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Report on in-plant training at Beximco Pharmaceuticals limited

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Department of Pharmacy
School of Pharmacy & Public Health

Independent University, Bangladesh

REPORT ON
IN-PLANT TRAINING
At
BEXIMCO PHARMACEUTICALS LIMITED

Submitted To
Mehdi Bin Samad
Lecturer

Dept. of Pharmacy, Independent University, Bangladesh.

PREPARED BY

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ID-2130215

Duration of Training: November 23 to December 03 2025

Enrolled Semester
Autumn-25

Student's Full Name & Signature:

Md. Atiqul Islam Shafin	

Acknowledgment

Writing the report on "In-plant Training in Beximco Pharmaceuticals Limited" for the B. Pharm (Hons) program gives me great pleasure. Encouraging students to develop their careers and creativity in the pharmaceutical field is the right course of action.

Furthermore, I would like to express my gratitude to Seagufta Afrin, PhD, Lecturer in the Department of Pharmacy at Independent University, Bangladesh, for granting me permission to complete an internship at Beximco Pharmaceuticals Limited. During my training, I received ongoing support and guidance from her.

I owe a debt of gratitude to every officer and worker at Beximco Pharmaceuticals Limited who contributed to our increased understanding. We also want to thank them for their tremendous assistance with our training program.

I wish for the continuous progress of **Beximco Pharmaceutical LTD.**

BEXIMCO PHARMA
here's to life
BEXIMCO PHARMACEUTICALS PLC.

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Date: 03-12-2025

TO WHOM IT MAY CONCERN

This is to certify that ***Md. Atiqul Islam Shafin,*** a student at the **School of Pharmacy & Public Health, Independent University, Bangladesh** has successfully completed In-plant Training from November 23, 2025, to December 03, 2025.

During this period, he observed various activities performed in different departments, equipment used at respective functional units, and steps involved in the production, preparation, and packaging of oral dosage products, including tablets, capsules, oral liquids, and suspensions.

He has also gained an overall understanding of materials management, warehousing, equipment maintenance, environmental control systems necessary for the production process, workplace health and safety protocols, and the quality management systems in the pharmaceutical laboratory.

We are confident that this training experience will significantly contribute to his academic and professional growth.

Mohammed Lutfur Rahman
Director Manufacturing

BEXIMCO PHARMACEUTICALS PLC.
Date 03.12.25
TONGI

Abstract

This report covers the in-plant training experience that the intern undertook November 23 to December 03 2025, at Beximco Pharmaceuticals Limited. The significant manufacturing process used in industry is covered in this report. It covers all production-related activities at the following sections: engineering, liquids, sterile, packaging, quality control (QC), quality assurance (QA), product development, and tablets (vitamins, iron, and other tablets), oral rehydration salt (ORS), and store. During training sessions, a total of nine distinct sections were visited and observed. There were various rooms in the sterile section, such as processing rooms, tool or dumping rooms, filtration, aseptic rooms for ophthalmic eye drops, water for injection (WFI), and filling rooms with class A injection filling process. The individual responsibilities of the other sections are also covered in more detail in the report. They uphold 5-M to create high-quality products, which include the standard operating procedure (SOP) for producing pharmaceuticals, as well as the manufacturing environment, equipment, and materials.

To ensure appropriate quality, the process rooms employ a variety of tools and equipment for handling, cleaning, disinfecting, sterilizing, hygienic practices, and sanitation, in addition to SOP and good manufacturing practice (GMP). BPL offers two product categories: non-sterile products and sterile products, both of which are based on microbiological ideas.

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Objectives of In-Plant Training

To earn our degree, we had to finish several pharmacy courses throughout the previous four years. Although I completed our practical classes using some simple tools and equipment and covered a lot of topics theoretically, I was unable to observe how these things were used in the pharmaceutical industry. Thus, I am here at your pharmaceutical sector to expand my theoretical knowledge, and the following my goals –

- For the development of our practical skills and techniques which are directly applicable to our careers.
- To realize and know how a pharmaceutical company runs.
- To know how its departments are interlinked and work together.
- To identify how GMP or cGMP is applied in the plant.
- To have an Idea about Standard Operating Procedures (SOPs).
- To get information about the QC, QA, R & D, Stability, and Microbiological activities for smooth and quality product manufacturing.
- To know how Pharmacists manage manufacturing problems.
- To see how quality is assured as well as controlled in each step starting from raw Material finished products.
- To learn about documentation record practices.
- To get an idea about the HRD activities for the regulation of the Pharmaceutical Industry.
- To get general Ideas about their project activities.
- To gather knowledge of the formal functional activities of the organization.
- To get information about IPC.
- To get information about how an engineering department works behind the success of the company.

Introduction

In Bangladesh, Beximco Pharmaceuticals Ltd (BPL) is a one of the top producer of active pharmaceutical ingredients (APIs) and pharmaceutical formulations. The corporation is one of the nation's biggest supplier of pharmaceuticals, and international regulatory agencies from Australia, the Gulf countries, Brazil, and other places have validated its cutting-edge manufacturing facilities. With approximately 400 medications in various dosage forms that cover broader therapeutic categories such antibiotics, antihypertensive, antidiabetics, anti-retroviral, anti-asthma inhalers, etc., the company is constantly expanding its portfolio. The business was established in 1976 and started producing and marketing products from Upjohn Inc. in the USA and Bayer AG in Germany in 1980 under license agreements. The company began producing its own formulations in 1983, and in 1992 it began to export. The parent firm and the manufacturer of intravenous fluids, Beximco Infusions Ltd., merged in 2005. Modern oral solid dosage plant completed in accordance with UK MHRA and US FDA standards, certified by key international regulatory authorities, was finished in the same year.

Beximco Pharma is currently the nation's top pharmaceutical exporter and the only business to have won the National Export Trophy (Gold), the top export award, a record three times. The company was the first to manufacture inhalers devoid of CFCs and is the biggest manufacturer of Metered Dose Inhalers (MDIs) in the nation. BPL is also the first company in the region to manufacture anti-retroviral medications (ARVs). While receiving training from the company, we made notes about our visits to various departments. This report will solely include the things we saw, learned, and were instructed on throughout our training. We anticipate that this report will be useful to us as we apply our knowledge to our workplace.

RESEARCH AND DEVELOPMENT (R & D)

The core of the pharmaceutical industry is the product development division. As the name suggests, product development oversees creating new products. This department creates new medications, and it is essential to the process of creating new medications as well as improving the quality of currently available medications. Additionally, this section resolves consumer complaints about popular products and troubleshoots issues that arise throughout the product's manufacturing process. Above all, the department's primary responsibility is documentation, specifically the creation of batch manufacturing records (BMRs) and batch packing records (BPRs).

Functions of product development

The product development department is responsible for the following functions,

- ✓ Formulation of new products.
- ✓ Reformulation of prevailing products.
- ✓ Troubleshooting related to manufacturing defects
- ✓ Preparation of BMR and BPR for a new product
- ✓ Development of present product
- ✓ Analytical method development for new product
- ✓ Stability study of new product according to established study protocol
- ✓ Preparation of sample for drug testing laboratories (DTL).

REGULATORY AFFAIRS

The government's goal to safeguard public health by regulating the efficacy and safety of products in a variety of industries, such as pharmaceuticals, veterinary care, medical devices, pesticides, agrochemicals, cosmetics, and complementary and alternative medicine, gave rise to the relatively new department of regulatory affairs.

Most businesses, whether they are little, creative biotechnology startups or large, global pharmaceutical enterprises, have specialized regulatory affairs staff members and don't depend on the knowledgeable counsel of independent regulatory consultants to fulfill their legal requirements.

There are three types of Regulatory Affairs:

1. Highly Regulated (FDA, TGA, MHRA certified)
2. Semi Regulated
3. Non-Regulated

The Regulatory Affairs Professionals:

The Regulatory Affairs Professionals are involved in the registration of drug products in respective countries prior to their marketing. They work with certain goals and play important role in the act of Regulatory Affairs.

Goals of Regulatory Affairs Professions

✓ Protection of human health.

✓ Ensuring safety, efficacy and quality of drugs.

✓ Ensure appropriateness and accuracy of product information.

Roles of Regulatory Affairs Professional

✓ Act as a liaison with regulatory agencies.

✓ Preparation of organized and scientifically valid NDA, ANDA, IND A, MAA, DMF submissions.

✓ Ensure adherence and compliance with all the applicable cGMP, ICH, GCP, GLP guidelines, regulations and laws.

✓ Providing expertise and regulatory intelligence in translating regulatory requirements into practical workable plans.

✓ Advise the companies on regulatory aspects and climate that would affect their proposed activities.

Importance of Regulatory Affairs Department

Drugs approval report for national and international are derived from Regulatory Affairs. Regulatory Affairs of Square pharmaceuticals deal with USA, AGS, MSRI, T GA, UK, EMEI, MCC and Brazil for certification. Now they deal with more than 40 countries and Regulatory Affairs also review their guidelines and fulfill country requirements (AC TD- the ASEAN.

Common Technical Dossier, CTD- Common Technical Document). If country requirements are not fulfilled, test improvement process and product quality improvement process are given by the Regulatory Affairs. Regulatory Affairs of Square pharmaceuticals deal with patent and generic products.

In today's competitive environment the reduction of the time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its Regulatory Affairs activities is therefore of considerable economic importance for the company. Therefore, Essential Drugs Company Limited (EDCL) has opened this department to make the organization economically feasible and viable.

VALIDATION

Validation is a process of establishing document evidence representing a procedure, process, or activity carried out in production or testing that maintains the desired level of compliance at all stages. Validation is required in every stage in building the industry to marketing the finished product of the industry to ensure quality product.

- ✓ Facilities validation
- ✓ HVAC system validation
- ✓ Computer system validation
- ✓ Equipment validation
- ✓ Process validation
- ✓ Analytical method validation
- ✓ Packaging validation
- ✓ Cold chain validation
- ✓ Cleaning validation.

Validation requires 4 qualification tools to perform its action along with the validation master plan, a document that describes how and when the validation program should be executed in a facility.

1. Design qualification (DQ)
2. Installation qualification (IQ)
3. Operational qualification (OQ)
4. Performance qualification (PQ)

Benefits of Validation Process:

- ✓ It provides the understanding of a process and decreases the risk of processing.
- ✓ It controls the costs.
- ✓ It reduces the regulatory noncompliance.
- ✓ A fully validated process may require less in-process control and end product.

PRODUCTION PLANNING & INVENTORY CONTROL

PPIC is the connecting point between marketing and factory. PPIC of SPL ensures proper storing and smooth supply of all input materials to meet market demand with a minimum size of inventory to ensure company growth.

Production planning, or production scheduling, is a term assigned to the planning of production in all aspects, from workforce activities to product delivery. Production planning is primarily concerned with the efficient use of resources. Inventory control is a critical part of the production system. Aside from the determination of the minimum level of stock a company can maintain safety against a balloon in customer demand, inventory control looks at the costs associated with maintaining inventory. Inventory control can comprise inventory of a finished product or inventory of materials used in making such products. Inventory control is affected by changes in customer demand, holding costs, ordering costs and back-order costs.

PPIC is involved in numerous works. Some of them are given below:

- It analyses the demand for a particular product for at least seven-months based on some Statistics and other factors.
- It receives the sales target for a particular product and makes a Strategy plan for that.
- PPIC usually makes a long plan. Because the raw material supply takes a long time. For example, by air it takes at least 3 months, by ship and road, it takes around 4-5 months to have the supply of raw materials.
- Always calculate the opening & closing Stock of warehouses and depots.
- Also involved in ABC Analysis for better production & inventory control.

Warehouse

Raw material Store is an area where raw materials and primary packaging materials are received, stored and finally distributed to the production department or to the distribution office as per requisition.

Area	Application
Unloading Bay	• Unloading received material • Conducting inspection of materials
Dedusting tunnel	• Removing adhering dust from the container.
Marshalling area	• Issuing a Good Received Note (GRN) for the received materials and sending it with Certificate of Analysis (COA) to the quality control (QC) department.
Quarantine area	• Transferring materials to the quarantine area. • Tagging a quarantine label to the container.
Passed area	• Storing of raw materials till it gets the “Passed Label”. • Tagging a “Passed Label” to the container
Fenced area	• Storing of passed raw materials for the use of production. • Storing of both quarantine and passed printed packaging foils
Sampling booth	• Collecting the raw materials samples for QC. • Tagging sample labels to the containers.
Cold storage	• Storing of heat sensitive materials such as Omeprazole
Rejected area	• Rejected raw materials, packaging materials are stored here. It is a separate room, where entry is strictly regulated.

Procedure performed by warehouse personnel.

Receive RM, unload materials in pallets, checking containers & label them, discarding defected containers. Cleaning containers (by vacuum & IPA), issuing GRN (Goods Receiver Note), then labeling as QUARANTINED and informing QC department for sampling. Issuing a BIN CARD, if QC department has given the container a PASSED label. Supplying raw materials according to the FIFO to production area.

Incoming raw material

↓

Unloading (In loading & unloading bay)

↓

Documentation in SAP (System application products)

↓

Separation according to Batch wise or product wise

↓

Keep it in the marshalling area

↓

Prepare GR. (Goods Received Note)

↓

Keeps the RM into Quarantine area attaching Quarantined Label?

↓

Sampling by QC

↓

Passed area if materials are passed by QC

Finished Goods Warehouse:

Raw materials are dispensed into the production unit and after the completion of production, the finished products are supplied to FGW. Then the finished goods are arranged the same as Raw Materials Warehouse (Quarantined, Sampled and Passed). The temperature and humidity are strictly maintained as it should not exceed 25°C &65 RH respectively.

Some Key points regarding the Warehouse:

✓ There are some consumable items (toothbrush, nylon tie etc.).

✓ Yellow net (for finished material, netting is done).

✓ Labeling is maintained in each and every panel.

✓ At every stage, QC test is done.

✓ RM Temp. below 250C, RH-below 65%

✓ FM- Temp.-below 250C.

✓ Emergency light.

✓ RH Store->WIP (work in progress)>passed

✓ Only Brand name is written in each label on the cartoon box, because this is the secondary packaging and it will not be viewed by the customer and so that generic name is labeled only on the primary packaging.

✓ Rack system or rack no. is maintained for identification if different stored materials.

✓ De-duster and dust collector system is introduced so that any dust particle will go out from the material which is brought from outside to the warehouse.

✓ Robopac (raping machine is used for final packaging of those products supposed to go outside of the country (export purpose).

✓ Helmet is used for safety purposes.

Important Documents of Production Area

Standard operating procedure (SOP):

This document contains validated procedures of different operations performed within production area.

Several types of SOPs exist, such as-

✓ SOP for cleaning

✓ SOP for controlling of label

✓ SOP for operating equipment

✓ SOP for daily accuracy of equipment etc.

Batch Manufacturing Record (BMR):

This document holds critical parameters corresponding to individual product manufacturing procedure. BMR consists of several parts such as

- ✓ Product formulation
- ✓ Steps involved in product preparation
- ✓ Reconciliation
- ✓ Calculation

BMR provides every minor detail regarding production procedure for ensuring quality products.

Log Book:

This is a written document of recording parameters during running any operations.

In process check (IPC):

It checks performance during production to monitor and if necessary, adjust to process to ensure that the product conforms to its specification.

Tablet Section

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods.

Essential quality of a good tablet:

1. They should be accurate and uniform in weight.
2. The drugs should be uniform distributed through the tablets.
3. The size and shape should be reasonable for easy administration.
4. The tablets should not be too hard that it may not be disintegrated in the stomach.
5. There should not be any incompatibilities.
6. They should be chemically, physically and microbiologically stable during storage.
7. They should not be broken during transportation or crumble in the hands of the patient.
8. They should be attractive in appearance.
9. They should not be any manufacturing defects like cracking, capping or discoloration.
10. After administration it should disintegrate readily.
11. They should be easy and Economical in production.

Advantages of the tablet dosage form:

1. They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
2. Cost is lowest of all oral dosage form.
3. Lighter and compact.
4. Easiest and cheapest to package and strip.
5. Easy to swallow with least tendency for hang-up.
6. Sustained release product is possible by enteric coating.

7. Objectionable odor and bitter taste can be masked by
coating technique.

8. Suitable for large-scale production.

9. Greatest chemical and microbial stability over all oral dosage

10. Product identification is easy and rapid requiring no additional steps when employing an embossed and/or monogrammed punch face.

Disadvantages of tablet dosage form:

1. Difficult to Swallow in case of children and unconscious patients.

2. Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.

3. Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.

4. Bitter testing drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating.

Methods of preparation of granules

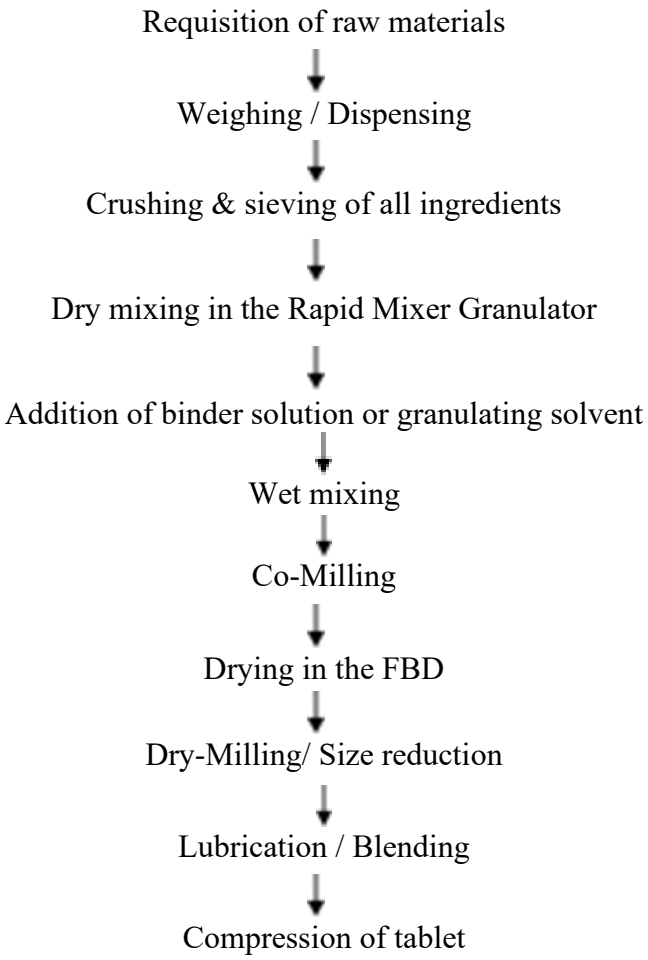
The manufacture of granulations for tablets compression may follow one or a combination of three established methods:

- ❖ Wet granulation
- ❖ Dry granulation
- ❖ Direct compression

Wet granulation: Wet granulation is a process of dry mixing, wet mixing and particle size enlargement and is a process of particle attachment. This method is popular due to the granulation meets all the qualities required for a good tablet.

Example: Calcium tablet, Paracetamol tablet.

Steps of Wet granulation:



Advantages of wet granulation:

- ✓ **Cost effectiveness:** The prime advantage of wet granulation is economic since it requires fewer unit operations. This means less equipment, lower power consumption, less space, less time and less labor leading to reduced production cost of tablets.
- ✓ **Stability:** Wet granulation is more suitable for moisture and heat sensitive APIs, since it eliminates drying steps and increases the stability of active ingredients by reducing detrimental effects.
- ✓ **Faster dissolution:** Disintegration or dissolution is the rate limiting step in absorption in the case of tablets of poorly soluble API prepared by wet granulation.

✓ **Less wear & tear of punches:** The high compaction pressure involved in the production of tablets by slugging or roller compaction can be avoided by adopting wet granulation. The chances of wear and tears of punches and dies are less.

✓ **Simplified validation:** Materials are "in process" for a shorter period, resulting in less chance for contamination or cross contamination, and making it easier to meet the requirement of current good manufacturing practices. Due to fewer unit operations, the validation and documentation requirements are reduced.

Limitations of wet granulation:

✓ It is an expensive process because of labor, time, and space requirements.

✓ Loss of material during various stages of processing.

✓ Stability concern for moisture sensitive or thermo labile drugs.

✓ Multiple processing steps add complexity and make validation control difficult.

✓ Any incompatibility between formulation components is aggravated.

✓ It is time consuming and requires a number of persons as many different steps.

Dry granulation:

In dry granulation process the powder mixture is compressed without the use of heat and solvent. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain a 'granules. This method is especially applicable to materials that cannot be prepared by wet granulation method due to their sensitivity to moisture or to the elevated temperature required for drying. Example: Aspirin tablet, Montelukast tablet, Magnesium Hydroxide etc.

Methods of dry granulation

Formation of granules using dry granulation process is generally achieved either by slugging technique or roller compaction. The two techniques are similar, but they can give different results,

✓ **Slugging technique:** This process involves compression of primary powder particles into large flat tablets or pallets using a tablet press or, more usually, a large heavy-duty rotary press. This process is often known as 'slugging', the compact made in the process (typically 25 mm diameter by about 10-15mm thick) being termed a 'slug'. The resultant compact is then milled using a hammer mill or other conventional milling equipment. The milled slugs are passed through a screen of desired mesh for sizing. Lubricant is added in the usual manner, and the granules compressed into tablets.

✓ **Roller compaction:** Roller compaction (also referred to as ribbon blending) is a relatively simple, more efficient and inexpensive form of dry granulation. It is a process where formulation ingredients are continuously passed between two counter-rotating rollers where it is densified and consolidated into a sheet of solid mass. Depending on the type of rollers used, the feed material may be compacted into dense ribbon-like materials known as flakes (smooth rolls) or dense briquettes (almond or stick-shaped) if the rollers have grooved or etched surfaces. The compacted materials are further milled, sized, lubricated and compressed into tablets.

Steps of dry Granulation:

Requisition of raw materials

↓

Weighing / Dispensing

↓

Compression into slugs or roll compaction

↓

Milling and screening of slugs

↓

Lubrication/ Blending

↓

Compression of tablet

Advantages of dry granulation:

- ✓ Requires less equipment and space.
- ✓ For moisture sensitive material.
- ✓ For heat sensitive material.
- ✓ For improved disintegration since powder particles are not bonded together by a binder.
- ✓ It eliminates the need for binder solutions, heavy mixing equipment and the costly and time-consuming drying step required for wet granulation.

Disadvantages of dry granulation:

- ✓ It requires a specialized heavy-duty tablet press to form slugs.
- ✓ It does not permit uniform color distribution as can be achieved with wet granulation where the dye can be incorporated into binder liquid.
- ✓ The process tends to create more dust than wet granulation, increasing the potential contamination.

Direct Compression:

The processing of drug with excipients can be achieved without any need of granulation and related unit operation. By simply mixing in a blender, formulation ingredients can be processed and compressed into tablets without any of the ingredients having to be changed. This procedure is called direct compression, and it is used in the manufacture of tablets when formulation ingredients can flow uniformly into a die cavity.

Steps of direct compression:

Requisition of raw materials

↓

Weighing / Dispensing

↓

Lubrication / Blending

↓

Compression of tablet

Advantages of direct Compression:

1. Low labor imparts.
2. Few processing steps.
3. Capping or splitting is reduced due to deacreation.

Disadvantages of direct Compression:

1. Diluents and other additives may interfere with the compressibility of the active ingredient and thus minimize the usefulness of the method due to difference in particle size and bulk density between the drug and diluent may lead to stratification within the powder.
2. Most materials cause relatively weak intermolecular action or are covered with films of absorbed gas that tend to hinder compaction. Diluents may interact with the drugs e.g. amine drug and lactose.
3. Because of the dry nature of direct compression, static charge build up can occur on the drug during routine, screening and mixing, which may prevent a uniform distribution of the drug on the mass.

Tablet Coating:

Tablet coating is the application of a coating material to the exterior of a tablet with the intention of conferring benefits and properties to the dosage form over the uncoated variety.

Purpose of tablet coating:

✓ Coating gives the tablet ingredients protection from environment, particularly light and moisture and thus increases chemical and physical stability of the tablets.

✓ Many drugs have a bitter or otherwise unpleasant taste; coating is effective way to mask such tastes.

✓ Coating helps to mask any unpleasant odors present in the tablet.

✓ Colored coatings also mask any differences in the appearance of raw materials and hence allay patient concern over tablets of differing appearance.

✓ Tablets that are coated are also somewhat easier to swallow than uncoated tablets.

✓ To improve pharmaceutical elegance using special color coating and contrasting printing.

✓ To incorporate another drug or formula adjuvant in the coating to

✓ To protect the drug from the gastric environment of the stomach with avoid chemical incompatibility or to provide sequential drug release.

✓ Colored coating aid in the rapid identification of product by the acid-resistant coating. Manufacturer, the dispensing pharmacist and the patient.

Critical Parameter for Tablet Coating:

✓ Pan speed (rpm)

✓ Spray Rate

✓ Inlet temperature (°C)

✓ Exhaust temperature (°C)

✓ Gun-to-bed distance (inch / cm)

✓ Atomizing air pressure

Capsules

Capsules are solid dosage form in which the drug is enclosed in either a hard or a soft, soluble gelatin shell. Hard capsules are used for filling solid substances such as powder, granules, etc. and soft capsules are used for filling liquid or oily substances. Recently, liquid filling hard gelatin capsules have gained popularity.

Manufacturing Procedure of capsules:

Take the hard gelatin capsule shell

↓

Fill the capsule with powder medicament/ granules with the disintegrate, diluents, etc., using capsule filling machine

↓

Sealing

↓

Polishing

↓

Transfer to blister packing

Advantages:

✓ Stable because it is solid dosage form.

✓ Dose accuracy is very much as it is solid dosages form.

✓ Minimal excipient and little pressure are required to compact the material.

✓ They are easy to handle and carry.

✓ Capsules are tasteless, odorless and can be easily administered.

✓ They are attractive in appearance.

✓ The drugs having unpleasant odor and taste are enclosed in a tasteless shell.

Disadvantages:

✓ Production cost is higher.

✓ Adulteration is very easy because drug is enclosed by shell.

✓ Capsules cannot be cut down so shorter dose is impossible.

✓ Gelatin coating is hydroscopic, absorbs moisture.

✓ Special conditions are required for storage.

Hard gelatin capsule

Hard gelatin capsules occupied the major position among the capsule dosage forms. Hard gelatin capsules are made of two shells: the capsule body/base and a shorter cap. The cap fits closely over the open end of the capsule body. Commercially for human use, hard gelatin capsules are available in several sizes, which vary from 000 to 5, the size 000 is the largest and the size 5 is the smallest.

Different sizes of hard gelatin capsules for human use.

The shells of the hard gelatin capsule are made from mixtures of gelatin, Sugar plasticizer, water, etc. Capsule shells may be colored by adding colorants such as titanium oxide added to the gelatin solution. Gelatin is a kind of protein obtained by partial hydrolysis of collagen from the animal skin, white connective tissue, and bones. Different color of the shells may be helpful to distinguish the finished capsules containing different drugs by the patients. Examples of hard capsules include

Amoxicillin, Tetracycline, Cephradine, Cloxacillin, etc.

Common Defects in Hard Gelatin Capsules

- **Lumpy or misshapen capsules:** If the capsules form lumps or are otherwise misshapen, check the conditions under which they were transported or stored. You should maintain empty capsules at a temperature between 15° and 30°C and a relative humidity between 40 and 65 percent. Avoid exposing empty capsules to a direct source of light or to heat. Don't transfer capsules suddenly from a high-temperature environment to a low- temperature one.

- **Improper rectification:** If the capsules are not being oriented properly (cap up), first make sure no one is using a plastic container to transport the capsules or a plastic scoop to load the capsule filler. Plastic can cause an electrostatic charge to develop, hindering rectification. Use stainless steel containers and scoops instead. Also check the gate knee and adjust it as necessary. Verify that the stroke of the pushers, or fingers, is set properly according to the joined length of the shells. Also check that the raceway is in good condition.

- **Failure to separate**: If the caps and bodies fail to separate, check the vacuum. On most capsule fillers, the gauge should read somewhere between 15 to 18 inches mercury. You may also need to adjust the gap between the machine's cap segments and body segments. Check the timing of the solenoid valve and how well the segment's' holes align with the raceway fingers. Check the filter bag and clean it periodically.

- **Telescoping:** This defect occurs when the cap and body misalign and the capsule body splits and a portion of it covers the cap. To eliminate this defect, make sure all the capsules are perfectly round. Also check the alignment of the cap and body bushings, or segments, using a gauge designed for that purpose. The environmental conditions in the filling room can also contribute to this problem. If you must stop the machine for more than 30 minutes, protect the capsule shells from direct exposure to the environment.
- **Popping:** If the capsules open or elongate after filling, it's likely due to excessive

locking pressure or overfilling. It's also possible that the locking mechanism is weak, but that's a defect rarely seen in capsules supplied by reputable manufacturers.

- **Brittleness:** Check your storage conditions. When capsules lose moisture, often due to poor storage practices, they become brittle. The threshold is approximately 12.5 percent moisture. Anything less will likely lead to brittleness. Filled capsules that include a hygroscopic active, or excipient can also cause brittleness. Capsules made from HPMC are less likely to become brittle.

Soft gelatin capsules

Soft gelatin capsules or soft gels are one-piece hermetically sealed soft shells containing liquid, suspension or semisolid form of medicament. Soft gelatin capsules are prepared by adding a plasticizer, such as glycerin or polyhydric alcohol (e.g., sorbitol), preservatives, color, solvent such as water, etc. to gelatin. The plasticizer makes elastic gelatin. Soft gelatin capsules come in

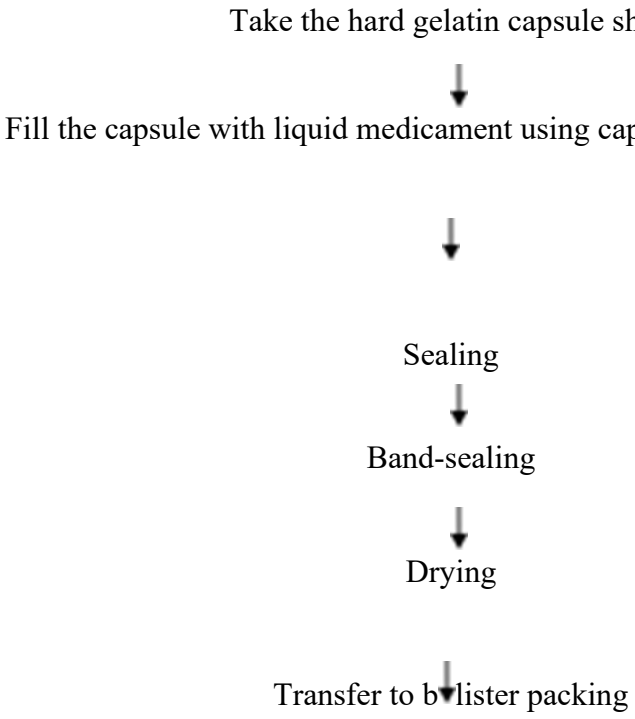
various shapes such as spherical, elliptical, oblong, special tube shapes with and without twist off, etc. Examples of soft capsules include Vit. E, Vit. D, Vit. A etc. Calcitonin, etc.

Liquid-filled hard gelatin capsules

The liquid-filled hard gelatin capsule is getting much attention because of its new concept of dosage form design. This type of capsules can accommodate liquid, semi-solid and waxy drugs into the hard shell usually made up of gelatin or hydroxypropyl methyl cellulose and enhance the stability and bioavailability of the drugs compared to hard gelatin capsules, e.g. Ibuprofen containing liquid filled hard gelatin capsule.

Liquid-fill hard capsule technology is becoming increasingly accepted by the pharmaceutical industry and while it can hardly be expected to replace more conventional dosage forms such as tablets and powder-filled capsules, it will become a mainstream alternative for those products with processing or clinical needs.

Process flow chart of liquid-filled hard gelatin capsule preparation:



Controlled release capsules

Cellulose derivatives such as hydroxy-propyl-methylcellulose, or Methocel, are used as a hydrophilic matrix material to prepare the controlled release capsules. When the polymer hydrates, it forms a gel of such consistency that controls the diffusion of drug from the shell, e.g. Diazepam controlled release capsule, Mesalamine controlled release capsule etc.

Oral Rehydrate Salt (ORS)

Oral Rehydrate Salt made by mixing salts of which the important one is common salt and sugar which is used to compensate for the loss of excessive fluid (water and salts) from the body that occurs during an episode of severe watery diarrhea as exemplified by cholera.

Component used in ORS

1. NaCl
2. KCl
3. Glucose anhydrate BP
4. Trisodium citrate dehydrate BP
5. Aerosol

Equipment and its working purpose:

1. Multi-mixing: Used for converting large granule into small size.

2. Russel Shifter: Mass the granule to produce homogenous size.
Mass size-20.

3. Cubic Blender: Mix the ingredients. RPM 5.5-6.

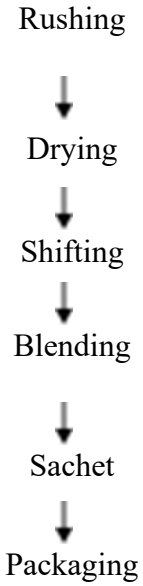
4. Young Tech Machine: Package the material at 22 rpm.

5. Klockner Hansel (model no-199): 120 sachet per min.

6. Robert Bosh GMBH (model no-17389)

7. Otto Hansel Machine (model no-196)

Manufacturing Process



Batch Size: 27,000

Engineering Department

The major rules of an engineering department in pharmaceutical company provide necessary driving force and logistic support to ensure smooth operation of plant utilizing its available strength with proper planning, organizing and controlling. In EDCL, Engineering Department is one of the vital departments associated with manufacturing pharmaceutical products which is employed with qualified professional engineers and technicians. The main responsibility of engineering department is to ensure smooth operation of plant machinery, utility services and validation of the system as per approved SOP.

Responsibility of engineering department

- ✓ To follow Good Engineering Practice.
- ✓ Preparation and Review of departmental SOPs
- ✓ Preparation and Review of PM schedule, checklist and attending breakdown.
- ✓ Observation and Guideline in installation activities of new equipment or projects at site.
- ✓ Implementation of SAP
- ✓ To review and undertake audits of vendor quality management system.
- ✓ Review and implementation of Technical Agreement.
- ✓ New vendor developments for different engineering services and follow up.
- ✓ To witness calibration and validation activities and review of calibration certificates.
- ✓ Support in installation activities of equipment's.
- ✓ Validation and Review of Site master plan and Coordination with contract persons
- ✓ Preparing all drawings and related system engineering documents, such as: P & I drawing, Utility drawing such as HVAC, Water system, Building and Room Drawings, Maintenance Requirements, Operational Manuals, Equipment Component Identification, Identification of Calibration Requirements, Equipment Installation and System Construction Procedures
- ✓ Co-ordination of the calibration activities for all critical instruments as identified by the validation team.
- ✓ Executing, Installation Qualification and Operational Qualification tasks and assisting in the execution of Performance Qualification.
- ✓ Maintenance of process & utility equipment.
- ✓ Responsible for handling change control, deviation, and incidents within the department.

- ✓ To ensure the ALCOA Data Integrity Checks.

Machine use in EDCL

HVAC

An HVAC system is Heating, Ventilation and Air-conditioning system that supply conditioned air to the areas of indoor surroundings to stimulate and maintain required temperature, humidity, ventilation and air-purity. HVAC system is the heart of Pharmaceutical Industries that purify the outside air and circulate all over the areas. HVAC system provides specific set of environmental conditions which required to make quality product.

A basic HVAC system works as explained below:

First, the system collects fresh air from outside the plant from where it is filtered using a filter. The filtered air goes through the supply duct and further filtration is done through the Air Handling Unit. The air handling unit then supplies the filtered air to different rooms within the manufacturing plant. HVAC System. The air supplied to each room is determined by the temperature and humidity that is required in the room. The HVAC system can effectively control the air condition of a given parameter through heating by adding thermal energy in an area to increase the temperature; the cooling is done through decreasing the thermal energy in an area to decrease the temperature. Humidifying is done by adding steam or water vapor in an area to increase the relative humidity while dehumidifying is done through getting rid of the humidity or water vapor in an area. The air is cleaned by removing the smoke, dust or pollen that contaminates the air. The air is ventilated by maintaining the gas ratio which can be done by adding external fresh air. Lastly, the system controls the air movement that is supplied in space which ensures that those in the place are comfortable.

Components of HVAC system:

❖ **Air-Conditioner**: An air conditioner is designed to change the air temperature and humidity within an area. The cooling is typically done using a simple refrigeration cycle.

❖ **Air Handling Unit (AHU):** The air handling unit is an equipment consisting of fans, heating and cooling coils, air control dampers, filters. It collects and mixes outdoor air with that returning from the building space. The air mixture is then cooled or heated, after which it is discharged into the building space through a duct.

❖ **Heating & Cooling Coils:** A heating coil is a piece of equipment built for efficient heat transfer from one medium to another. A cooling coil cools air blown across it and into the building occupied space.

❖ **Dehumidifiers/Heater:** In dehumidifier evaporator and condenser coils are placed in the same air path, and the entire unit is placed in the environment. Having the condenser coil in the same air path as the evaporator coil produces cool, dehumidified air. The air next passes over the condenser coil, rewarming the dehumidified air.

❖ **Filter (Pre & Hepa):** A particulate air filter is a device composed of fibrous materials which removes solid particulates such as dust, pollen grains, mold, and bacteria from the air. A chemical air filter consists of an absorbent or catalyst for the removal of airborne molecular contaminants such as volatile organic compounds or ozone. Air filters are used in applications where air quality is important.

❖ **Dust Extractor:** A dust collection system is an air quality improvement system. Dust collection systems work on the basic formula of capture, convey and collect.

❖ **Ducting (For Delivery of Controlled Air):** Ducts are used to deliver and remove air. A duct system is often called ductwork.

❖ **Supply Fans**: Flow rate is controlled by inlet vans or outlet dampers on the fan. The supply fan speed is controlled to maintain pressure in the supply

duct.

- ❖ **Smoke Detectors:** A smoke detector is a device that detects smoke, typically as an indicator of fire.
- ❖ **Damper**: A plate or gate placed in a duct to control air flow by increasing friction in the duct.
- ❖ **Humidity/Temp. Sensors:** This function board is used to measure humidity. Temperature sensors are devices used to measure the temperature. A pressure sensor measures pressure, typically of gases or liquids.

Liquid Section

The aqueous solutions of medicines that are used to produce internal and external therapeutic effects are known as liquid dosage forms. A solution is a liquid preparation that contains one or more soluble chemical substances dissolved in a specified solvent. Liquid dosage form mainly divided into,

A. Solution
B. Syrup
C. Suspension
D. Emulsion.

Solution:

Pharmaceutical solutions are made by dissolving a solute into a solvent. The solutes can be one or more active ingredients or excipients that are homogeneously dispersed at the molecular level (i.e., dissolved) in the solvent. The solvent can be a single liquid excipient or a combination of miscible liquids (i.e., co solvent mixture).

Types of solutions:

- ➢ **Syrup -** Syrup is a saturated sugar solution. Thus, aqueous solutions containing sugar at or close to its saturation concentration of 67% w/w are called syrups. In

special circumstances, it may be replaced as a whole or in part by other sugars (e.g., glucose/dextrose) or non-sugar (e.g., sorbitol, glycerin, and propylene glycol). Most syrup contain the following components in addition to the purified water and drug(s): (a) sugar, usually sucrose or other sugar substitutes are used to provide sweetness and viscosity, (b) antimicrobial preservatives, (c) flavorants, and (d) colorants. Syrups may also contain solubilizing agents, thickeners, or stabilizers.

➢ **Elixir -** is sweetened hydro alcoholic (combinations of water and ethanol) solutions are termed elixirs. Compared to syrup, elixirs are usually less sweet and less viscous, because they contain a lower proportion of sugar and are consequently less effective than syrups in masking the taste of drugs. Elixirs containing over 10%–12% alcohol are usually self-preserving and do not require the addition of antimicrobial agents for preservation.

➢ **Tincture:** Tinctures are alcoholic or hydro alcoholic solutions of vegetable drugs' chemical or soluble components. The extraction process is used to make the majority of tinctures. Tinctures can contain anywhere from 15% to 80% alcohol, depending on how they are made.

➢ **Oil-based solutions:** While the majority of solution dosage forms are based on water, some solutions are based on oil. For instance, progesterone injections consist of the hormone in a vegetable oil that is suitable for intramuscular application. Additionally, an olive oil-based solution of cyclosporine A is available for oral and ophthalmic use. Due to concerns about palatability, oral dosage forms containing oily solutions are generally not preferred.

➢ **Miscellaneous solutions:** Hydroalcoholic solutions of aromatic materials are termed spirits. *Mouth-washes* are solutions used to cleanse the mouth or treat diseases of the oral membrane. *Antibacterial topical solutions* (e.g., benzalkonium chloride and strong iodine) kill bacteria when applied to the skin or mucous membrane.

Sucrose Syrup manufacturing Process:

➢ Collect the weighing tag of sucrose ingredient (1200 kg) and attach with BMR.

➢ Take 600 Liter Purified water (DM) in 2200 Liter Steam Jacketed Vat.

➢ After adding both Water and Sucrose ingredient then raise the temperature to 100°c to dissolve the 1200 kg sucrose ingredient.

➢ Maintain stirring at 1400 rpm for 60 minutes to make a clear solution.

➢ Then cool the syrup at a temperature of 35°c with continuous stirring (Silverson Stirrer).

➢ This is pharmaceutical grade syrup preparation.

Suspension:

In a pharmaceutical suspension, insoluble solid particles are dispersed in a liquid medium, resulting in a coarse dispersion. (Shake the particles to suspend them). There are two phases,

➢ Internal Phase - consisting of solid, non-soluble particles Using a single or combination of suspending agents, they are kept uniform throughout the suspending vehicle.

➢ External Phase - (suspending medium) typically consists of water. Sometimes, it could be a non-ingested organic or oily liquid. Usually, liquid is oil or water.

Desired Features of suspension:

➢ The suspended particles should not settle rapidly.

➢ Using a moderate amount of shaking, the sediment must be easily resuspended.

➢ It should be easy to pour yet not watery and no grittiness.

➢ It should be physically, chemically and microbiologically stable. (no growth of

fungi, bacteria, oxidation).

Classification of Suspension:

➢ Oral suspension (e.g., Aluminum Hydroxide and magnesium carbonate to reduce acidity) antacid

➢ Externally applied suspension (e.g., calamine lotion for itching)

➢ Parenteral suspension (e.g., Cholera and Tetanus vaccines)

Preparation of Paracetamol Suspension:

➢ Check and receive all raw materials listed in BMR for Name, Quantity and collect the weighing tags of each ingredient and attach with BMR.

➢ Preparation of Sucrose syrup in 2200 Liter Steam Jacketed Vat. Temperature maintain at 100°c and maintain stirring at 1400 rpm for 60 minutes to make clear solution.

➢ Addition of Active and Excipients Pharmaceutical ingredient: Take the following material (Microcrystalline cellulose, Carboxymethylcellulose sodium, Colloidal anhydrous Silica) in 450L Purified water in Master vat on stirring to make homogenous slurry.

➢ Dissolve the material (Sodium Methyl Hydroxybenzoate, Sodium Propyl Hydroxybenzoate) in 50L purified water then transfer this dissolved material into Master Vat through 100 Mesh nylon screens with continuous stirring (Silverson Stirrer).

➢ Filter the sucrose syrup through 100 Mesh nylon Screen that before made and transfer it to Master Vat and Stir for 10 minutes.

➢ Take the following material (Glycerol, Polysorbate 80) in a separate Vat By passing through 100 Mesh nylon screen and add the materials (Paracetamol fine

powder, purified water) and transfer both mixture into Master Vat slowly with continuous Stirring by (Silverson Stirrer).

➢ After adding all material then transfer to Master Vat and finally adjust the volume up to 3000L with purified water and stir for 20 minutes including recycling of the contents for 7 minutes.

➢ Check the PH of the bulk product PH range (4.5 to 6.00).

➢ Affix in-process label on the Master Vat indicating Name of the product, Batch No, Batch size, Mfg., Date and Exp. Date.

➢ Filling the suspension into amber glass bottles and Volumes take range (59-61) ml.

➢ Total Volume is 50000 bottles.

➢ Tertiary Pack Size is 30 bottles.

Emulsion:

The dispersed phase can be stabilized by the presence of an emulsifier. In the continuous phase, one liquid is uniformly dispersed as globules.

Types of Emulsions used in Pharmacy:

➢ **O/W:** oil droplets in water (external) oral injections topical lotions (more preferable b/c easier to consume).

➢ **W/O:** water droplets in oil (external) topical oily and aqueous creams, pastes, gel rectal ointments.

Intention of Use of emulsions:

➢ The majority of these preparations are used for the effects of the therapeutic agents they contain.

➢ Non-medicated ones are used for physical effects such as protectants or lubricants.

List of Liquid oral Products in EDCL:

1) Paracetamol syrup (60ml)

2) Paracetamol suspension (60ml)

3) Chloroquine phosphate syrup (60ml0

4) Levamisole syrup (450ml)

5) Zinc sulphate syrup (100ml)

List of Topical Products in EDCL:

1) Neomycin ointment (10gm)

2) Benzyl benzoate (1L)

The scientifically complete removal of all germs, including the strongest bacteria and spores, is known as sterilization. It is a condition that is difficult to either achieve or demonstrate. There are various inorganic and organic compounds that kill bacteria; however, they may not always be completely successful and can sometimes leave hazardous or undesired residues.

Although moist heat (steam) sterilization can give good results and simple validation, ultraviolet and ionizing radiation do not. These antimicrobials damage or change DNA to prevent replication. Like their forebears, modern scientists turn to steam if sterility is a strict need.

Most, but not all, microorganisms die at temperatures exceeding 80°C. As their environment's temperature rises, microorganisms become more active. Prions demand a considerably higher deactivation temperature and longer deactivation times. With a transmission of 2500 joules per gram of steam, condensation of steam molecules on colder microorganisms effectively raises the temperature at which they are destroyed. The substantially reduced heat transmission of hot dry gases and boundary layer effects,

which can shield and protect microorganisms, make other heating methods inefficient.

Sterile Section

- ➢ Steam Sterilization.
- ➢ Flash Sterilization.
- ➢ Low-Temperature Sterilization Technologies.
- ➢ Ethylene Oxide “Gas” Sterilization.
- ➢ Hydrogen Peroxide Gas Plasma.
- ➢ Peracetic Acid Sterilization.
- ➢ Microbicidal Activity of Low-Temperature Sterilization Technologies.
- ➢ Bioburden of Surgical Devices.

Instrument use for injection (ampoule Preparation)

- ➢ Auto ampoule filling and sealing machine
- ➢ Ampoule Washing machine
- ➢ Autoclave
- ➢ Dry heat Sterilizer
- ➢ Charge vat
- ➢ Cartilage filter unit

Flow Chart of ampoule filling and sealing

Injectable products are dispensed in ampoules according to the procedure given.

Ampoule unboxing

↓

Ampoule Washing

↓

Sterilization (in case of aseptically filled ampoules)

↓

Ampoules filling (under laminar air flow)

↓

Ampoule Sealing

↓

Terminal sterilization

↓

Ampoule inspection

↓

Sealed ampoules

DM flow chart of ampoules washing:

Ampoules are placed manually on tray

↓

Passed through change box to ampoules washing room

↓

Ampoules trays are placed in washing machine where a flash of DM+ WFI flows upper and lower part of machine

↓

After certain period of time, it is removed and the ampoules are replaced from that tray to another tray

↓

Performed dry heat sterilization for dehydrogenation at 260^0C temperature for 1hour

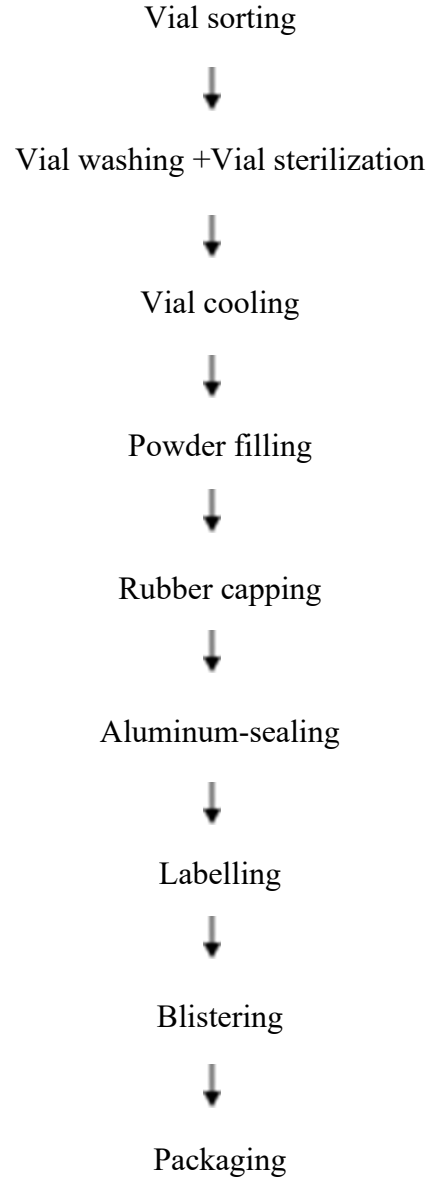
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Allowed to cool and remove it for filling and sealing in aseptic area

Different sterilization techniques and their uses

Sterilization techniques	Temperature (Degree Celsius)	Exposure time (Hours)	Pressure (Bar)	Use
Dry heat sterilization (DBS)	180	3	1.1	Vials
	220	2.5	1.1	
	250	1	1.1	

Preparation of vial involves the following steps:



Machinery Packaging,

Machine name
Semi-automatic bottle filling machine
Semi-automatic cap closer machine
Semi-automatic infusion cap sealing machine
Ampoule filling and sealing machine
Automatic steam sterilizer
Dry heat sterilizer
Charging vessel

Packaging:

➢ Package Foil Layer: 2-layer, Aluminum and Politian.

➢ Empty package weight: 1.15 gm.

➢ Drug with STD weight: 11.40 gm.

➢ Package length: 18/17.

➢ 1 box contains 20 sachets.

➢ 1 cartoon contains 20 boxes.

Packaging

A Pharmaceutical Package container is an article or device which contains the

Pharmaceutical Product and the container may or may not be in direct contact with the product. The container which is designed for pharmaceutical purpose must be stable.

Ideal Qualities of a Pharmaceutical Package

1. It should have sufficient mechanical strength to withstand handling, filling, closing and transportation.
2. It should not react with the contents stored in it.
3. It should be of such shape that it can be elegant, and the content can be easily drawn from it.
4. It should not leach alkali in the contents.
5. The container should not support mold growth.
6. The container must bear the heat when it is sterilized.

Types of Packaging

Primary Packaging: Primary packaging are those packages which are in direct contact with the pharmaceutical formulation. The main aim of primary package is to protect the formulation from environmental, chemical, mechanical and/or other hazards.

Secondary Packaging: The package external to Primary package is known as secondary package. This package provides additional protection during warehousing and provides information about drug product for e.g. Leaflets.

Tertiary packaging: Examples: Barrel, crate, container, pallets, slip sheet. It is outer package of secondary packaging and prevents damage to the products. It is used for bulk handling and shipping.

Material used in packaging

1. Glass

2. Plastic

3. Rubber

4. Metal

5. Paper AND Board

Blister types:

1. ALU-ALU for capsule.
2. ALU-PVC for tablet.
3. ALU-PVDC.

Packaging Machineries



Horn Noack N- 740: Blister

✓ Drug: Calcium and Vit-D-3 tablet

✓ Batch size: 1 lakh.

✓ Alu. Foil: Width-189 mm, Thickness-20 micrometer.

✓ PVC Film: Width-192 mm, Thickness- 400 (+, -) 5 micrometer.

✓ Packet forming tem. – (575-660) degree calceus.

✓ Sealing forming tem. – (200-260) degree calceus.

Process: Forming heater form pocket after that sealing roller seal it. Here is used pump to cool the pocket by cooling water.



Hoonga HMV6: Blister

✓ Drug: Ciprofloxacin tablet 500 mg.

✓ Batch size: 2 lakhs.

✓ Alu. Foil: Width-264 mm, Thickness-20 micrometer.

✓ PVC Film: Width-264 mm, Thickness- (250-260) micrometer.

✓ Packet forming tem. – 133-degree calceus.

✓ Sealing forming tem. – 145-degree calceus.

Process: Forming heater form the packets. Feeding box fill the tablet in the pocket. After that sealing, seal the package and print batch number.



CAM-MX 166: Blister

✓ Drug: Chlorphenamine teb-4 mg

✓ Batch size: 10 lakhs.

✓ Alu. Foil: Width-217 mm, Thickness-20 micro meter.

✓ PVC Film: Width-217 mm, Thickness- (310-320) micro meter.

✓ Packet forming tem. – 130-degree calceus.

✓ Sealing forming tem. – 180-degree calceus.

Proces: Forming- form the pocket at 130-degree tem. Hopper- filling the tablet in the pocket by channel. Sealing- Seal the packet at 180-degree tem and also print the batch.

QA (Quality Assurance) Department

The most important department in the pharmaceutical industry is quality assurance. A pharmaceutical company's research, raw material store, quality control, manufacturing, and sales all go through the QA department's approval. Quality assurance (QA) is the central point of all activities. Quality assurance (QA) ensures that pharmaceutical products are produced in accordance with a safe and consistent quality standard. The QA department is in charge of allowing a variety of practices that lead to the production of high-quality goods. Quality Assurance provides a disciplined atmosphere for manufacturing and other activities in a manufacturing company. QA delegates responsibilities to every person in the company Quality Assurance provides a disciplined atmosphere for manufacturing and other activities in a manufacturing company. QA delegates responsibilities to every person in the company.

Instrument used in QA Department:

✓ HPLC (High performance liquid chromatography)

✓ AAS (Atomic absorption spectrophotometer)

✓ GC (Gas Chromatography)

✓TLC (Thin layer Chromatography)

✓ IR (Infra-Red Spectrophotometer)

✓ Reflective Index

✓ Viscometer

✓ Karl fisher Reagent for water analysis

✓ PH meter

✓ UV spectrophotometer

✓ Dissolution machine

✓ Hardness tester

✓ Friability tester

Role of Quality Assurance in Pharmaceutical Industry: In the pharmaceutical manufacturing company, quality assurance plays a significant role. In a pharmaceutical manufacturing company, all work begins and ends at the level of quality assurance. Nobody is allowed to work outside of the company's standard operating procedures (SOPs), and QA fully controls and implements the SOPs. In this section, every Quality Assurance function is described in details.

Quality Assurance role in raw material store: Personnel from the quality assurance (QA) department are in charge of verifying all incoming raw materials, APIs, excipients, dissolved, and chemicals. They will thoroughly examine the bill number, batch number, and manufacturing date, expiration date, details about the vendor and manufacturer, and whether the container's packing seals and labels are still intact. The material moves on to the next step, which is a sampling of the same, if visual inspection confirms that all parameters have been met. Quality Assurance role in Quality Control: In addition to QC, Quality Assurance shares responsibility for the department of quality control. Every testing procedure in the QC department begins with the QA-issued standard operating procedure (SOP), and QA must continuously oversee all analysis activities. In the quality control department, QA is responsible for issuing standard operating procedures (SOPs) for all activities and instruments. QA is also responsible for validating all testing procedures and instrument performance. Process and equipment performance validation is carried out by QA within a predetermined time frame.

Test Performed in QC Department:

✓ Hardness test

✓ Friability test

✓ LOD (Loss on Dry) test at 105°c

✓ Disintegration test

✓ Dissolution test

✓ HPLC

✓ Assay by titration/spectrophotometer/IR/UV

Microbiological Quality Control of Pharmaceutical Products:

Microbiological quality control is an essential part of the pharmaceutical production process. Pharmaceutical firms must guarantee the quality and safety of their products by rigorously testing raw materials, equipment, ambient surfaces, and final preparations for microbiological contaminants that might have been unintentionally introduced during or after the manufacturing process. The currently approved microbiological quality control assays include growth promotion, microbial enumeration, and antibiotic efficacy testing. To ensure that microbial growth is encouraged, for example, growth promotion testing is a frequently used quality control assay that measures the nutritional characteristics of culture media.

Laboratory Microbiology Test Performed:

✓ Air born Particle counter

✓ Colony counter

✓ Sterilization method at 121°c for 20 min by HIRAY AMA machine

✓ Water Test (a- Drinking water: 500cfu/ml b- DM water: 100cfu/ml c- Distilled water/WFI: <10cfu/100ml

✓ Limit test: A) Bacteria by Tryptone Soya Agar B) Fungi by Potato Dextrose Agar

✓ Specific culture media

✓ Zone of inhibition test

✓ Growth Promotion test

✓ Culture training

✓ Air born particle counter test

Process Validation: A step-by-step procedure known as process validation is intended to guarantee that a manufacturing process can consistently produce high-quality goods. A validation team led by the head of quality assurance for pharmaceutical manufacturers performs it.

Three Stages of process Validation:

Stage 1: Process Design-Consider the following sources and methods to capture process information.

✓ Product development activities

✓ Functionality and limitations of production equipment

✓ Predicted contributions to variability

✓ Risk analysis tools

✓ Experiments or demonstrations at laboratory or pilot scale

✓ Computer-based or virtual simulations

Stage 2: Process Qualification - A protocol and a report should be used to carry out process performance qualification,

✓ Introduction, Objectives, and Scope

✓ Production, Quality Assurance (QA), and Quality Control (QC) Responsibilities and Prerequisites (e.g. manufacturing records)

✓ Process Validation Study Plan based on Quality Risk Management (QRM)

✓ Validation Team (Research and Development, Engineering, Production, QA, and QC)

✓ Product Details and Design Considerations

✓ List of Materials, Vendors, and Master Formula

✓ In-process Test and Specifications or Critical Quality Attributes (CQA)

✓ In-process Test and Specifications or Critical Quality Attributes (CQA)

✓ Analytical Method Validation

✓ Finished Product Specification

Stage 3: Continued Process Verification- The third stage of process validation, which follows process design and qualification, entails setting up systems to constantly ensure that the validated process remains in this state during routine production. Statistical process control (SPC), continuous monitoring and sampling of process parameters and quality attributes, and scheduled maintenance of the facility, utilities, and equipment are all common components of continued process verification. Throughout the validation process, good documentation practices must be followed.

Product Development

Developing dosage forms with the best quality and lowest cost in the shortest amount of time is the industry's biggest problem. In this area, our Product Development Department is essential. Our pharmaceutical products are created in a methodical manner to attain the appropriate level of quality for their intended usage. This department is staffed by highly qualified individuals who have a sufficient understanding of pharmaceutical technology and are well equipped with a variety of production machines and equipment for small-scale production.

All items are developed using thorough standard manufacturing processes with appropriate formulations. After conducting thorough stability research, including an accelerated stability study, the expiry duration of items is calculated. All technical documents, including the Product Development, Production, and Quality Control Departments' active involvement, include the Master Formula, Standard Manufacturing Process, Standard Product Specifications, Standard Specifications of Raw and Packaging Material, all types of test methods, Batch Manufacturing Records (BMR), validation of test methods & Process Validation, and finally the Product Master File.

Product development division is outfitted with ERWEKA Multi-Purpose Equipment’s, including all required attachments for sieving, mixing, granulating, tableting, coating & polishing, liquid mixing, dosing & filling, and all additional equipment’s for capsule filling and ointment dosing & filling units. In addition to the QC laboratory, there is a separate testing lab with all essential testing equipment and resources for stability studies, such as an operational climate oven for rapid stability studies.

During Our training period we observed:

Development of pantoprazole

Function of product development section: The principal functions include the following,

- ✓ Source validation for new product
- ✓ SOP development for new product
- ✓ Troubleshooting for existing product
- ✓ Modification of an existing formulation for cost reduction
- ✓ Development of formulation of new

Products other functions of PD section including:

✓ Improvement of formulation of existing products

✓ Comparative studies with other company's sample

✓ Determination of the batch size

✓ Method development for testing the raw materials and finished products

✓ Determination of easy production process

✓ Stability study of new and existing products

✓ Determination of compatibility of excipients with the active ingredients

Preparation of MO (Manufacture Order)

❖ Costing study

❖ Pilot batch production

❖ Lebel design, packing material design and approval

Product development activities:

❖ Receiving of project paper

❖ Collection of innovator sample

❖ Pre-formulation study

❖ Formulation design

❖ Collection of raw materials

❖ Product development trial

❖ Process development batch

❖ Process development report

❖ Process validation

❖ Process validation report

❖ Commercial manufacturing

Machine used in this section:

ER WEKA- Multipurpose equipment with all necessary attachment for: -

1. Sieving
2. Mixing
3. Granulating
4. Tableting
5. Coating and Polishing
6. Liquid mixing
7. Dosing and filling for capsule, ointment

There is a separate testing laboratory with all necessary testing facilities apart from QC laboratory and facilities for stability study including climate over for accelerated stability study in functioning continuously.

Standard operating procedure (SOP) for stability study:

Assurance of stability is a primary goal for a pharmaceutical company. Stable products don't have to be outdated; instead, they just need to fulfill specific standards for identity, strength, purity, and other attributes over the whole of their stated shelf life. Stability may be impacted by physical, chemical, or microbiological changes that take place during or after the manufacture of a product. Therefore, all the tests and studies are part of the stability research program for new goods.

Objective

The primary objective for stability study is to assure desired quality, purity, strength, identity, efficacy etc. in the finished marketed products of EDCL during its shelf-life.

Policies:

ASS will be used to assess new products' stability and shelf life. After six months, the shelf life will be assessed using the data and plot of the ASS and may, if needed, be sent to the regulatory agency. The recipe is first approved by the regulatory agency after the formulation, packaging,

etc. are examined. If the recipe works, the regulatory body looks over the annexure, which contains the shelf-life estimate, stability research report, packing material, even

box, etc. You can use information from the relevant room temperature to calculate shelf life.

The first three scale-up production batches produced following approval shall adhere to the expedited methodology outlined in the approved medication application.

The requirements for stability study

- ❖ Potency assay: all active ingredients.
- ❖ Container: appearance of inner wall and cap interior
- ❖ Integrity of seals
- ❖ Appearance and adhesion of label
- ❖ Dosage form
- ❖ Physical characteristics

Determination of Shelf-life:

Based on the application of Arrhenius equation,

$$\text{Log } t = \text{Log}A - 2.30RT$$

- ❖ A= constant
- ❖ E_a= Energy of activation
- ❖ R= Molar gas constant
- ❖ T= Thermodynamic temperature in Kelvin scale, which indicates the effect of temperature on the rate constant K, of chemical reaction.

Recommendation:

During our internship at **Beximco Pharmaceuticals Limited**, we observed the company's strong commitment to quality and excellence. Based on our experience, we anticipate that Beximco will continue to strengthen its position and emerge as a market leader in Bangladesh's pharmaceutical industry.

The central warehouse demonstrates exemplary pharmaceutical practices and is well organized. Other warehouse facilities within the factory may benefit from adopting similar standards and operational practices.

The Product Research and Development (R&D) unit is well equipped with modern instruments and advanced facilities. However, recruiting additional skilled personnel would help reduce the workload on existing staff and further enhance the company's capacity in formulation and analytical development, enabling it to remain a pacesetter in innovation.

Although the solid dosage unit of Track I does not fully meet ideal environmental cleanliness standards, it is operated by a dedicated and skilled workforce committed to producing quality products. The setup for powder for suspension manufacturing was observed to be particularly well maintained. The liquid, cream, and ointment departments were also satisfactory; however, improved cleanroom practices would further enhance product quality and compliance.

The infusions department operates within a controlled manufacturing area, though the packaging section does not fully meet optimal cleanroom standards. A dedicated Quality Control (QC) and Quality Assurance (QA) team actively monitors both environmental and product parameters, ensuring consistent quality.

The overall Quality Control department is highly active and efficient. Increasing the workforce in this department would improve operational efficiency. The company's Quality Assurance system is particularly impressive, with multiple checkpoints across departments, reflecting strong adherence to Good Manufacturing Practices (GMP)**.**

Finally, closer collaboration between the **internship program**, **training**, and **human resources departments** is recommended. Such coordination would allow interns to gain a comprehensive understanding of departmental activities without disrupting routine operations at the operational level.

Conclusion:

Visiting and observing the various divisions of a pharmaceutical manufacturing company firsthand was both encouraging and inspiring. This experience not only motivated us to study our academic subjects more thoroughly but also helped us realize the immense dedication, discipline, and teamwork required to build and sustain a pharmaceutical company of such high standards.

Our in-plant training at **Beximco Pharmaceuticals Limited (BPL)** provided exposure to a wide range of dosage forms. The two-week observation period across multiple departments significantly strengthened our understanding of theoretical concepts by allowing us to see their practical applications. We observed manufacturing processes, quality control activities, packaging operations, and other essential functions involved in pharmaceutical production, which greatly enriched our learning experience.

Throughout our training, we encountered advanced technologies and modern equipment and gained valuable insights into their industrial applications. We also explored the vast industrial premises of BPL, including its own power generation facilities and a liquid nitrogen plant. Furthermore, we observed strict quality assurance practices at every stage of production, ensuring the manufacture of high-quality pharmaceutical products suitable for both national and international markets. It was evident that BPL employees are highly trained and committed to strictly following **Good Manufacturing Practice (GMP)** guidelines.

Beximco Pharmaceuticals Limited has consistently maintained a position among the top three pharmaceutical companies in Bangladesh in terms of market share for over five years. It was truly an honor to witness the internal operations of an organization of such stature and excellence.

Finally, we would like to express our sincere gratitude to **Beximco Pharmaceuticals Limited** and all its personnel for providing us with this invaluable opportunity. We are deeply thankful for the knowledge, experience, and inspiration gained throughout our journey with BPL, which will undoubtedly contribute to our future professional development.