

A COMPREHENSIVE REPORT ON SUMMER INTERNSHIP AT LIFE PHARMACEUTICALS

Abstract

Two weeks long summer internship at Life Pharmaceuticals, Kolkata was a nice first-hand experience on different processes, equipments, instruments used in Production and Quality Control units of a Pharmaceutical Industry. Situated at Uluberia, Howrah, Life Pharmaceuticals, Kolkata is manufacturing tablets and parenteral products for last three decades or so with the help of about 50 employees.

They have a patent product CHROMOSTAT®

Life Pharmaceuticals Pvt Ltd.'s Corporate Identification Number is (CIN) U24232WB1964PTC026271 and its registration number is 26271. It's registered address is 3/2B ORIENT ROW KOLKATA WB 700017 IN .

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LIFE PHARMACEUTICALS

DIFFERENT UNITS IN THIS COMPANY

- Raw Material Storage House
- Water Plant
- Air Handling Unit
- Production Unit
 - Tablet Production Unit
 - Parenteral Production Unit
- Quality Control and Quality Assurance Unit

Raw Materials Storage House

DIFFERENT SECTION IN THIS AREA

- **Dedusting unit**
 - **Raw Materials Passed Section**
 - **Raw materials unpassed section**
 - **Raw materials store room**
 - **Vitamins and biological materials store room**
 - **Raw materials rejection store room**
 - **Dispensing room**
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- Raw materials, packed in cartoon, enter through the entry gate and dedusting of the packaging materials are done.
 - Samples are collected from raw materials and sent it to Quality Control (QC) department for testing purpose.
 - QC approved materials are kept in Raw Materials Passed Section and others are kept in Raw Materials Unpassed Section.
 - Finally, the raw materials (QC approved) are kept in raw materials store room.
 - Vitamins and other biological materials are kept separately in an air-conditioned room, namely Vitamins and Biological store room.
 - Waste materials are kept in rejection room.
 - Raw materials are weighed under LAF Hood kept in Dispensing room.

AIR HANDLING UNIT (AHU) - air of the production area is regulated and circulated by HVAC (heating ventilation air condition) system.

Components of AHU-

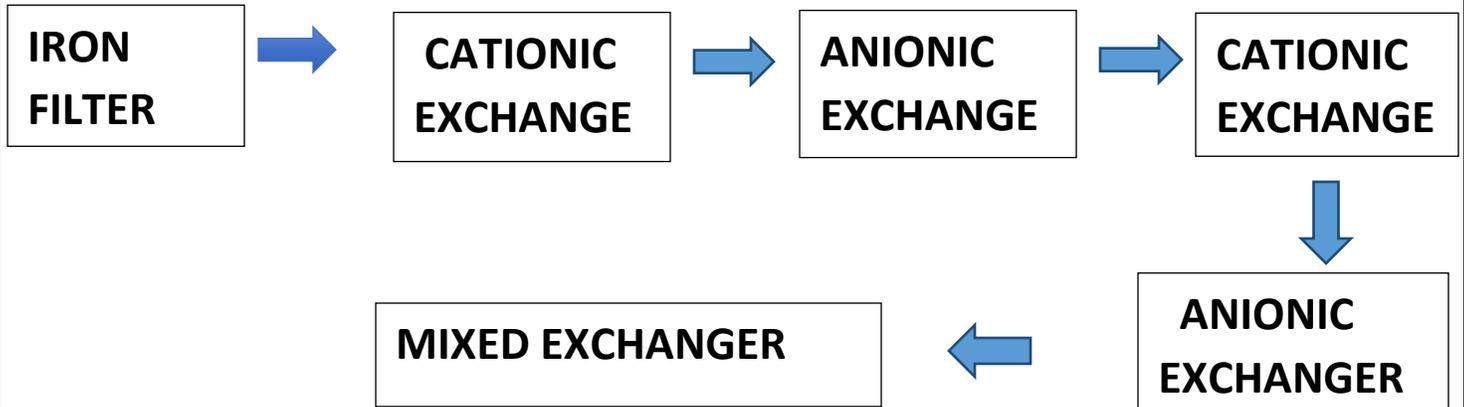
- **Housing-** made up of metal and contains all the other components.
 - **Fan-** centrifugal fan is used to circulate the air to the various parts of the section in the building. Types of fan are used: backward, forward, curved, inclined.
 - **Filter-**HEPA filter is used. It is able to achieve efficiencies up to 99.97%, removing minute particles and air born bacteria from the air.
 - **Humidifier-**heating coil is used to control the humidity level of the air.
 - **Cooling coil-** is used to cool and dehumidify the air.
 - **Mixing box-** this is the place where the outside air and the return air are mixed to provide the correct proportion of air to be distributed.
- **Smoke test** is done for validation of H-VAC.

WATER PLANT

Demineralized Water and Water for Injection is mainly used for Production.

DEMINERALIZED WATER PRODUCTION

- Six different types of ion exchanger are used.



Water comes out from the mixed ion exchanger and passes through the UV pump, here conductivity of the water is checked by Online Conductivity meter and finally stored in VAT (150 L/ 300 L).

WATER FOR INJECTION PRODUCTION

Equipment: 1) Boiler
2) Multi Column Distillation Still

Boiler: portable water is heated above 100°C to produce steam which is used in multi column distillation still.

Multi-Column Distillation Still: capacity – 100 lit/ hr.
Pressure – 90 lb.

Description- It has two control device a) Feed water
b) Cooling water

Principle: Double Distillation.

Working procedure:

1. Demineralized water is heated with steam i.e. produced by boiler at 124°C
2. Then it is condensed by Cooling Water control device.
3. 1 & 2 are repeated again i.e. double distillation is done.
4. Finally, water for injection is produced.

- USES -**
- 1) Ampule washing
 - 2) Parenteral formulation

PRODUCTION UNIT: Mainly Tablets and Parenterals are produced here.

TABLET PRODUCTION UNIT: Class D is maintained throughout this area.

Equipments:

- **DRY GRANULATION EQUIPMENT**

- 1) **Roller Compactor (Gran-01)**

- Mesh size- 40; Capacity- 60Kg; Mfg. by- Hindustan

- Construction-it contains

- i. **Feeding system-** which conveys the powder to the compaction area between the rolls.
 - ii. **Compaction unit-** it contains two counter rotating rolls, powder is compacted to ribbon, between these two rolls.
 - iii. **Size reduction unit-**milling the ribbons to the desired particle size.

- Uses: size reduction and granulation.

- 2) **Double Cone Blender (Precikot)**

- Capacity- 300 Kg;

- Uses- Mixing of granules, dry powder, heavy and abrasive materials.

- **WET GRANULATION EQUIPMENT**

- 1) **Rapid Mixer Granulator or RMG (Precikot)**

- Capacity- 30 KG

- Working principle-formation of granules occurs by rising, whirling, tumbling motion of material. During the addition of binder solution to the powder impeller and chopper are operated at low speed after the formation of wet mass impeller and chopper are operated at high speed to form the granules.

- Uses-In rapid mixer granulator mixing, densification and agglomeration is achieved using shear mixing (breaking inter-molecular forces) and compaction forces exerted by impeller on the powder mass.

- 2) **MASS MIXER**

- Capacity-50 KG

- Used in mixing.

- **DRYER**

- 1) **FLUIDIZED BED DRYER**

- Capacity- 30 KG; Temperature used- 60°C

- Power- 440 Volt

- It consists of – air preparatory unit, product container, exhaust filter and blower, control panel spray nozzle, solution deliver, distribution plate.

- Uses- used to reduce the moisture of granules.

- 2) **TRAY DRIER (KILBURN DRYING OVEN)**

- Mfg. by-McNeill & Barry limited;

- Capacity -48 KG; motor H.P- 15 kilowatt, total AMPs-15.4.

- Used in drying of granules.

- **LUBRICATOR**

- 1) **Drum mixer**

- RPM: 40-45

- Uses- mixing and lubrication.

- **TABLET PUNCHING MACHINE (CADMACH)**

- Station -27, power supply-440 volt.

- Uses- used in compression of granules

- **BLISTER PACKAGING MACHINE-** primary packaging of the tablet is done by this machine.

- Rapid pack 240**

- Forming temperature-155°C; sealing temperature- 213°C

- **COATING MACHINE**

- 1) **Film coating machine (UNICOTA-36)**

- Capacity-60KG; Temperature maintained -220°C; rpm – 4-5; mesh size -100;

Coating solution- INSTACOAT+ titanium di-oxide+ Isopropyl alcohol+ methylene chloride (for TRANXEMIC ACID).

Spraying of coating solution is done by spraying gun.

2) PANCOTA

Conventional coating machine, spraying of coating solution is done manually.

- **TABLET POLISHING MACHINE**

Uses- polishing of tablet.

In process quality control- hardness testing, disintegration test, weight variation test, content uniformity test is done to check the quality of the tablet.

PARENTERAL PRODUCTION UNIT

Different section of this unit –

- **Ampule washing and drying room-** here washing and drying of the ampule is done.
Ampule washing machine (OLO-60)
Ampules are washed with demineralized water two times and finally washed with water for injection.
Ampule drying machine (DHS)
Dry heat sterilization of Ampules are done by heating at 240°-260°C for 70 min. Sterilization of these ampules are done before filling and sealing.
- **Solution preparation room –** Class C is maintained throughout this room. Active pharmaceutical ingredients are diluted with water for injection (within 24 hr. of production) to prepare the solution. Sterilization of the solution is done with membrane filter (pore size-.25 micron). Then a sample of the solution, sent to quality control unit for sterility testing.
- **Ampule filling and sealing room-** Class B is maintained in ampule filling and sealing room and under the LAF (laminar air flow) hood class A is maintained.
Ampule filling sealing machine- filling of the solution into ampule and sealing of the ampule is done by this equipment.
- **Changing room-** sterilized apron, gloves, hair mask, and shoe cover should be wear before entering into the production area.
- **In-process quality control room-**
- Ampules are kept against black and white background to check white and black particles manually.
 - After filling and sealing, samples are sent to QC unit for microbial testing that is **pyrogen test/ bacterial endotoxin test.**
Reagent used in this test-

C.S.F (*E.coli*) O55:B5 (in powder)

Strength- 33 mg/ vial; volume-50 ml

- LAL reagent water is used to dissolve it.
- Store at 2°C to 8°C.

LYSATE

Volume-1.8 ml; wave length- 0.125EU/ ml

- Store at 2°C to 8°C.

LAL REAGENT WATER

Store at 15 to 30°C

Volume-100 ml

Endotoxin content- <0.005 EU/ ml

- **Ampule labeling** – ampules are labeled manually.
- **Secondary packaging** – ampules are packed into small boxes than in a cartoon.

QUALITY CONTROL AND QUALITY ASSURANCE UNIT

QUALITY CONTROL – a system of maintaining standards in manufactured products by testing a sample of the product against specification (that mentioned in pharmacopeia).

Different apparatus used in QC

- **INCUBATOR**- It is used to grow and maintain the microbial culture. It maintains optimal temperature (35-37°C), humidity and other condition like carbon di oxide, oxygen.
- **BOD INCUBATOR**: Bio- oxygen demand incubator is used to maintain temperature (22°C) for storage or incubation of bacterial culture where high ° of constant temperature accuracy is required.
- **LAMINAR AIR FLOW CABINET**- is a carefully enclosed bench designed to prevent contamination of semiconductor wafers, biological samples or any particle sensitive materials. Air is drawn through a HEPA filter and blown in a very smooth, laminar flow towards the user. Due to the direction of air flow sample is protected.

Cabinet is made up of stainless steel (grade- 316L).

- **STABILITY TEST CHAMBER (REMI)**

Temperature and relative humidity is maintained.

- **SPECTROPHPTOMETRY**

Double beam spectrophotometer (ELICO)

Uses- quantitative measurement of the reflection or transmission properties of a material as a function of wavelength.

- **HPLC /High Performance Liquid Chromatography (SHIMADZU)**

HPLC column – C (18)

250x 4.60 cm

Used to separate, identify and quantify each component in a mixture.

- **DISINTREGATION TEST APPARATUS**

Mfg. by -Electro Meta Corporation

- Single pan
- Temperature maintained: $37\pm 2^{\circ}\text{C}$

Used to measure disintegration time of a dosage form like tablet, capsules, and suppositories etc.

- **FRAIBILITY TEST APPARATUS**

Mfg.by- Campbell Electronics

Used to determine the physical strength of tablet.

- **MONSANTO HARDNESS TESTER**

Used to determine hardness of the tablet.

- **POLARIMETER**

Mfg.by-TOSHNIWA INSTS. & ENGINEERING.CO

Used to measure the angle of rotation caused by polarized light.

- **SIMPLE MICROSCOPE**

Uses- for determination particle size, morphology and roughness of the raw materials, finished product etc.

- **REFRACTOMETER**

Used to measure refractive index.

- **MOISTURE BALANCE**

Provide a primary method for accurate moisture measurement by using the loss on drying (LOD) method.

Tablet granules are kept at 105°C for 15 min.

- **ULTRASONIC CLEANER (SONICA)**

Uses – degassing and cleaning

- **DIGITAL POTENTIOMETER**

Range -200 mv-2000mv

Different electrodes are-

1. Reference electrode (Type RE-20); pH- 7
2. Glass electrode (Type GE 15)
3. Silver electrode (TYPE SE 70)
4. Platinum electrode (TYPE PE 60)

- **DIGITAL COLONY COUNTER**

It is designed for quick and accurate counting of bacterial and mould counting in petri dishes.

- **ELECTRONIC DIGITAL BALANCE**

Used for weighing substances to the milligram (0.000g)

- **UV-DETECTOR**

Range – (254 nm -366 nm)

Uses- Detection and identification of analytic sample by measuring of absorption of the sample.

- **VACUUM GAUGE**

Uses- used to check loss on drying of different biological materials like vitamin (to prevent degradation by heating).

For vitamins 12-25 lb. pressure is applied.

- **HOT AIR OVEN**

Used in dry heat sterilization of

1. Glassware (like petri dishes, flasks, test tubes),
2. Materials that contain oil,
3. Metal instrument like scalpels, scissors and blades.

Temperature used- **160°C for 2 hrs.**

- **WATER BATH**

Used for heating (some chemical reactions require elevated temperature).

- **AUTOCLAVE**

It is used to sterilize equipment (glass wares) and supplies (liquid media, nonflammable liquids) by subjecting them to high - pressure saturated steam at **121°C** at **15 lbs.** pressure for **15 minutes**.

- **MUFFLE FURNACE**

Used for converting the materials in absolute ash. This ash is used for performing the analysis of different chemical properties of the materials that are being tested.

Temperature used-up to 1200°C.

- **CRUCIBLE FURNACE**

Use- used for heating above 800°C

QUALITY ASSURANCE UNIT

- They prepare, approve and monitor the implementation of key documents like SOP (standard operating procedure), BMR (Batch Manufacturing Record), BPR (Batch Packaging Record), BP quality manual, validation master plan etc.
- They check the qualification of raw materials, vendors, testing methods, document control, equipment calibration, data recording, and formulation of API batches.
- They ensure the specifications and test procedure for raw materials, packing materials, in-process testing, APIs, stability testing etc.
- They approve an equipment calibration, qualification and maintenance schedules, as well as qualification of HVAC, gas and power distribution system.
- They review and approve manufacturing records and QC testing data before any intermediate, API or finished batch is released.