

Manufacturing of dry powder injection of Ceftriaxone + Sulbactam 1.5gmIP

A Internship Report submitted
for the partial fulfilment of the Degree of Master of Science

By

Miloni B. Nandani

Enrolment No:

210621026

[M.Sc. Biotechnology]



Under the supervision of

Sukrut Patel

Manager -Production department

DEPARTMENT OF BIOTECHNOLOGY

ATMIYA UNIVERSITY

‘YOGIDHAM GURUKUL’ KALAWAD ROAD

RAJKOT (GUJARAT) – 360005

2022-23



C E R T I F I C A T E

This is to certify that this training report entitled **Manufacturing of dry powder injection of Ceftriaxone + Sulbactam 1.5gm IP** was successfully carried out by Miss. **Miloni B. Nandan** towards the partial fulfilment of requirements for the degree of Master of Science in Biotechnology of Atmiya University, Rajkot. It is an authentic record of his/her own work, carried out by him/her under the guidance of Name of Supervisor for a period of 3 months during the academic year of 2022-23. The content of this report, in full or in parts, has not been submitted for the award of any other degree or certificate in this or any other University.

Signature

Dr.Nutan Prakash Vishwakarma

Head of the Department

Signature

Mr.Sukrut Patel

Supervisor



DECLARATION

I hereby declare that the work incorporated in the present dissertation report entitled **“Manufacturing of dry powder injection of Ceftriaxone + Sulbactam 1.5gmIP”** is my own work and is original. This work (in part or in full) has not been submitted to any University for the award of any Degree or a Diploma.

Date:5th April 2023

Miloni B. Nandani



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ABSTRACT

- ✓ SanoletLifecare Private Limited is a private company .
- ✓ This company manufactures dry powder of injection using different antibiotics.
- ✓ This company has departments named Production department, QC department, QA department & Engineering department. Different tests like Sterility test , BET test, Sterility test are done to check the quality of the product,
- ✓ The study of this concept is necessary for getting real time practical experience .
- ✓ In this study I have given a short introduction about my internship along with the activities which I have performed during my internship period.
- ✓ I also relate the practical practice with the theoretical concepts that I have observed during my internship.



ABBREVIATIONS

Annual General Meeting (AGM)

Ministry of Corporate Affairs (MCA)

No(Number)

United State Pharmacopeia(USP)

Manufacturing(Mig.)

Master Formula Record(MFR)

Batch Manufacturing Record(BMR)

Batch Packaging Record(BPR)

Not Applicable(NA)

Quality Assurance(OA)

Quality Control(QC)

Expiry(Exp.)

Raw Material(RM)

Packaging Material(PM)

In Process Quality Assurance(IPQA)

Bacterial Endotoxin Test(BET)

Regulatory Affairs(RA)



COMPANY INFORMATION

- ✓ Sanolet Life care Private Limited is a Private incorporated on 21 September 2020. It is classified as Non-govt. company and is registered at Registrar of Companies, Ahmedabad. Its authorized share capital is Rs. 11,000,000 and its paid up capital is Rs. 10,100,000.
- ✓ Sanolet Life care Private Limited's Annual General Meeting (AGM) was last
- ✓ held on 30 November 2021 and as per records from Ministry of Corporate Affairs
- ✓ (MCA), its balance sheet was last filed on 31 March 2021.
- ✓ Directors of Sanolet Life care Private Limited are KiranbhaiKanubhaiBunde, TejaskumarMaganlalPadodara, Hiren Vasantlal Shah and Sachin IshvarbhaiSardava.



DIFFERENT DEPARTMENTS OF COPMANY ARE:

- ❖ Production Department
- ❖ QA Department
- ❖ QC Department
- ❖ Engineering Department



PRODUCT INFORMATION

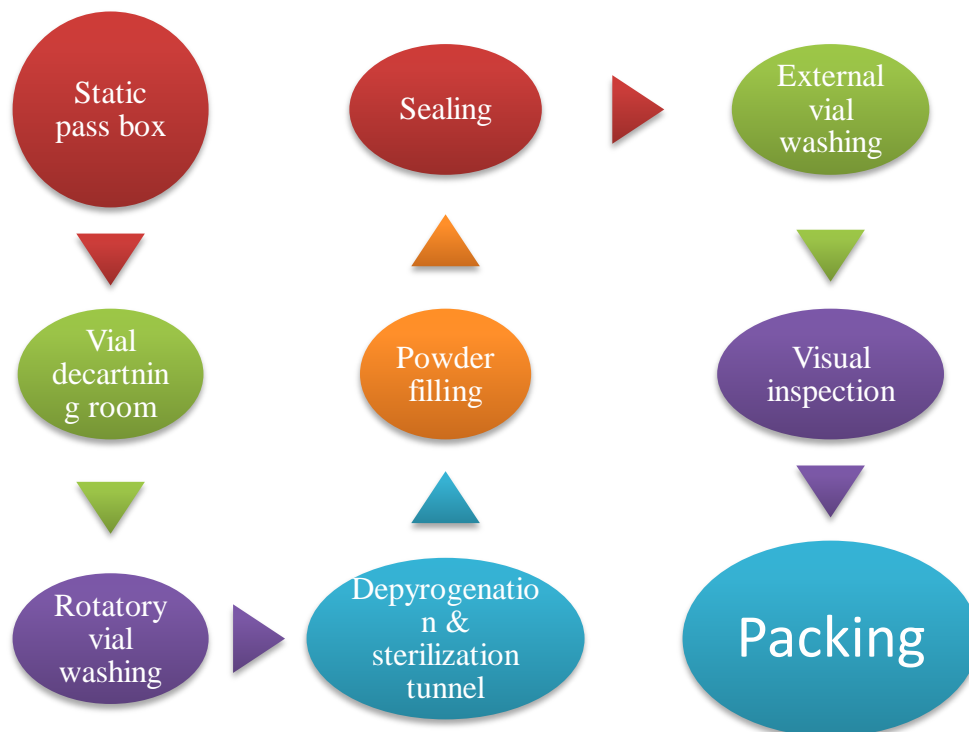
- ✓ CEFTRIAXONE+SULBACTAM contains Ceftriaxone and Sulbactam. Ceftriaxone is a cephalosporin antibiotic, whereas Sulbactam is a beta-lactamase inhibitor. CEFTRIAXONE+SULBACTAM has broad-spectrum activity and is effective against both gram-positive and gram-negative bacteria. It makes the drug effective in multiple serious bacterial infections.
- ✓ Ceftriaxone is a broad-spectrum cephalosporin antibiotic used for the treatment of bacterial infections in various locations, such as in the respiratory tract, skin, soft tissue, and urinary tract.
- ✓ Sulbactam is a β -lactamase inhibitor. This drug is given in combination with β -lactam antibiotics to inhibit β -lactamase, an enzyme produced by bacteria that destroys the antibiotics.



PRODUCTION DEPARTMENT

- A production department is a group of functions within a business that is responsible for the manufacture of goods.
- Production department includes documents like Batch Manufacturing Record (BMR) & Batch Packaging Record (BPR).

Production line flowchart:





BATCH MANUFACTURING RECORD (BMR)

BMR NO :BMR/SC0015/00

Product Name :Ceftriaxone & Sulbactam (IP) 1.5gm

Generic Name :Ceftriaxone 1000MG & Sulbactam 500MG for injection

Product Code :SC0015

Batch NO :22DC118

Effective Date :29/05/2022

Composition: Each vial contains: Sterile ceftriaxone & Sulbactam IP Eq. to Ceftriaxone& Sulbactam anhydrous 1.5gm

Product Description:7.5ml clear glass vial USP II IHS,20mm grey butyl rubber stopper with 20mm,CL blue Hip off seal IMS containing a white coloured powder.

Storagecondition:Store below 25°C Do not freeze, protect from light and moisture.

Effective date: 29/05/2022

Effective Batch NO.NA

Product Specification:IP

Shelf Life:24 months.

Standard Batch size: 5000 vials

Mfg License No:G/28/1843

Superseded version NO:NA

Reason for change:New product

MFR NO:MFR/ SC0015/00



Actual Batch size:5000 vial

Mfg Date:01/2023

Exp. Date: 12/2024

Fill weight:As per calculation +_2%-

BMR Issued by (QA):

✓

BMR Received by (Production):

✓

Batch Start Date:

Batch Completion date:



Table of Content

1. List of abbreviations
2. Signature log sheet
3. Bill of raw material
 - i. Before start the process line clearance shall be taken as per SOP No.
 - ii. Name of area: RM store, previous product name, previous product batch number.
 - iii. Raw material requirement, standard fill weight
4. Bill of primary packing material
5. General instruction
6. Equipment & machine cleaning record
7. Glass vial washing
 - i. Line clearance for decartoning of vials
 - ii. Decartoning of vials
 - iii. Washing of vials
 - iv. Vial washing verification
 - v. Clarity check (Minimum 8 vials to be checked at interval of 1hr)
 - vi. No. of vials rejected during decartoning& washing
 - vii. No. of washed vials sent for Depyrogenation
 - viii. Check the parameters before starting the depyrogenation& sterilization
8. Depyrogenation& sterilization of washed vials
 - i. Line clearance for vial washing &depyrogenation of tunnel
 - ii. No. of vials rjctrd during depyrogenation
 - iii. No. of vials sent for filling
9. Flip Off seal sanitization record
10. Washing & sterilization of rubber stopper , blander & machine parts
11. Environmental control of sterile area
 - i. Fogging status



- ii.** Cleaning before start of filling
- iii.** Control checks
 - a.** Working of AHU system
 - b.** Working of dehumidifier
 - c.** Fogging with disinfectant solution containing 11% H₂SO₄ & 0.01% AgNO₃

- 12.** Equipments stability record
- 13.** Weighing & Bulk mixing record
- 14.** Filling & sealing record
- 15.** Visual Inspection & Rejection record
- 16.** Batch Reconciliation
- 17.** Batch yields details
- 18.** Batch summary report
- 19.** BMR review history



BATCH PACKAGING RECORD

Product Name:Ceftriaxone & Sulbactam 1.5gm

Generic Name: Ceftriaxone 1000MG & Sulbactam 500MG for injection

BPR NO:BPR/SC0015/00

Batch NO:22DC118

Effective Date:29/05/2022

Composition: Each vial contains: Sterile ceftriaxone & Sulbactam IP Eq. to Ceftriaxone& Sulbactam anhydrous 1.5gm

Storage condition:Store below 25°C Do not freeze, protect from light and moisture.

Effective date: 29/05/2022

Effective Batch NO.NA

Product Specification:IP

Shelf Life:24 months.

Standard Batch size: 5000 vials

Mfg License No:G/28/1843

Actual Batch size:5000 vial

Mfg Date:01/2023

Exp. Date: 12/2024

Fill weight:As per calculation +_2%-



BMR Issued by (QA)

✓

BMR Received by (Production):

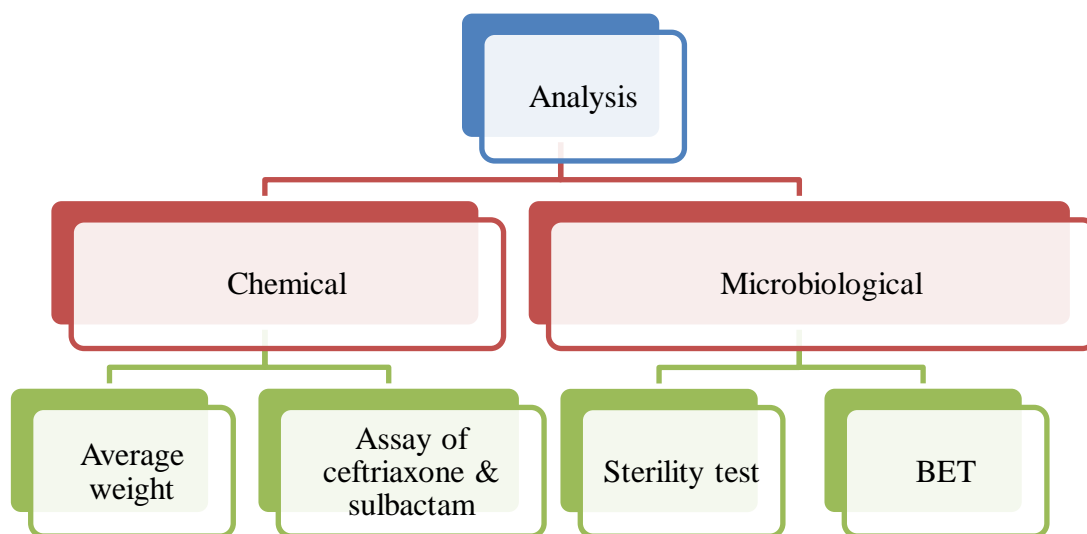
✓

Batch Start Date& Batch Completion date:



QUALITY CONTROL DEPARTMENT

- ✓ The aim of QC in the pharmaceutical industry is to verify and test the medicines at various stages of production to ensure every product is of the good quality.





- **Average weight:** Cefoperazone & Sulbactam

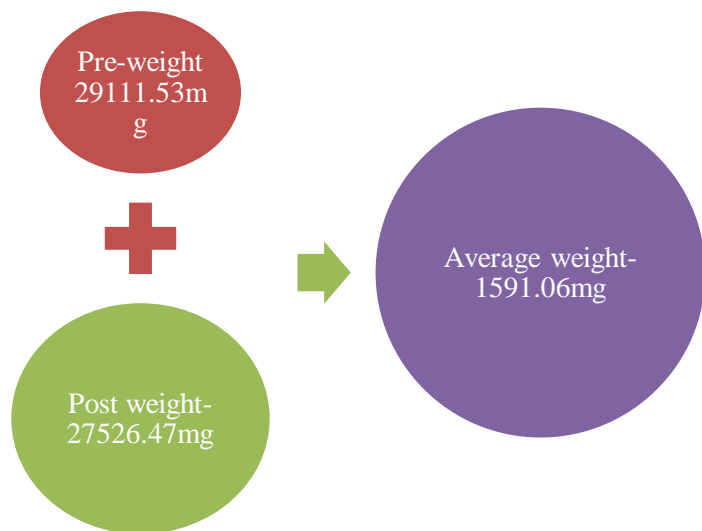
Take a vial & remove the seal

- Weigh the powder present in vial (pre weight)

Wash th vial with ethonal & dry it in hot air oven

- Weigh the vial again (post weight)

RESULT:





•Assay of ceftriaxone & sulbactam:

- ✓ The assay is based on the inhibitory effect of ceftriaxone on the strain of *Bacillus subtilis* is used as test organism.
- ✓ Assay of sulbactam a beta lactamase inhibitor, in serum in the presence of ampicillin were compared.

•Sterility Test:

- ✓ Sterility testing is required to ensure viable contaminating microorganisms are not evident in a product. This testing is conducted by direct inoculation or membrane filtration methods and can be performed in an isolator or cleanroom environment.
- ✓ Membrane Filtration: Sterile, enclosed units allow for the simultaneous filtration of equal volumes of test samples through two membrane filters.



•Bacterial Endotoxin Test (BET):

Principle:

- ✓ A bacterial endotoxin test (BET), such as LAL (limulus ameocyte lysate), is an in vitro assay used to detect bacterial endotoxins. The bacterial endotoxin test uses the lysate from blood cells to detect bacterial endotoxins.

Procedure:

1. Take 2 test tubes.
2. Add 100 μ L of sample to the tubes.
3. Now add 100 μ L of LAL reagent in assay tubes and incubate tubes for 60 minutes.
4. Now invert the tubes and observe the result.
5. If solid medium remain intact the product is considered to contain endotoxin.

RESULT:



Endotoxin absent



Endotoxin present



QUALITY ASSURANCE DEPARTMENT (QA)

○ QA ensures that the medication being manufactured are consistent, reliable and are safe for public release.

QA includes:

- **Warehouse**– RM(Raw material) store and PM(Packing material) store
- **Production department**
- ***IPQA(In process quality assurance)** is responsible for carrying out all the processes as per SOP during manufacturing to ensure quality.
- **RA(Regulatory affairs)** acts as the interface between the pharmaceutical industry and drug regulatory authorities



ENGINEERING DEPARTMENT

Pharmaceutical engineering focuses on designing, building, and improving manufacturing facilities that produce drugs.

Why Determination of hardness of water is necessary?

- Hardness of water is due to the presence of dissolved salts of calcium, magnesium and other metal ions.
- The determination of hardness is a useful analytical process for measuring the quality of water for household and industrial uses.
- below 75 mg/L-soft
- 76 to 150 mg/L -moderately hard
- 151 to 300 mg/L-hard
- more than 300 mg/ - very hard

❖ Air Handling Unit:

- No cross contamination through air in product manufacture area.
- Air lock (cascade, bubble)
- Filters (HEFA, fine-filter,pre-filter)
- Validation (integrity-to know leakage)
- Particle count (0.5 to 5 micron)
- Recovery:Time-10min
- Instrument - Air burn particle counter
- Print out of result-Cycle per min (Viable/non-viable particle count)



PACKAGING & STORAGE DEPARTMENT

✓ **Primary packaging :**

It is the material that first envelopes the product and holds it.

- Vials
- Seal rubber
- Stopper

✓ **Secondary packaging :**

It is outside the primary packaging used to group primary package together.

- Label
- Carton

✓ **Tertiary packaging:**

It is done for bulk handling and shipping.

- ✓ Raw material and Packing materials which are used in the manufacturing of batches shall be received and stored at required storage conditions.

- Shipper Box
- Plastic shrink



• **References:**

<https://go.drugbank.com/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4668432/>

<https://www.1mg.com/generics/ceftriaxone-sulbactam-400880>