.
	Remarks of Evaluator	The firm has not performed testing as per official pharmacopeia.
	Decision of RB in 331st meeting	*Registration Board deferred the case for submission of specifications, analytical procedures and COAs as per official pharmacopoeia.*
Decision: The case was discussed in 331st meeting of Registration Board. No response received from the firm. Case was deferred for clarification by the firm.		

Imported Human Biological (GDK Flu Quadrivalent Vaccine) applied by M/s Lab Diagnostic Systems (SMC) Pvt. Ltd.

13.	**Name, address of Applicant / Importer**	Lab Diagnostic Systems (SMC) Pvt. Ltd. Plot 36-A, PSIC SIE, Taxila Rawalpindi
	Details of Drug Sale License of importer	License No: 01-374-0006-96845D **Address:** 36-A, PSIC, SIE, Taxila Rawalpindi Validity: 04/08/2024
	Name and address of marketing authorization holder (abroad)	Name: Jiangsu GDK Biological Technology Co., Ltd. Address: No. 12, Yujin Road, Taizhou Pharmaceutical Hi tech Industrial Development Zone, Jiangsu Province, China
	Name, address of manufacturer(s)	Name: Jiangsu GDK Biotechnology Technology Co., Ltd. Address: No. 12, Yujin Road, Taizhou Pharmaceutical Hi tech Industrial Development Zone, Jiangsu Province, China
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free Sale certificate, GMP certificate)	Firm has submitted legalized CoPP (No.Jiangsu20230116) issued by Jiangsu Medical Product Administration, China. The COPP specifies that the product is licensed for sale in country of origin. The COPP also specifies the GMP status of manufacturer.
	Details of letter of authorization / sole agency agreement	Firm has submitted legalized Distribution Certificate from **M/s** Jiangsu GDK Biological Technology Co., Ltd. China.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	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	Form -5F

		Dy. No.: 478 R&I dated: 13/09/2023
	Details of fee submitted	Rs: 150,000 Dated: 18/08/2023 Deposit Slip No. 9971882166
	The proposed proprietary name / brand name	GDK Flu Quadrivalent Vaccine
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 0.5 mL dose contains 15 µg of hemagglutinin protein (60 µg total) from each of the following four influenza subtypes or lineages: A/H1N1, A/H3N2, B Victoria, B Yamagata 0.5ml/piece/box.
	Dosage form of applied drug	Pre-Filled Syringe
	Pharmacotherapeutic Group of (API)	Quadrivalent influenza Vaccine
	Reference to Finished product specifications	Chinese Pharmacopoeia
	Proposed Pack size	1's PFS
	Proposed unit price	As per SRO
	Shelf Life	12 months
	Storage Conditions	2°C – 8°C
	The status in reference regulatory authorities	INFLUVAC® Tetra 2021 USFDA
	For generic drugs (me-too status)	-
	Module-II (Quality Overall Summary	Firm has submitted QOS as per ICH guidelines. Firm has summarized information related to general properties, manufacturers, description of manufacturing process and controls, characterization, 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	Name: Jiangsu GDK Biological Technology Co., Ltd. Address: No. 12, Yujin Road, Taizhou, Jiangsu Province, 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, container closure system.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability data of 3 batches as; Long term stability data (6±2°C) at 0,1,2,3,6,9,12 and 15 months. Stress testing (37±2°C) at 0,1,3,5,7,10,14, and 21 days. Accelerated stability study (25±2°C) at 0,1,3,5,7,10,14 and 21 days.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control 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	Method verification was carried out for identification, osmotic pressure molar concentration, free formaldehyde content, hemagglutinin content, protein content, ovalbumin content, sterility test and bacterial endotoxin

		test on applied vaccine. Chinese Pharmacopeia was followed for specifications.
	Container closure system of the drug product	The container closure system consists of primary packaging materials and secondary packaging materials. The primary packaging materials include assemblages for prefilled syringes (with stainless steel needles), chlorobutyl rubber stoppers for prefilled syringes and plungers for prefilled syringes; secondary packaging materials include labels, package inserts, boxes, medium boxes, cartons, PVC sheets, and composite films.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches at real time and accelerated conditions. The real time stability data provided is conducted at 6 ± 2 °C for 18 months. The accelerated stability data provided is of 03 batches and is conducted at 25 ± 2 °C for 06 months.
	Module-IV (Non-Clinical)	Firm has submitted; Toxicity study in mice. Active systemic anaphylaxis study in guinea pigs. Muscle irritation study in rabbits.
	Module-V (Clinical)	Firm has submitted, • A single center open label phase 1 clinical trial investigating safety in 41 health individuals aged 18-49 years old. • A phase III clinical trial with single center, randomized, double blind, positive controlled, non-inferiority design investigating immunogenicity and safety in volunteers over 3 years of age.
	Remarks of Evaluator	• The brand name on CoPP is different from the brand name on Form5-F (CTD). • Stability data submitted by the firm does not include batch size, relative humidity and pack size. • Repeat dose toxicity studies are not provided in detail in Module 4 of CTD. • Phase III clinical trial is monocentric.
	Decision of RB in **331st meeting**	**Registration Board after due deliberation decided to defer the case for submission of following deficient information/documents:** 1) Repeat Dose Toxicity Studies, 2) Rationale/guideline for selection of monocentric phase III clinical trial, 3) clarification of brand name and parameters of stability data i.e batch size, relative humidity and pack size. The matter of short availability of influenza vaccine in the country was discussed in detail and the board noted that in order to make the product available in the country, more competitors should come in market, the Board constituted the following panel for virtual GMP inspection of manufacturer abroad: • *Ms. Haleema Sharif (Deputy Director BE&R)* • *Mr. Akbar Ali (Deputy Director QA&LT)*
	Remarks of BE&R	The firm has submitted the following; • Repeat dose toxicity studies • Stability data with required parameters/conditions • Clarification on brand name that the CoPP is with Generic name and Form 5-F is with brand name and Letter of Authorization from manufacturer is also with brand name. • The firm has submitted declaration from principal that all the Chinese manufacturers of influenza

		vaccine are conducting monocentric phase III clinical trials. *The manufacturer has developed the product as per "Chinese Pharmacopoeia" while the product monograph is available in "European Pharmacopoeia".*
	Decision: Keeping in view above; Registration Board after detailed deliberation, legalized CoPP and availability of product in country of origin, approved the product subject to compliance of specifications as per Drug Specification Rules 1978 and current Import Policy for finished drugs.	

End of Document