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Eskayef Pharmaceuticals Limited in plant training report

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ESKAYEF PHARMACEUTICALS LIMITED

Report on In-Plant Training

Eskayef Pharmaceuticals Limited

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ACKNOWLEDGEMENTS

All praise to Almighty God who has given me the opportunity to undertake and complete this in-plant training and finally write up the report.

I would like to thank Mr. Latifur Rahman, Chairman, Transcom Group & Mrs. Simeen Hossain, Managing Director & Chief Executive Officer, Eskayef Pharmaceutical Limited for their kind acceptance to arrange 12 days in plant Training from 19th January to 2th February 2026 in Eskayef Pharmaceuticals Limited, where I have earned practical knowledge about a pharmaceutical company in different sections.

I would also like to thank Abdullah Al Wahid Executive Director of Plant, Rupganj plant Eskayef Pharmaceuticals Limited and Mohammad Ismail Bablu Executive General Manager Quality Eskayef Pharmaceuticals Limited for their kind acceptance to perform in plant Training in a company.

I would like to convey a big thank you to Mr. Rajkumar Karmakar , General Manager & Mr. Mohammad Moniruzzaman Senior QA Manager Rupganj plant Eskayef Pharmaceuticals Limited for his constant support and enthusiasm to all the trainees during training period.

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With Regards,

Sumaiya Islam

LETTER OF TRANSMITTAL

12 April , 2026

Mr. Berun Kumar Roy

Production Manager, Eskayef Pharmaceutic Limited, Rupganj Plant

Subject : Submission of In Plent Training Report.

Dear Sir,

With due respect, I would like to inform you thag it is a great pleasure for me to submit the ln Plant Training report as a requirement for the completion of the training program. Thank you very much for your help & support in ananging the study program. This report, which I would like to submit to you for your evaluation, is a discussion of my observations.

I am very grateful to my supervisor, Eskayef Pharmaceuticals authority, and the university for giving me the opportunity to complete my training program smoothly. I have tied to combine all the necessary data available in order to come up with a complete report. Besides several constraints, I have givan all my efforts to make this report meaningful.

I sincerely believe and hope that you will find this study very interesting, information and enlightening. I beg your kind excuse for the unintentional error that may take place in the report

in spite of my best efforts. I sincerely hope that this report will meet your approval.

Thank you very much for your kind cooperation without which the Training program cannot be completed. I like to take every opportunity to express my gratitude of indebtedness to you.

I, therefore, would like to request you to accept my report and oblige me with the honour of completing my training. Thank you

Regards

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Introduction

One of Bangladesh's biggest and fastest-growing pharmaceutical companies is Eskayef Pharmaceuticals Ltd. The business, which is a member other Transcom Group, is also known as SK+F and has its headquarters in Dhaka, the capital of Bangladesh. When the business was reorganized to become GlaxoSmithKline in 2000, the former SmithKline & French facilities in Bangladesh gave rise to SK+F Eskayef Pharmaceuticals Limited. Eskayef envisions a leading role for it self as a catalyst for improvement of the healthcare environment. The company's mission is to maintain people's health and combat disease to enhance the quality of human life so that people may live longer, healthier and more meaningful lives. The chairman of Transcom group planted a seed of dream in 1885. As the years went by the seed began to grow and soon turned into a full-grown tree with its leaves branching out in innumerable ventures .

Today, TRANSCOM is one of the leading conglomerate companies of the country. The dream has turned into reality by the pragmatic vision of Mr. Latifur Rahmrn, the Chairman of TRANSCOM GROUP and Eskayf Bangladesh Limited and the company proudly stands symbolising the epic tree of the seed that was planted 120 years ago.

Eskayefs manufacturing facility has transcended the frontiers after the accreditation of UK MHRA (United Kingdom Medicines and Healthcare products Regulatory Agency). Eskayef has been growing rnore globally since 2005 and exporting bulk pellets and finished products in Asi4 Africa, Central America, Europ€ and Australia. The company is also tied up with the world leader in eye care solution Allergan Inc. Ireland. The company often manufactures insulin in a world clr.cs facility which is being exported to Novo Nordisk.

The company $ arted its production of pharmaceuticals with the manufacture of generic products for the domestic market but has since moved into bulk products and the veterinary market. SK+F Eskayef currently manufactures and markets 28 different animal health product in 57 different dosage forms.

Mission

To produce and sell goods of the highest caliber while also helping to enhance the general health and wellbeing of the populace.

Vision

To dominate the domestic pharmaceutical business, gain recognition as a multinational corporation from Bangladesh, and establish ourselves as a reliable and efficient role model for our partners, clients, medical professionals, and the general public.

Facilities

One of Bangladesh's pharmaceutical enterprises with the quickest rate of growth, Eskayef produces and distributes a varity of medicinal l medications, bulk pellets, and goods for the health and nutrition of animals. Currently, the companys yearly sales turnover exceeds BDT 4.50 billion.

From its founding, Eskayefs business has grown quickly, placing it at the top of the list of pharmaceutical businesses in Bangladesh today. It produces and distributes 126 prescription drugs in 294 dosage forms, and 22 of those medications are market leaders in terms of brand recognition. Thanks to its highly qualified, experienced, and competent staff as well as its unwavering standards of quality control, Eskayef has become one of the most well-known brands in Bangladesh's pharmaceutical sector.

Manufacturing zones of Eskayef

o Mirpur Plant

o Toagi Plant

o Rupganj Plant

o Shalna Planl

HSE (Health Safety and Environment)

HSE is the state of complete physical, mental, and social well-being and rest merely the dance of disease. Safety is regarded as the awareness to stay alert to every task. Last but not the least, all our sounds make up our environment. To incorporate all these three into a singularity is the primary objective of HSE department

Objectives of HSE are:

o To promote occupational health.

o The development of wort organisation and working cultures that should reflect essential value systems adopted by the undertaking concemed, and include effective managerial systems, personnel policy, principles for participation, and voluntary quality related management practices to improve occupational safety

and health.

0 The maintenance and promotion of worker health and working capacity.

o The improvement of working conditions and the working environment to become conducive to

Safety and health:

HSE training is instrumental to ensure mental and physical well being of all the party involved.com benefit and also having to enforce policy facilitating laws for the employees and to ensure no crime. Many rules and regulations are in place to ensure the practice of safety in the workplace such as BLA, CCRS7, Electricity Act, etc. 5045001, established in 2018, assures the HSE of organisation that the pharmaceutical industries must comply with such inter national certifications. HSE training prepares us to combat against amergoes such as natural, constructional and operational We must handle rach disaster with extreme precaution and by ensuring the following parameters

Prevention

Preparcdness

Response and

Recovery

Eskayef ensures the safety of employees and uho of the erotient very seriously and the huge piece ofthe budget for safety training and to properly tocate the toxic waste product by the factory by either using an incinerator or CTP. They have a contract with Moulds Cement Gladesh To help them with their waste management. Furthermore, they also arc ensuring proper safety tools Installation by maintaining Pillar Hydrant, Sensor, Manual Call Room, Extinguisher, CCTV etc.

Rupgani Plant

Rupganj plant is located in Murapara" Rupganj, Narayanganj - 1464

Rupganj plant is divided into five distinct unit:

General Manufacturing Unit

Oncology Unit

Penicillin Unit

Penem Unit

Cosmetics Unit (currently not running)

Warehouse

A Pharmaceutical warehouse is a place where raw materials (RM), packaging materials (PM) and finished goods (FG) are kept for storage according to their storing conditions. To accommodate huge raw materials, Eskayef Rupganj plant currently has seven vast warehouses namely warehouse 0l ,02,03,04,05,06 and 07 .

o Warehouse l: Under construction for soft gel.

o Warehouse 2: The capacity of Warehouse 0l is 7, 34,000 square feet. lt maintains a Conholled room temperature below 25 degree Celsius (15-25"C) and used for raw materials only which includes both API and excipients which need to be stored at this temperature range. The basic functioning ofa warehouse is to receive the raw materials which include both excipients and active ingredients, properly and store them in the correct storing conditions as required. When a raw material comes to the industry it is received in the loading/unloading bay. Here when the raw materials are brough! the materials are checked whether the correct materials have been brought correct amount, manufacturing date, expiry date and from the approved source. The source is checked by the approved source list given. After all these checking the material is unloaded. The

sample of raw material is taken and sent to the Quality control lab for testing to ensure the identity of the product. In case of API all the containers that is 100% checking is done and for excipients the checking is done by using a formula [Vn+1n= no. of container]

if 100 containers are there then samples from I I containmen will be taken and checked. But in case of propylene glycol 100% identity test is done after the Reed Pharma Tragdy.

After these ar€ sent for sampling these materials and before receiving they arr given R.R no and labelled QUARANTINE and kept in the warehouse. If the materials are appved form the QC then they are labelled PASSED and if not then they are labelled REJECT. The containers from where samples are taken after sampling are labelled SAMPLED. If the materials are purchased from a local manufacturer then they are rcturned before the billing happens in case the materials are rejected but if exported then they are kept in the reject room (located in warehouse l) and after 3 months with proper

authorization desuoyed.

There is a cool room under construction:

o Warehouse 3: Raw materials of penicillin.

o Warehouse 4 Packaging materials of penicillin.

o Warehouse 5. Under reconstruction.

Warehouse 6: Raw materials of Agrovet are kept here. Ambient temp€rature is maintained here.

o Warehouse 7: Mixture of RM & PM (Maxi. PM). This warehouse maintains a temperature below 45oC (Ambient temperature). It is mainly used for storing packaging materials (shippers, bottles, vials, rubber stoppers, E-cup, foil etc.).

Different units of warehouse:

Quarantine Area

o Released Area

o Dispensing Area

Finished Product Area

o Rejected Area

o Packaging Products Area Special Arca

o QC Sampling Room

o Change Room for Warehouse Officers & Workers

o Change Room for QC Officer

The main functions of Warehouse:

o Material Receiving

o Storing

o Dispensing.

Materials Receiving System:

Upon receiving the shipment's labelling should be carefully to make sure that they belong to the same source approval. Only materials from the same batch receive the same Receiving Record (RR) number.

o The RR is the identification number for that raw material.

o The shipment should be inspected visually for damage.

o The materials are then carefully labelled 'Quarantine" with the RR number.

o Rejected materials should be clearly separated from the 'released' materials.

Rejected packaging materials containing the company's logo are deshoyed. For raw materials that are rejected the vendor is contacted immediately.

Storage:

* Raw materials and finished products are stored according to their chemical or physical properties.

*Some raw materials and finished products are kep in normal room Condition.

*In order to prevent mix-up of printed containers and labelling materials, each printed packaging material is stored properly identified with the specific GRN number and code number and at the time issues the identity is checked very carefully.

Working process for Raw Material & Packaging Material:

They receive materials which are purchased by purrhasing department Keep record and send Sampling booth for sampling pass label about those. + materials to QC + QC collects sample + perform test and provide approval or rejected tag +

If QC tests are passed, then supply raw materials, packaging materials, excipients to the concened depertmnent according to product order sheet and product requisition in the first in first out process.

Keep records about that.

Working process for Finished Goods:

After packaging of final product, QA gives the NOT RELEASED yellow tag in the shipping carton + Stored in the outer portion of the ware house-2. +

After all the performed tests by QC are passed, they give the RELEASED green tag removing the previous one. (lf not passed, a HOLD label is given). +

Then these RELEASED goods are moved to the inner portion ofthe ware house-2

+ According to market demand, the released products are distributed in First in first out

process to the depots. Conditions for storage:

Storage	Ambient	cold	cool	CRT
Temperature	below 4OaC	2-8C	8-15C	15-25C
RH	-	20RH%	35%RH	55%RH

There is one cool room for essence and color. Capsule room- 15.5"C-24.4oC & RH 39-61% Ambient temperature is set at the warehouse. However, for moisture sensitive products, specific RH and RT is maintained. Three types of areas are maintained for storing materials :

*Cold temperature area (2-8'C) for storing insulin, omeprazole powder etc.
*Cool temperature area (8-150 c) for storing colouring, flavouring material etc.
*Relative humidity area for storing capsule shells and other types of blistering material.

General manufacturing unit (Production)

In general manufacturing unit, two types of dosage form are prepared: Solid Dosage form:

o Tablet (Vet)

Powder for Suspension (PFS)

Liquid Dosage Form:

o Solution (Vet)

Among these two types of dosage form:

Human product:

NRG(PFS):

Losectil 20mg (PFS)

Losectil 40 mg (PFS)

Juicy (PFS)

Esobgul

Animal prcduct:

o Marbo vet Bolus

o Xinc B Vet O/S

Tablet (Vet)Production in GMU:

Tablet is defined as a compressed unit solid dosage form containing medicaments with or without excipients.

o lntended mainly for oral administration

o Most commonly are disk shaped with convex surfaces

o Available in special shapes like round, oval, oblong, cylindrical, squart, triangular.

Tablet formulation and design may be described as a process where the formulator ensures that the correct amount of drug in the right form is delivered at or over the proper time at the proper rate and in the desired location, while having the chemical integrity protected to that point. Tablet constitutes a major class of dosage form. It is the preferred class of product due to minimum bullk stability, and uniform dose etc. Tablet formulation is critical as different problems may arise during the steps involved.

Types of tablets :

1 Oral Tablet for Ingestion

2 Compressed tablet or standard compress tablets Multiple compressed tablets

3 Repea.t action tablets

4 Delayed action and enteric coated tablets

5 Sugar and chocolate coated tablets

6 Film coated tablets

7 Chewable tablets

Tablet Used in Oral

Cavity: o Buccal

tablets

Sublingual tablets

Troches tablets

Dental cones

Tablet Administered by Other Routes:

implantation tablets

Vaginal tablets

Tablet Used to Prepare Solution :

Effervescent tablets

Dispensing tablets

Hypodermic tablets

Tablets triturate

Filler or diluent

A filler, such as sucrose or lactose, is included to increase the size of the tablet. This is necessary as often the amount of 'active' is so tiny that the tablet would be too small to handle without it.

Disintegrating agent :

Disintegrating agents help the tablet to break down into small fragments, when it is ingested. This helps the medicine to dissolve and be taken up by the body so that it can act more quickly. Disintegrating agents may include potato or cocoa butter.
Examples: include sodium starch glycolate, crosslinked sodium carboxymethyl cellulose (croscarmellose).

Binder:

A binder, such as glucose or sucrose, is added to hold the tablet together after it has been compressed stopping it from breaking down and stopping it from forming lumps. Examples: Microcrystalline cellulose, Hydroxy-propyl Cellulose, Starch, Gelatin, Sucrose.

Glidant:

The glidant helps to keep the powder making up the tablet flowing as the tablet.

Examples:

include colloidal silicon dioxide, talc, and magnesium carbonate.

Lubricant:

Lubricants ensure that the tablet has a smooth surface and that the powder does not stick to the equipment used to make the tablet.

Examples: Magnesium stearate, Stearic acid, Hydrogenated vegetable oils and (PEG).

Anti-adherent:

The anti-adherent also stops the powder from sticking to the equipment as the tablet is being made. Examples: magnesium stearate.

Sweetener:

Function: To make the ingredients more palatable, especially in chewable tablets Such as antacid or liquids like cough syrup. Therefore, tooth decay is sometimes associated with cough syrup abuse. Sugar can be used to disguise unpleasant tastes or smells.

Flavour :

Flavouring agents help to make the tablot taste b€tter.

Colorant:

Colours are added to help you to recognize your tablet and to make it easier to take your medicine correctly.

GENERAL MANUFACTURING STEPS OF TABLET:

Manufacturing Area

+

Dispensing Unit

+

Granulation Unit

+

Compression Unit

+

Coating Unit

+

Off line Packaging

+

On line Packaging

Manufacturing ring Area:

Dispensing:

Dispensing means the materials arc supplied to the production areas by weighing according to the BMR (Batch Manufacturing Record) and released from the RM store.

Close attention is paid to dangers of cross-contamination. Dispensing of raw materials is done in the presence of authorised personnel from the production and QA. The remaining stock is recorded to make reconciliation of the stock possible at any time. Raw materials from warehouses and dispensed materials are kept in different lines in the dispensing area where CNC is maintained .Temperature in the dispensing area: 19 24oC and RH:. 45-6O0/"

Dispensing booth is covered with PVC curtains. Dispensing is done under laminar air flow (flow rate 0.36-0.55 m/s) to minimise dust generation and microbial contamination. Inside the dispensing booth, there are two portions

o Class C area- weighing of RM is done here. There is a HEPA (High Effrciency Particulate Air) Filter in the upper portion in this area. There are also pre filters & mid filters in the lower portion of the booth.

o Class D area- transferring of RM is done here.

Air Lock System:

Acts as a transit point for raw materials before proceeding into the next step (dispensing).

Wash Bay:

Machine equipment, drums etc. are cleaned using potable water, hot portable water, 70% Isopropyl alcohol and finally purified water. Drying is done with compressed air

and finally rubbed with lint free clean cloth and is transferred to the clean room.

Clean Store:

It consists of pressure. Materials (cleaned) are brought from the wash bay and stored until further use. Stores cleaned accessories such as IPA bottles, Mesh, Drums, empty cleaned containers etc.

Special Notes:

Balances of different Enges are used for dispensing. Minimum 1 mg & maximum 65kg can be weighed with the balances.

o During dispensing, excipients are weighed first followed by API (Active Pharmaceutical Ingredient) and colour.

Colour excipients are dispensed followed by APL After taking the weight of the required raw materials, they are sent to dispensing bulk and the remaining (extra) are retumed back to the warehouse.

o Within 45 days of dispensing dispensed material must go for production.

o Full line clearance is maintained to avoid contamination.

o For inhalers dispensing is done in the production area

o For light sensitive materials booth light is offduring operation and materials are taken into black bag.

Daily balance check is done.

Every data is uploaded into the database & log book is also maintained.

For solid manufacturing positive pressure is maintained in the room and negative pressurre in the corridor. Temperature is maintained between CRT and around 407o humidity is maintained.

Granulation:

Granulation is the process in which the powder particles of raw materials are made to form larger particles in order to facilitate compression for the production oftablets. All the materials are received from the dispensing unit and granulation is performed. For suitable granulation, it is required to have 30-40% powder and 60-70% granules and also l-5% moisture in compressing particles. In tablets & capsules granules are the intermediate product & having size of 0.2 to 0.5 mm.

Granulation

Area.

Mixing

Drying

Sieving

Slurry or paste preparation for wet granulation

Types of Granulations:

Granulation process can be divided into three

types-

o Direct Compression.

o Dry Granulation

o Wet Granulation

Wet granulation:

Wet granulation method is a process of size enlargement in which fine powder particles are agglomerated or brought together into larger, strong and relatively permanent structures called granules using a suitable non-toxic granulating fluid such as water, isopropanol or ethanol (or mixtures thereo0. The granulating fluid can be used alone or as a solvent containing binder or granulating agent.

Machineries observed in Granulation Unit :

Name	Origin	capacity
High Shear Granulator	Glatt India	300kg
High Shear Granulator	Cosmec Italy	500kg
Fluid Bed Granulator	Nano Pharma Tec, China	0-6,100kg
High Speed mixer	Sejong Korea	670l

Generally, the wet granulation procedure is used in the general manufacturing unit (GMU). The steps of wet granulation are given below

Wet Granulation Steps:

Dispensing + Sieving of raw mate rial + API and excipient mixing without binder solution and lubricant + Wet mixing + Drying of granules (FBD) + Sieving and milling + Drying of granules + Final sizing/Ir4illing of granules + Drying (lf required) + Lubrication

Documen8 used in Granulation Process:

Production order sheet (POS): Raw materials come from the warehouse according to POS.

Product changeover certificate: It contains previous and current product Names

Batch Manufacturing Record: lt contains name of - C Raw materials

Preparation procedure

Monitoring record

Batch packaging record

Analytical record sheet

Product release and distribution certificate.

Blending

Blending is mainly the process of mixing. In pharmaceuticals, lubricants are mixed with granules after granulation to increase flow property.

Machine name: Mix bin

Company: CosMec. (Country: Italy)

Recipe is s€t in the personnel logic control (PLC). Rotation of the IBC bin is done in both clockwise & anticlockwise directions.

Compression:

After the preparation of granules and mixing of the ingrcdients they are compressed to get the final product. The compression is done either by single punch machine or multi-station machine (rotary press).

There are two types of tablet presses:

Single rotary press

Double rotary press

The Usual Part of a Rotary Tablet Press or Multi-Stetion Tablet Press :

Hopper : The hopper holds the granule / powder mixture (API plus excipients) that are to be compressed into a tablet.

Feeder: Mechanised feeder can be used to force granules from hoppers into the die cavlty.

Dies: This is where the powder granules are compressed into tablets and it determines,

The diameter of the tablet.

The size of the tablet

To some extent the thickness of the tablet.

Punches: This comprises the upper and the lower punches. They move within the die bore to compress granules into tablets. The basic difference between upper and lower punch.

Tooling Station: The upper punch, the lower punch and the die which accommodate one station in a tablet press,

Tooling Set: A complete set of punches and dies to accommodate all stations in a tablet press. The dies and punches and their setup on a compression machine is called tooling. is the size of its tips. The lower punch's tip is comparatively large.

Dies and punches Tooling Type	Tablet Punch Barrel diameter	Tablet Outer Diameter of Die
D	25.40mm	38.10mm
B	19.00mm	30.16mm
BB	19.00mm	24.00mm
DD	25.40mm	30.16mm

Turret: Most high-speed tablet presses take the form of a rotating tunet that holds any number of punohes. As they rotate around turrot, the punches come into contact with cams which control the punch's vertical position .

Cam tracks: This guides the movement of both the upper and lower punches. There are two ofc am tracks guide,

o Upper cam track guide

o Lower cam track guide

Ejection Cam:Guides the lower punch upwards facilitating the ejection of the tablet from the die cavity after compression.

Precompresrion Rollers: This roller gives the granules an initial compression force to get rid of excess air that might be entrapped in the die.

Main Compression Rollers:This roller applies the final compression forre needed for the formation of a tablet.

Takeoff Blade: This is fitted in front of the feeder housing and it deflecs the tablet down the discharge chutes.

Discharge Chute: This is where the t8blet after being deflected by the take 'off blade passes through for collection.

Tablet Deduster: In almost all cases, tablets coming out of a tablet machine bear excess powder on its surface and are run through the tablet dedustor to remove that excess powder.

Metal Detector: It checks presence or absence of the trace amount of metal in a compressed tablet.

Steps in Compression:

Granules are loaded into hopper + Feeder + Fill Cam + Pre-Compression + Main Compression + Ejection chute by scrapper + Tablet Dedusgr + Metal Detector + Tablet Collection.

Coating:

Coated tablets are tablets covered with one or more layers of mixtures of various

substances such as natural or synthetic resins, gums, gelatin, inactive and insoluble fillers, sugars, plasticizers, waxes, colouring matter authorised by the competent authority and sometimes flavouring substances and active subsances. The substances used as coatings are usually applied as a solution or suspension in conditions in which evaporation of the vehicle occurs.

When the coating is a very thin polymeric coating, the tablets are known as film coated tablets.

The purpose of tablet coating:

0 Cover the unpleasant taste, odour and colour.

o Physical and chemical protection in medicine from the environment (light, moisture, and air).

o Control of drug release as in enteric coating or sustained release.

o improve the appearance of tablets.

In Eskayef, three types of coating are performed:

1.Film Coating (FCT):

Thin layer of coating

Mainly used to delay the dissolution

To prevent the tablet degradation due to absorption of moisture

2.Enteric Coating @CT):

o To be released in the intesthe

o Involves 2-3 steps

Sugar Coating (SCT):

o ThickJayer of coating

o For pellets & cephalosporin

FILMCOATING:

In film coating two polymers are highly used. One is HPMC and another is Eudragit L100 and L.50 (liquid).

In aqueous solution water is used as solvent but in organic solution-methanol, methylene chloride and PEG 6000 are used. The distance between spray gun and tablet bed, in case of organic solvent is 34 inches and incase of aqueous solvents is 8 inches. Pan rotation is within 3-15/hr. It varies from product to product. Air pressure is maintained to 1.54 kg.

Reasons for film corting:

o To improve product appearance and identification.

o To improve the ease of swallowing by making the tablets smoother to improve the strength of the tablet.

o Increase the mechanical resistance of the tablet

o To create modified relapse form

Process of film coating:

Tablet loading into coating pan + Warm up cycle (30'C) + Spray cycle l; (lnitial spraying) 450'C + Spray cycle 2; (Final spraying) + Drying 45-60'C + Cooling

ENTERIC COATING:

There are two steps for enteric coating:

Sub-coating: Sub coating is performed by using either organic or a HPMC as polymer aqueous solution. This process performs for 5 hours.

Enteric coating: Enteric coating is performed by using eudragit L-100 or L- 50 over the sub coating. This is to do Cellulose acetone for 15 hours.

Enteric film coating agents:

Cellulose acetate phthalate

Acrylate polymers

Hydroxypropyl methylcellulose phthalate

Polyvinyl acetate phthalate

Machines used for coating:

Perforated coating pans.

Air flow metres are there for checking the gun pressure. . Guider blades inside the pan helps moving the tables from right to left.

o Paddles inside the pan help moving the tablets from up to down.

o Angle and distance of the guns needs to be set at optimum distance.

GMU Liquid Docage Form (Vet Solution):

ln the General Manufacturing Unit, different types of oral solution are produced as veterinary products. Some of the commercially available veterinary oral products are as below- o Amprol L Vet Solution

o Avian pH Solution

o Ciproflox Vet Solution

o Eskavit

0 Hepatonic Solution

Liquid Dosage Form Manufacturing:

This area has three mixing tanks of 600 kg, 800 kg & 1400 kg capacity with three different types of propellers.

The area also has one compounding cell of6200 kg capacity. Tanks are made in China

Cleaning of the tanks is done with portable water and hot portable water .

General manufacturing process of oral liq[ids:

Weighing of active ingredients and excipients

+

Mixing of excipients with certain amount of water by mechanical stirrer

+

Addition of excipients and mixing

+

Volume adjusted and Passing through a pump to the storage vessel

+

Transfer of the solution to the filling vessel through 5O-micron Cartridge filter

+

Filling, Flushing of Nihogen (N2)

+

Sealing of Bottles (glass or pet) containing oral liquid

Condition for manufacturing of oral liquids :

Relative Humidity: Not more than 55%. Temperature: Below

30'C In the packaging unit, filled & sealed bottles are

sequentially:

o Labelled

o Packed with an insert in the intermediate carton o Final

packed in master carton .

MACHINES USED IN THE ORAL LIQUID MANUFACTURING UNIT:

Name of Machine	Function	Capacity
Steam Jacketed Vessel ,China	Mixing	3000L
Steam jacketed Vessel,China	Storage / Mixing	2000L
Cartridge Filter	Filtration	-
Bottle Filling & Sealing Machine	Filling & Sealing of Oral Liquid	2300bottles/hr

GMU Packaging:

Packaging:

Packaging is the process by which the pharmaceuticals are suitably packaged so that they should retain their therapeutic effectiveness from the time of their packaging till they arc still consumed.

Categories of pharmaceutica of packaging materials:

l.Primary packaging:

Primary packaging system is the material that first envelops the product and holds if

Example: Ampoules, vials, prefilled syringes, strip package, blister packaging.

2.Secondary packaging:

Secondary packaging system is outside the primary packaging and used to group primary packages together. Example: Cartoons, Boxes, Injection trays, Comrgated.

3.Tertiary Packaging:

Tertiary packaging system is used for bulk handling and shipping Example: Barrell, Containers, Edge protector.

Strip packaging:

Comprise one or more pockets of materials, each of which contains a single dose of the products. Types of dosage form they may be presented in strip packs include tablets,

capsules, granules, suppositories, eye drops, and liquid medicines.

Composition of strip packs:

The pack is composed of two layen of film or laminate materials. The layer can be the same or dissimilar. Example: Aluminum, Cellulose, Polyvinyl chloride, polyvinylidene chloride.

Blister Pack: Consists of a base layer, which contains cavities containing pharmaceuticals products

and a lid that is sealed by hea! pressure or both. They are more rigid and less bulky than strip packs and cannot be used for powder, semisolids or liquids.

Composition of blister pack:

The base layer materials used for blister packs are similar to those used for strip packs.

The most commonly used examples include: Aluminium PVC, PVC/PVDC, Polypropylene.

Blistering:

Blistering is the process of making a blister or enclosing the tablets and capsules into plastic packing.

flow chart of blistering

Schematic of a Blister Packaging Process + Pocket forming + Product loading + Sealing + Coding + Perforation + Cutting into individual blisters

Flow chart of strip packing prooess:

Tablets or capsules in hopper + Tablets/capsules in vibrating disc + Enter through toed channel + Pressing + Hot roller having particular dies shape + Tablets or capsules enter between two alu roll strips + Strip packaging + Poly-coated alu rolls (coated with plastic materials) come from two sides.

Liquid Auto filling Machine:

High Speed Oral Syrup Filling Machine Production Line is suitable for 20-l00ml metal screw thread cap glass bottle oral liquid washing, drying, filling and capping(roll). The Machine Production Line composed of the washing machine, tunnel oven, liquid filling capping(roll) machine.

Secondary Packaging:

This Is outside the primary packaging, perhaps used to goup primary packages together.

Example- Boxes, cartons.

Oncology (Production)

Oncology unit is separated from other units because of the hypersensitivity of the oncology product. There are two types of products are manufactured in Rupganj plant :

Tablet

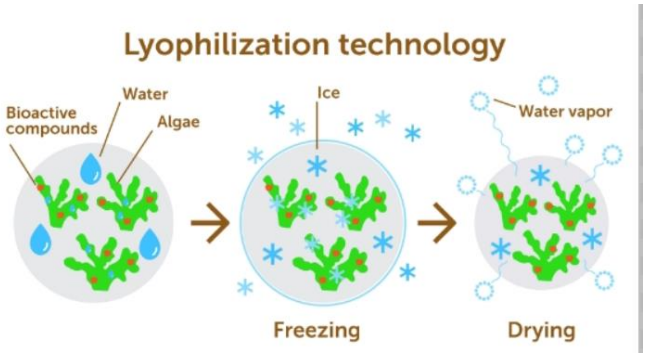
Sterile product:

1. Liquid injection
2. Lyophilized powder for injection

First time in the history of Bangladesh, the ESKAYEF Oncology facility has been built with the most advanced ISOLATOR TECIINOLOGY.

First time in Bangladesh true OEL validated Oncology facility and in compliance with all the major global regulatory authorities like FDA, I\{mA, TGd WHO and EUROPEAN MEDICINE AGENCY.

Isolator technology has been applied in every step of the manufacturing process of tablets, liquid injections and lyophilized Injections to ensure the safety ofpeople and to avoid Cross Contamination of Oncology Products.



Isolator Technology :

The isolator is the aseptic barrier between the sterile product and the environment. The better this banier works, the safer the sterile product. Some mainlenance personnel are particularly distinguished in keeping the isolators in good shape for a very long time.

Importance of isolator technology

The isolator ensures the production area and the personnel/environment are separate.

Ensures a protected environment that is free from viable microorganisms.

It prevents contamination from one area spreading to the other.

This technology provides a higher level of containment than the traditional clean room and uses an integrated decontamination system,

Some isolator equipment used in the oncology unit of Eskayef Pharmaceuticals Ltd., Rupganj plant.

l,eak Test of Isolator:

Negative pressure is maintained inside the isolator. The isolator is closed to test for Ieakage. The pressure is then applied inside the isolator for 15 minutes to see if it can retain the negative pressure. If there is no change in pressure after 15 minutes, there is no leakage in the isolator.

Vials washing for Injection Production:

Vials are washed using a vertical ultrasonic vial washing machine. Here, the inner side Of the vials are washed by using water for injection whereas the outer side are washed by using purified water. At last, compressed air is used to dry the vials .

Vial Size	A	B	C
Volume	7.5ml	1ml	30ml
Temperature for washing	310-340C	295-325C	3320-350C
Temperature for washing	115mm/min	110mm/min	60 mm/min

Sterilisation Technique:

Sterilisation refers to any process that removes, kills, or deactivates all forms of life (particularly microorganisms such as fungi, bacteriq spores, and unicellular eukaryotic organisms) and other biological agents such as prions present in or on a specific surface, object, or fluid .

Sterilisation technique is used to wash the vials, rubber, stopper, change part, filteq and flip of seal, etc. This test is done to ensure that the products made retain the highest quality and are safe to use.

Methods of sterilization and disinfection

Physical

Heat

dry heat flaming , hot air oven, incineration , infera red

moist heat - below 10ooc, at 1OO"c, above 100C

Radiation : non-ionization , ionization

Chemical

Liquid : alchoole, aldehydes , phenolics, halogens , heavy metals , surface active , dyes .

Gaseous : formaldehyde , ethylene , plasma .

Mechanical : membrance , sintered glass , asbestos .

In Eskayet three types of sterilisation technique are used:

Dry heat Sterilisation (DHS)

Sterilisation by dry heat is accomplished by conduction. The heat is absorbed by the

outside surface of the item, then passes towards the centre of the item, layer by layer. The entire item will eventually reach the temperature required for sterilisation to take place.

Dry heat does most of the damage by oxidising molecules. The essential cell constituents are destroyed and the organism dies. The temperature is maintained for almost an hour to kill the most diflicult ofthe resistant spores.

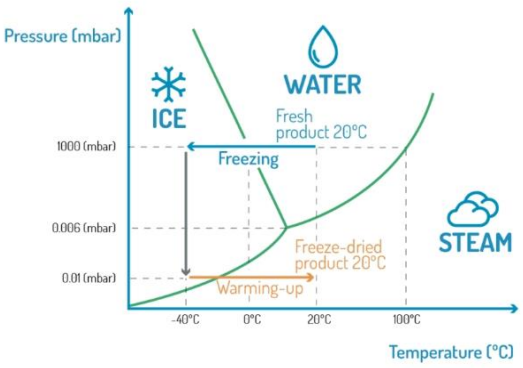
The most common time.temperature relationships for sterilisation with hot air sterilisers are:

*l70oC (340'F) for 30 minutes

*160oC (320oF) for 60 minutes

* l50oC (300'F) for 150 minutes or longer depending on the volume.

Bacillus atrophaeus spores should be used to monitor the sterilisation process for dry heat because they are more resistant to dry heat than the spores of Geobacillusstearothermophilus. The primary lethal process is considered to b€ the oxidation of cell constituents.



In Eskayef Pharmaceuticals Ltd.260'C temperature for 35 minutes is applied for DHS purposes.

Moist heat Sterilisation in Autoclave:

Moist heat destroys microorganisms by the irreversible denaturation of enzymes and structural proteins. The temperature at which denaturation occurs varies inversely with

the amount of water present. Sterilisation in saturated steam thus requires precise control of time, temperature, and pressure.

The recommendation for sterilisation in an autoclave is l5 minutes at 12l'C (200 kPa). The temperature should be used to control and monitor the process, the pressure is mainly used to obtain the required steam temp€ratur€. In EskayefPharmaceuticals Ltd., l22oC for 30 minutes is applied for extra caution to kill the microbes.

Filtration technique:

Filtration is the preferred method of sterilising heat sensitive liquid and gases without exposur€ to denaturation heat. Rather than destroying contaminating microorganisms, it simply r€moves them. It is the method of choice for sterilising antibiotic solutions, toxic chemicals, radioisotopes, vaccines, and carbohydrates, which are all heat sensitive.

The selection of filters for sterilisation must account for the size range of the contaminants to be excluded. The most commonly used filter is composed of nitocellulose and has a pore size of 0.22pm. The size of the bacteria ranges from 0.3 to 0.5 pm whereas the size of the viruses ranges from 20 nm to 0.36 pm. Thus, a filter of 0.22um retains all bacteria and spores but not all viruses.

Production of liquid injection:

Eskayef Pharmaceuticals Ltd., produce two types of sterile products at the oncology unit in their Rupganj plant. One is liquid for injection and another is lyophilized powder for injection.

- The producb that ane marketed as liquid for injec'tion are as follows:
- *Carbotor 150
- Carbotor 450
- Paclitor 30
- Paclitor 100
- *Paclitor 300
- Cistor 10
- *Cistor 50
- Cytosor 100
- Docetor 2.

Flowchart of production proc63 of liquid injection:

Dispensing of raw materials + Weight checking + Collect of WFI in tank + Mixing/Bulk preparation + Filtration + Capping + External vial washing + Vial inspection + Secondary packaging

Production of Lyophilized Powder for injection:

In Eskayef Pharmaceuticals Ltd., there is a dedicated oncology building in Rupganj plant. Here, the lyophilized powder for injection is produced. This process is done because of processing a liquid with taste (and thereby simplifying aseptic handling) and enhancing the stability ofa dry powder as well as the product stability in a dry state. Besides, it also removes water without having to heat the product excessively. Lyophilization or freeze drying is a process in which water is removed from a product after it is frozen and placed under a vacuum, allowing the ice to change directly from solid to vapour without passing through a liquid phase.

Products that are marketed as lyophilized powder for injection:

- Pemetor 100
- Pemetor 500
- Doxotor l0
- Doxotor 50
- Gemtor Ig
- Gemtor 200
- Oxator 50
- Oxator 100

Flowchart of production process of lyophilized powder :
Dispensing + Weight + Collect +Mixing /Bu + Lyophilized + Half + Filing + Filtration + 2-3 days freezing , primary + Cake formati + Full stoppering + Capping + Extern al + Vail inspection + Secondary packing .

Penicillin

There is a dedicated Penicillin production unit in Rupganj Plant due to the hypersensitivity ofpenicillin. In this production unit, the following two types of dosage

- ✓ form are manufactured.
- ✓ Solid Dooage
- ✓ Form: Tablet
- ✓ Capsule
- ✓ Powder for Suspension (PFS)
- ✓ Sterile Dosage Form
- ✓ lV Injection

The following products are manufactured in Rupganj plant

Tablet	Capsule	PFS	IV/LM
Augment 625	Flucloxin 500	Augments PFS	Augment injection
Augment 375	Flucloxin	Flucloxin 100 ml	Flucloxin 500 mg
Augment 1g	-		

Capsule Manufacturing

Capsules:

Capsule is a kind of solid dosage form with hard or soft gelatin of various shapes and capacities which contain a single dose of active ingredients.

Types of capsules:

Hard Gelatin Capsule:

Contains dry powdere.d ingredients or pellets. o Have two parts: body and cap.

Body: contains the contents.

Cap: SeaVcover the body after filling of contents Soft Gelatin Capsule:

Contains liquid or semi-solid matrix.

Having only one-piece outer soft gelatin shell

Properties of Gelatin:

A protein in nature so hotein is digested by proteolytic enzymes hence Gelatin is therapeutically inert.

- ✓ Insoluble in cold water
- ✓ Soluble in hot water

Protein is digested by a pmteolyic enzyme

Obtained from the hydrolysis of collagen from animal connective tissue, bone, skin

Chemical & physical properties of Gelatin depend upon the source of collagen & the manner of extraction.

There are two types of gelatins:

Type A: Derived mainly from pork skins by acid processing

Type B: Obtained from bones and animal skins by alkaline processing.

Blends of both types of gelatin are used to obtain gelatin solutions with the viscosity and bloom stength characteristics desirable for capsule manufacturing of Hard Soft

gelatin Capsules.

Manufacturing steps:

Dispensing + Processing + Encapsulation + Polishing + Packaging

- Common problems occurred during encepsuletion:
- Blank shell
- Shell lock in channel
- Shell breaking
- Improper filling of shell
- Improper fitting of shell in dies if compressed air pressure is not adjusted
- properly

Machireries used in Capsule Area:

Machine Name	Manufacturer	Origin	Capacity
Semi Auto capsule filling	P+am pharmaceutical	India	1500-1700cap/hr
Automatic capsule filling	Hanli	Korea	3000cap/hr

Powder for Suspension(PFS):

Powders for oral suspension are preparations consisting of solid, loose, dry particles of varying degrees of fine particle size. They are developed as powder mixtures of typical ingredients required for an aqueous suspension. In the Rupganj plant, Augment and Flucloxin are manufactured as powder for suspension.

Manufacturing steps of PFS:

Raw Material + Dispensing + Mixing + Blending + Filling (Bottle washed by Dry heat) + Labelling + Secondary Packaging

Engineering

SK+F Limited has a strong engineering departmen! which renders their services to act as a supportive hand for smooth production. The engineering deparfinent of Eskayef Bangladesh Limited consists ofa team ofdedicated engineers, pharmacists, technicians

and workers responsible for facilitating production.

The following wings are included under this department:

o Project

o Project Maintenance

o Calibration

Project:

Project means planned set of interrelated tasks to be executed over a fixed period and within certain cost and other limitations.

For example, SK+F limited has recently completed their project Faraaz Ayaaz Hossain Building (FAHB), here they planned and designed the overall technical support for installation of all equipment and provides utility service as required in FAHB building of the plan! more specifically can be mentioned their project on rryAC system.

Project Maintenance:

The Project Department planned, designed a new task and finally implemented it then they handed it over to the project maintenance depafinent. The maintenance department is actually a helping department of the project department that helps to maintain the particular project such as the air, water, electricity, machines and equipment in the industry, identi! any technical problem and solve it promptly. lt deals with procurement, installation, and renovation of machines. This department is responsible for maintenance of machines and equipment and it checks instnrments at varying intervals depending on class of instrument.

Project maintenance department usually deals with the following system:

Power house ,Heat, ventilation and air conditioning systern (HVAC system) ,Water plant Air Compressor ,Chiller system ,Steam generation in a boiler and supplied plant.

Effluent Treafnent Plant (ETP)

HVAC system:

The HVAC systern means "Heating Ventilation and Air Conditioning system". The total system is an automatic process and is maintained by a software system named metari . The process is maintained in the different areas by conaolling the air pressure (positive and negative).

Function of HVAC in pharmaceuticals:

In the pharmaceutical industry the importance of the HVAC system cannot be described

in words as it helps to maintain different classes of clean room (i.e class A, B, C, D and so on).

HVAC system main performs the following function in pharmaceuticals:

1. To maintain specified temperature (i.e-24"C)
2. To maintain specific relative humidity
3. To remove dust particles from production area
4. To hold the air contamination within acceptable limits.
5. To maintain proper air flow to ensure cross contamination does not occur. . To

prevent microbial contamination in some area using HEPA filter

Table 1 air classification clean area classification 0.5um particles /ft	ISO designation	>0,5particles	Microbiological active air action levels	Microbiology settling plates action levels
100	5	3520	1	1
1000	6	35200	7	3
10,000	7	352000	10	5
100,000	8	3520000	100	50

Zoning concept:

Zoning concept is properly maintained in SK+F plant by the HVAC system. There are mainly five zones,

Zoon	Used for
A	Sterile filling
B	Surrounding of sterile filling
C	Sterile product labelling & packing
D	Non – sterile production
E	Non classified

Elffluent treatment plant:

Effluent treatment plant ETP alongside ensures treatment of toxic chemicals and proper disposal of used water in the entire plant.

The waste water is brought in the equalisation tank and stored. In the flash mixer tank there is a level which when crossed water is brought up into it by a centrifugal pump. In the meantime the chemicals required to treat waste water is dosed. There are five chemicals needed to do so

o Alum 2.5kg per 1000L

o Lime3.l25kgper1000L

o Polymer 37.59 per 1000L

o Urea5009per 1000L

o DAP @iammonium phosphate) 5009 per 1000L

Calibration:

Calibration is a comparison between measurements - one of known magnitude or corectness made or set with one device and another measurement made in as similar a way as possible with a second device.

The device with the known or assigned correctness is called the standard. The second device is the unit under test, test instrument, or any of several other names for the device being calibrated.

Calibration may be called for:

- ✓ new instrument
- ✓ after an instrument has been repaired or modified
- ✓ when a specified time period has elapsed
- ✓ when a specified usage (operating hours) has elapsed
- ✓ before and/or after a critical measurement

after an even! for example

after an instrument has had a shoclq vibration, or has been exposed to an adverse condition which potentially may have put it out of calibration or damage

It sudden changes in weather

whenever observations appear questionable or instrument indications do not match the output of surrogate instrument.

Quality Control

Quality control is concened with sampling, specification & testing to ensure that the necessary & relevant tests are caried out & the materials are not released for use until the quality has been judged as per regulation.

According to GMP (Good Manufacturing Practice), Quality control can be defined broadly as the regular control of quality, ensured by pharmacists and technicians, responsible for the acceptance or rejection of incoming raw materials, packaging components and finished products. Quality control for in process tests and inspections to assure that systems are being controlled and monitored, are also important. Moreover,

it is the crucial part of Quality Assurance (QA).

Quality Control Department mainly checks the quality of 3 types of materials:

- ✓ Raw Materials (RM)
- ✓ Packaging Materials (PM)
- ✓ Finished Goods (FG)

Major responsibilities of quality control department:

o Sampling adequately for testing purpose (physical, chemical and biological)

o Issuing release, reject or quarantine advice for each batch of raw and packaging materials.

a Assessment ofthe intermediate products for further processing.

Assessment of the bulk products for their release, reprocess and reject, etc o

Ensure precision and accuracy ofall testing methods.

o Performing environmental monitoring checks. calibration and standardisation of laboratory equipment.

o Testing of any retum goods.

o Analysis of complaint samples with their corresponding receiving samples.

Monitoring batch-wise full quality control test records with sigrature of the person who performs the test.

o Preparing analysis reports for the tested samples, and recording and investigating any results that are Out of Specifications (OOS).

Instruments used in QC lab of Eskayef Pharmaceutical Ltd.:

Karl fischer titratior	Metrohm	Switzerland
Dissolution tester	Pharma test	Germany
HPLC Water purification	Thermo scientific	USA
UV-Vis Spectrophotometer	Thermo scientific	USA
Viscometer	LAMY Rheology instrument	France
Mechanical shaker	GFL	Germany
Hardness test	Pharma test	Germany
Analytical balance	Sartorius	Germany
Polarimeter	Anton – Paar	Germany
PH meter	Metrohm	Switzerland
Potentiometer titration	Metrohm	Switzerland
Karl fisher coulometer	Metrohm	Switzerland
Glass drying oven	Ecocell	South korea
FTIR Spectrometer	Perkin elmer	USA
Inductively coupled plasma	Perkin elmer	USA
Optical emission spectrometer		

Microwave sample preparation	Norvex	USA
Desiccator	Perkin elmer	Portugal
Fluorescence spectrometer	Wincom company Ltd.	USA
Ultrasonic bath	Elmasonic	Germany
Tapped density test	Wincom company ltd.	China

The following tests are performed by the Quality Control (QC) department to ensure quality products to the consumer.

Generally, two type of test are done by QC:

Qualitative test

Quantitative test

Qualitative teat

- Disintegration test
- Size, shape, appearance
- Viscosity
- 0Dose uniformity
- Absorbance
- measurement for
- Hardness
- detection of materials
- Conductivity test
- Friability
- Dissolution test

Quantitative test:

- .pH
- Melting point check
- COD, BOD test
- Potency
- Particle size analysis
- Impurities

Purpose of instruments used in the QC laboratory:

High-performance liquid chromatography (HPLC):

HPLC is the form of liquid chromatogaphy that is generally used in the pharmaceutical industry, as it can provide the precise results that are required. The results can be used to analyse finished drug products and their ingredients quantitatively and qualitatively during the manufacturing process. This is achieved through the separation, quantification and identification of components in a mixture and can be used to reveal

the identity of a drug.

One of the main benefits of HPLC is its ability to elucidate the structure and determine the quantities of impurities in pharmaceutical formulations.3 HPLC is especially suitable for compounds that are not easily volatilized, thermally unstable and have high molecular weights. Therefore, it can quantify a drug in its pure and dosage form.

Karl Fisher Titrator:

Karl Fischer titration is a titrimetric method commonly used in a pharmaceutical industry for the determination of water content in different substances. Because water content determination is a critical parameter to ensure product quality and to assure the chemical and physical properties of the product.

The principle of Karl Fischer titration is based on the oxidation reaction between sulphur dioxide and iodine. Water reacts with sulphur dioxide and iodine to form hydrogen iodide and sulphur trioxide. An endpoint is reached when all the water is consumed.

12+ SO2 + H202III+SO1

Dissolution Tester:

In the pharmaceutical industry, drug dissolution testing is routinely used to provide

critical in vitro drug release information for both quality control purposes, i.e.. to assess batchto-batch consistency of solid oral dosage forms such as tablets, and drug development, i.e., to predict in vivo drug release profiles.

Tapped Density Tester:

Tapped density, a significant parameter for investigating the compressibility and flowability of pharmaceutical powders, is extremely useful for promoting the QbD and GMPs approach.

Disintegration Tester:

The disintegration test determines how quickly the tablet breaks down into smaller particles, allowing for a larger surface area and availability of the drug when administered to a patient. It is a physical process that represents the breakage of inter particle interactions generated during tablet compaction of granular particles of the active pharmaceutical ingredient (API) and excipients.

UV Visible Spectroscopy:

It is a type of absorption spectroscopy that uses the ultra violet & visible part of the electromagnetic spectrum. UV & Visible spectrum is obtained by passing UV & Visible light through a mnsparent layer of the substance being examined & then recording the transmitted light. When a beam of electromagnetic radiation is passed through a sample, the radiation can be either transmitted or absorbed; depending upon the structure of the molecule. So, the radiation not absorbed that is transmitted can be measured by UV and Visible spectrometry.

Applications of tIV Spectroscopy:

Detection of Impurities

It is useful in the structure elucidation oforganic molecules, such as in detecting the presence or absence of unsaturation, the presence of heteroatoms.

Gas Chromatognphy:

Gas chromatography diffent from other forms of chromatography in that the mobile phase is a gas and the components ar€ separated as vapours. It is thus used to separate and detect small molecular weight compounds in the gas phase.

Infrarcd (IR) Spectroscopy: spectoscopy (IR spectroscopy or vibrational spectroscopy) is the measurement of the interaction of infrared radiation with matter by absorption. emission, or reflection.

Principle of Infrared Spectroscopy:

IR spectroscopy was on the principle that molecules absorb specific frequencies that are characteristic of their structure. At temperatures above absolute zero, all the atoms in molecules are in continuous vibration with respect to each other. The IR spectroscopy a sample is recorded by passing a beam of IR radiation through the sample. When the auency of a specific vibration is equal to the frequency of the IR radiation directed on the molecule, the molecule absorbs the radiation. The examination of the transmitted light reveals how much energy was absorbed at each frequency (or wavelength).

Total Oryanic Carbon (TOC) Analyzer:

Total Organic Carbon Analysis is an analyical technique used to detemine water quality. It is essential because water purity is critical for a number of industries including pharmaceutical, manufacturing, power generation and water supplying. The presence of bacteria or other inorganic compounds can indicate filtration, storage or

system failure. Contamination can also create problems such as damaging industrial systems or negatively impacting product quality which will threaten profiability and the health of consumers.

Atomic Absorption Spectrophotometer (AAS):

AAS is an analytical technique used to determine the concentration of metal atomVions in a sample.

Principle of atomic absorption spectroscopys

Firstly, all atoms or ions can absorb light at specific, unique wavelengths. The amount of light absorbed at this wavelength is directly proportional to the concentration of the absorbing ions or atoms.

The electrons within an atom exist at various energy levels. When the atom is exposed to its own unique wavelength, it can absorb the energy (photons) and electrons move from a ground state to excited states. The radiant energy absorbed by the electrons is directly related to the transition that occurs during this process. Furthermore, since the electronic structure of every element is unique, the radiation absorbed represents a unique property of each element and it can be measured.

Particle size analyzer:

Particle size analysis is used to characterise the size distribution of particles in a given: sample. Particle size analysis can be applied to solid materials, suspensions, emulsions and even aerosols.

The main reason for analysing a sample is to determine their size and shape and in tum their uniformity. Uniformity is key to any product, especially formulations, as highly polydisperse (non-uniform) formulations won't work as intended, and in some cases, the properties of the formulation become localised, rather than throughout the whole formulation.

Stability Storage and Testing:

There is a dedicated stability chamber where the Finished Goods @Gs) are stored for further testing to ensure that the products released in the market are safe to use. Three months apart (i.e., 3 months, 6 months, 9 months, etc.), the QC departrment tests the products stored in the stability chamber.

The producs are stored in four chambers where different environmental condition exists such As:

Storage condition	Temperature	Relative humidity
Real time storage condition	25C	60%RH
Intermediate storage condition	30C	65%RH
Intermediate storage condition	30C	75%RH
Accelerated storage condition	40 C	75%RH

MICROBIOLOGY

Pharmaceutical microbiology provides knowledge and understanding of the significance of the presence of bacteria, yeasts, molds, viruses, and toxins in pharmaceutical raw materials, inrcrmediates, products, and pharmaceutical production environments, as well as the microbiological control of pharmaceutical products, production environments, and people.

Microbiology is one of the crucial departrments in Eskayef Pharmaceuticals Limited. It introduces risk assessment and practical contamination control strategies, as well as protocols and techniques associated with the operation and assurance of clean-room, aseptic-room, and controlled environments for preventing any possible microbial conlamination,

Eskayef Pharmaceuticals Limited has more than 30 microbiologists working in is Rupganj and Tongi plants. There arc two labs in the Rupganj plant where microbiologists primarily analyse raw materials, finished goods, and water. Oncology, agrovet, and general products are typically analysed in one lab, while penicillin and penem poducts are analysed in the other.

Instruments used in the microbiology laboratory:

- Analyical Balance
- Autoclave
- lncubator
- Hot air oven
- Magnetic Stirrer
- pH Metre
- Laminar Air Flow/ Laminar Hood
- Microscope
- Water Bath
- Vortex Mixer/ Vortexer
- Colony Counter
- Petri dish rotator
- Hot plate o Water Distiller o Air sampler, etc.

Tests to be performed:

Micmbial limit test:

Microbial Limits Testing (MLT) is used to determine whether a non-sterile pharmaceutical product complies with an established microbial quality specifioation.

Sterility test:

Sterility testing is required to ensur€ viable contaminating microorganisms are not evident in a product. This testing is conducted by direct inoculation or membrane filnation methods and can be performed in an isolator or cleanroom environment.

Anatorin test:

The Anatoxin-a Strip Test for Water is a quick immunochromatographic test desigred specifically for qualitative Anatoxin-a screening in fresh water. The Anatoxin-a Strip Test only provides preliminary qualitative results.

Endotoxin test:

The Bacterial Endotoxin Test can be used to identiff harmful pymgens in pharmaceutical products and injection water using a gel clot method.

Liquid particle count (LPC):

Liquid particle counting is used to measure the size and distribution of particles in a liquid or on solid samples. The particle distribution and size are measured by inadiating a liquid sample with a laser diode and detecting the scattered light. The properites of the scattered light are related to the particle size.

Environment monitoring test:

Microbiological Envimnmental Monitoring Testing is done as a means of measuring the levels of contamination in the Air, Water, and Surfaces.

Air monitoring test:

Bio Sampler: The microbial contamination in the air is measured by collecting and enumerating the airborne viable particles using a bio sampler.

Settle Plates: To obtain qualitative data and identiS potential trends in airbome contamination, passive air monitoring using settle plates is performed.

Surfaces monitoring test:

Swab Test: This test consists of testing the required surfaces with a moistened swab

Contrct Plote Test: This test consists ofexposing a contact plate to the tested surface.

Growth promotion test (GPT):

The growth promotion test is a quality control requirement that confirms the ability of

a new batch of media to support growth ofa predetermined selection of representative microorganisms.

Media fill Process simulation test:

A media fill is the execution of an aseptic manufacturing procedure using a sterile microbiological growth medium instead of the drug solution to determine whether the aseptic procedures are sufficient to prevent contamination during actual drug production. Media fill is generally performed twice in a year and it takes 14 days to accomplish.

Acceptance criteria:

The following is acceptance criteria for media fill test validation: . Test size is less than 50$ units:

No contaminated units should be detected. .Test size is 5000 to 10,000 units:

One contaminated unit should result in an investigation, including consideration Of a repeat media fill test.. Two contaminated units are considered cause for revalidation, following investigation.

When filling mor€ than 10,fi[units: One contaminated unit should result in an investigation

Two contaminated units are considered cause for revalidation, following investigation.

Water analysis ,Chemical analysis, The following tests are performed in chemical analysis:

Total organic carbon (IOC):. Total organic carbon is the amount ofcarbon found in an organic compound and is often used as a non-specific indicator of water quality or cleanliness of pharmaceutical manufacturing equipment.

Conductivity:

Water conductivity is used to measure water purity and suitability to use in pharmaceutical applications. The conductivity of water is important because it tells how many dissolved substances, chemicals, and minerals are present. Higher concentrations of these impurities result in higher conductivity.

Heavy metals test:

Heavy metals constitute transition and post-transition elements along with metalloids, namely, arsenic and selenium. The heavy metals test det€cts and estimates metallic impurities colored by sulphide ions by comparing them to a lead standard.

Nitrlte test:

A Nitrate Test is a chemical test used to determine the presence of nitrate ions in solution. A common nitrate test, known as the brown ring test can be performed by adding iron (ll) sulphate to a solution of a nitrate, then slowly adding concentrated sulfuric acid such that the acid forms a layer below the aqueous solution. A brown ring will form at the junction of the two layers, indicating the present of the nitrate ion.

Microbiological analysis:

Microbial limit test:

Microbial Limits Testing (MLT) is used to determine whether a non-sterile pharmaceutical product complies with an established specification for microbial quality.

Microbial limit for different type water:

Type of water	Limit
Purified water	100CFU/ml
WFI	10CFU/ml
Portable water	500CFU/ml

Microbial limit for different types water:

This test is performed for water for injection (WFl). Generally, Gel-clot LAL test and Kinetic turbidimetric LAL test (KTA) are performed to identify pyrogen in injection water.

Temperature related with Microorganisms:

- For fungal 20-25 "C (cool incubator).
- For bacteria 30-35 oC (warm incubator).
- For a pyrogen test 37 oC (warm incubator).

Validation and Documentation

Validation is a process of establishing documentary evidence demonstrating that a procedure, process, or activity carried out in production or testing maintains the desired level of compliance at all stages. In the Pharma Industry it is very important apart from final testing and compliance of product with standard that the process adapted to produce itself must assure that process will consistently produce the expected results.

Types of validation:

ln Eskayef Pharmaceuticals Ltd., the following type of validation are performed:

Validation:

Process validation is defined as the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products. Process validation is a requirement of current Good Manufacturing Practices (CGMP$ for finished pharmaceuticals, Process validation involves a series of activities taking place over the lifecycle ofthe product and process. The Process validation activities can be described in three stages:

Stage I - Process Design: The commercial process is defined during this stage based on knowledge gained through development and scale-up activities.

Stage 2 - Process Qualification: During this stage, the process design is confirmed as being capable of reproducible commercial manufacturing.

Stage 3 - Continued Process Verification: Ongoing assurance is gained during routine production that the process remains in a state of control.

Cleaning Validation:

It is a documented-evidence to assure that a cleaning process removes residues of the active pharmaceutical ingredients of the product manufactured in an equipment which is suitable for processing medicinal products.

In cleaning validation of equipment, the following paremeters are checked:

API residues are checked whether they presont or not.

Cleaning agent residue are also checked to know their presenoe o Impurities presence

Generally, two methods are used in cleaning validation:

Cleaning Assesment:

It is used to detect the API. In this process, the active ingredient is detected and evaluated to determine whether the Permitted Daily Exposure @DE) remains in the acceptance criteria.

To accomplish this proces, two tests are usually done.

Chemical test:

If the API is changed in the production unit, then the chemical test is needed. Here, the residues of the previous product are detected.

Microbiological test:

It is needed to see whether any microbs are present or not. If API is not changed during production, then only microbiological tests are needed during production of different batches.

Maximum Allowable Carry Over (MACO):

It is the acceptable transfened amount from the previous product into the next batch.

Based On therapeutic daily dose the acceptance criteria can be calculated by the following equation:

MACO = TDD previous x MBS next / SF x TDD next

Here'

SF x TDD next

TDD previous Std. therapeutic daily dose for the investigated product (mg/day)

TDD next = Std. therapeutic daily dose for the next product (mg/day) MBS next = Minimum batch size for the next product where MACO can end up (mg) SF = Safety factor.

- Cleaning validation program:
- Selection of cleaning Level (Type)
- Selection of cleaning method
- Selection of sampling method
- Selection of Scientific basis for the contamination limit (acceptance criteria)
- Selection of Worst case related to the equipment

Selection of Worst case related to the product

Establishing the storage period after cleaning (hold time study)

Selection of analiycal method

Documentation .

Packaging Validation:

It is done to confirm that the resulting product from a specified packaging process consistently conforms to product attributes & requirements.

Analytical Validation:

Analytical validation is the process used to confirm that the analytical procedure employed for a specific test is suitable for its intended us . results from this validation can be used to judge the quality , reliability and consistency of analytical results , it is an integral part of any good analytical practice.

Computer System Validation :

Computer validation is a proof to ensure system are consistenty documented in accordance with the predetermined specifications and quality function attributes throughout their lifecycle Depending on when its performed .its divided into four types :

Prospective validation

Establishing documented evidence prior to process implementation that a system dose what it propsed to do based on pre planned . This approach to validation is normally undertaken whenever the process for new formulation ,must be validated before pharmaceutical production commences. This approach often leads to transfer of the manufacturing

Retrospective validation.

Retrospective validation is used for facilities , processes, and process control in operation use that have not undergone a formally documented validation process . valitadtion of theses is possible using historical data to provide .processes and will be inappropriate where there have been recent changes in the composition of product, operating processes or equipment.

Concurrent validation :

Concurrent validation is used for establishing documented evidence that a facility and processes do what they purport to do, based on information generated during actual imputation of the process. This approach involves monitoring of critical processing steps and end product testing of current production, to show that the manufacturing process is in a state of control.

Revalidation :

Revalidation means repeating the original validation effort or any part of it, and includes

investigative review of existing performance data. This approach is essential to maintain

the validated status of the plan! equipment manufacturing processes and computer systems.

Possible reasons for starting the revalidation process include:

The transfer ofa product from one plant to another.

*Changes to the product, the plant, the manufacturing process, tle cleaning

process, or changes that could affect product quality.

*The necessity of periodic checking of the validation results.

*Significant (usually order of magnitude) increase or decrease in batch size.

*Sequential batches that fail to meet product and process specifications. The scope of revalidation procedures depends on the extent of the changes and the effect upon the product.

Documentation:

Documentation is the vital part for a pharmaceutical company. It is necessary to document each and every process and methods used in manufacturing as it acts as an indicator whenever any problem occurs with the product. Good Documentation Practice (GDP) describes standards by which documents are created and maintained.

Eskayef Pharmaceuticals Ltd. strictly adheres to documentation requirements.

Everything is well documented here because the concept is that without documentation,

one did nothing. Each stage ofthe process and method is documented and validated to

ensure EU-GMP compliance. Features of documentation include

It should be contemporaneous with the event they record.

It should not be handwritten.

When electronically produced it should be checked for error.

It should be free from erors.

It should be approved, signed and dated by authorised personnel.

The documents which are reserved in SK+F are following

Site master file:

The site master file (SMF) is prepared by the pharmaceutical manufacturer and should contain specific information about the quality management policies and activities of the site, the production and/or quality control of pharmaceutical manufacturing operations carried out at the named site and any closely integrated operations at adjacent and nearby buildings. If only part ofa pharmaceutical operation is carried out on the site, an SMF need only describe those operations, e.g., analysis, packaging, etc.

Validation master plan

A Validation Master Plan, also known as a "VMP," outlines the principle involved in facility qualification, defines the areas and systems to be validated, and provides a written program for achieving and maintaining a qualified facility.

Standard Operating Procedure (S.O.P):

An authorised written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g., equipment operation, maintenance and cleaning, cleaning of premises and environmental control; sampling and inspection);

Validation protocol:

Validation Protocol is defined as a written plan describing the process to be validated, including production equipment and how validation will be conducted. A Validation Protocol is necessary to define the specific items and activities that will constitute a cleaning validation study.

Specification :

Specification is a critical quality standard that establishes the set of criteria to which a

drug substance or drug product should conform to be considered acceptable for its intended use. The specifications are proposed and justified by the manufacturer and approved by regulatory authorities as conditions of approval.

Specification

contains - R.M., specification, Packaging material specification. o In process specification

Finished product specification

Batch documentation:

It is a written record that documents the entire manufacturing process and the history of

1. a product batch
2. *Batch Document contains:
3. BMR batch manufacturing Record
4. *COFA (Certificate of Analysis)
5. *Line clearance
6. Cleaned tag
7. BPR (Batch Packaging Record)
8. *Print outs

Q.M.S documentation:

A quality management system (QMS) is the core of any quality and compliance process. It is a regulatory requirement that the Food and Drug Adminisration (FDA) and other global regulatory bodies consider critical. An automated QMS system reduces audit time and findings and lowers the risk of product recalls.

QMS document contains:

1. *Deviation management
2. OOS (Out of Specification)
3. *CAPA (Conective & Preventive Action)
4. *Change control
5. *Marketing complaint handling
6. Rejection
7. Audit report
8. Vendor evaluation

Other documentation contains:

1. *Validation repo(
2. *Control direction
3. *Log books
4. Maintenance record
5. Calibration record
6. Environment maintenance record

Quality Assurance

Quality Assurance department is responsible for assuring that the quality policies adopted by a company are followed and, in most organisations, it serves as the contactnwith regulatory agencies and are the final authority for product acceptance or rejection' It also helps to prepare the standard operating procedures (SOP) related to the control of quality

Quality assurance means the sum total of the organised arrangements made with the object of ensuring that products will be at the quality required by their intended use. It is thus GMP plus factors outside the scope of ISO guidelines.

The function of QA starts from raw materials and continues up to released products.

The function of QA in a pharmaceutical is given below.

Quality assurance department

1. 1.Quality control =* Raw materials Q.C, *Finished product Q.C, *Packing materials Q.C,*Stability test
2. Documentation
3. Iprocess quality
4. Microbiology .

Before purchasing:

Environment of the suppliers is also sensitive for purchasing of raw materials. QA checks the environment before purchasing the active pharmaceutical ingredients (API).

In warehouse

Identification of raw materials (RM / PM) o Check the quality by QC

Orientalion ofraw materials.

Orientation of packaging materials.

QA inspection and report submission to the head of QC.

Sampling for, Lab sample ,Microbiological sample. , Retention sample.

Released and rejection works of raw materials and packaging materials

In production area:

Before starting of manufacturing the cleaning operation or changeover of machineries

is checked by the Q.A.

o Line clearance.

o In process QC.

For solid production the following tests are done:

- Weight variation
- Hardness

- Thickness
- Diameter
- Friability
- Disintegration Test

For L.C.O.:

- Weight
- Volume checking.

In aseptic area:

Air particle monitoring, microbiological tests (swab test), wat€r test and treatment are done by the microbiological deparfinent under the supervision of QA.

In packeging area:

QA officer give tho line cloarance for starting of packaging operation after assuring the following points:

- *Absence of product of previous order.
- Absence of packaging material belonging to the previous order.
- *Cleanliness.
- *QA officer checks the batch no. Mfg. & Expiry date.
- *. Random checking ofblisten & strips.
- *Random wt. checking for cream and ointrnent.
- *Random volume checking for liquid during filling. o Check the inner and shipping cartoon.
- Evaluation and repacking of accidental damaged goods.

Instruments Used for QA Tests:

SL no	Name	Manufacture	Origin
1	LOD Over	Memmart	Germany
2	Disintegration test	Pharmatest	Germany
3	Moisture analyzer	Sartorius	Germany
4	Friability test	Pharmatest	Germany
5	Tap density tester	Metrohm	Switzerland
6	Smartest 50	Pharma tron	Switzerland
7	KF titrimeter	Metrohm	Switzerland

Quality Management System :

The complaint handling part is based upon three areas: minor, major and critical.

Depending upon the criticality of the complaint it is decided who shall handle the situation QA, GM or Head of Eskayef.

The Quality management system reviews document through four areas:

1.Assesses Deviation- When an established process is given but cannot be followed and this comes from the production, warehouse, calibration etc. Depending upon the criticality of the deviation it is decided who to handle it.

2. Out of specification-This comes from the QC when any product shows results out of the specification stated.

3.Change Request- The change request if needed comes from production, QC, calibration, warehouse and accordingly done after proper justification that why the change is needed.

4 CAPA (Corrective action and preventive action)- This includes immediate action or an alam type system is made via documentation for future perspective.

Deviation:

A deviation is a departure from standard procedure or specifications resulting in non conforming material or proceses or where there have been unusual or unexplained events which have the potential to impact on product quality, system integrity or personal safety.

Deviation manegement:

A process flow diagram for deviation management is given below.

- *Deviation initiator
- *Description of discrepancy
- *Formation of investigation team and investigation ofthe discrepancy
- *Root cause analysis
- *Proposed Corrective/Preventive action
- *Proposed agreed by QA
- *Action taken by relevant department
- *Close out comment of QA
- *Approval of head ofQA
- *Follow up/ Verification
- *Action taken effectively
- *Deviation closed

Out of Specification (OOS):

Out of specification (OOS) means an examination, measurment, or test result that does not comply with pre-established criteria.

Out of Trend (OOT):

A result that does not follow the expected trend either in comparison with other batches or with respect to previous results collected during a stability study.

Change control:

Change control is a procedure that ensures changes are implemented in a controlled and coordinated manner. The change control program evaluates all changes that could affect the production and control of the drug product, intermediate or API.

Quality Management System (QMS):

Pharmaceutical Quality Management System (QMS) is a set of procedures and practices that contribute to product quality.

It targets individual processes and personnel involved in product manufacfuring and prevents them from drifting away from quality standards such as ISO and ICH Ql0.

QMS should be done when deviation, change request, OOS or OOT occur in the pharmaceutical industry.

Elements of Pharmaceutical Quality Management System:

There are four elements of a Pharmaceutical Quality System. The drug manufacturer can incorporate these elements as p€r product life cycle requirements, and ther€ is no fixed scheme for applying these elements.

The four elemenb arc:

Process performance and product quality monitoring system 2) Corrective action and preventive action (CAPA) system Change management system

Management review of process performance and product quality

Process Performance and Product Quality Monitoring System:

An effective monitoring system provides assurance of the continued capability of processes and controls to produc a prduct of desired quality and to identiry areas for continual improvement.

Risk assessment techniques can be used to detect shortcomings in-process components. Specialised tools and feedback can also be used to perform analysis on given parameters.

The inspection system is checked randomly by both production personnel and the Quality Department to identif faults or malfunctions.

Corrcctive Action and Preventive Action (CAPA) System:

CAPA or corrective action and preventive action provide a structure for discovering the

main cause of problems and resolving those problems. In addition, it verifies the conditions and solutions for future use and then looks for other possible issues and solutions.

The illustrated CAPA process is given below:

- Identification
- Evaluation
- lnvestigation
- Analysis
- Follow Up
- Implementation
- Action Plan

After necessary Corrective and Preventive actions are applied, the CAPA is sent again to auditors for approvals. Upon approval, the CAPA is closed, and the format is made part of the records.

Change Management System:

Innovation, improvement the outputs of process performance and product quality monitoring, and CAPA drive change. To evaluate, approve, and implement these changes properly, a company should have an effective change management system. There is generally a difference in formality of change management processes prior to the initial regulatory submission and after submission, where changes to the regulatory filing might be required under regional requirements.

Management Review of Process Performance and Product Quelity:

Management review is a process of reviewing process and product quality across various management hierarchy levels to escalate urgent quality and product problems. The purpose of management review is to propose improve.

input review output

Management Process Adult Findings

Nonconforman Customer Corrective and + Management Review + Customer Related Product lmprovements QMS lmprovements Process lmprovements Resource.

Conclusion

Eskayef Pharmaceuticals Limited is renowned for its innovative endeavors, which often stem from thorough product testing and market analysis conducted in Bangladesh. With all different kinds of dosage forms---tablet, pill, synrp, suspension, crcam, ointment, gel, inhaler, and certain raw materials-its chemical division is nearly saturated. Being a part of such a prestigious industry as this makes me incredibly proud.

To speak the truth, it's the 'In plant Training' which visualises our four years' academic course in less than a month only. It helps us to undentand the complicated steps of tablet coating, methods of granulation, physics of compression, liquid filling and such difficult topics of pharmaceutics which we just leam by heart in our academic session in the deparment. So we cant but thank Eskayef Pharmaceuticals Limited as we all assume the knowledge we gathered from this training will of course be the assets for our future life. At the same time, it is our bad luck we failed to work with the marketing department of Eskayef Pharmaceuticals Limited which would be supportive to enrich our knowledge.

The extraordinary faces of Eskayef Pharmaceuticals Limited are - here everything is systematic and the good affiliation between the colleagues and boss -subordinates workers. They are very helpful to each other as well as to the trainees. We have got immense support from all the members of Eskayef Pharmaceuticals Limited.

However, today Eskayef Pharmaceuticals Limited has not only attained the apex of its development for the dedication of its employees, proper management, and proper application of science and technology and for the standard of products but also has succeeded in attaining a good position in the world market.

We are really proud to have firsthand knowledge and practical experience from a company like this. We pray for the onward development of Eskayef Pharmaceuticals Limited.

END

SK+F

ESKAYEF PHARMACEUTICALS LIMITED

CERTIFICATE

OF IN-PLANT TRAINING

Enthusiastically certify that

Sumaiya Islam

Son / Daughter of Nurul Islam & Rashida Islam from the department of Pharmacy, Independent University Bangladesh, has successfully completed In-Plant Training in this company from January 19, 2026 to February 02, 2026.

During this training period he / she was engaged and gathered knowledge on different units and operations of Technical Division like Warehouse, Manufacturing units of Solid Dosage, Liquid & Parenteral Preparations, Quality Assurance, Quality Control, Microbiology, Validation & Documentation and Engineering department.

ESKAYEF PHARMACEUTICALS LIMITED SK+F

Executive Director - Plant

Date: April 26, 2026

www.skfbd.com