Manufacturing of Dry Powder of Injection of Cefoperazone Sodium IP 1000 mg

A Dissertation Report submitted

for the partial fulfilment of the Degree of Master of Science

By

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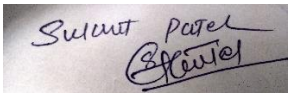
2022-23

(On letterhead of the Department)

CE R T IFICATE

This is to certify that this training report entitled "Manufacturing of dry powder of injection of Cefoperazone Sodium IP 1000 mg" was successfully carried out by Miss Rutva J. Karkar 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	Signature
Dr. Nutan Parakash Vishwakarma	Mr. Sukrut Patel
(Head of the Department)	(Supervisor)

D E C L A R A T I O N

I hereby declare that the work incorporated in the present dissertation report entitled "**Manufacturing of dry powder of injection of Cefoperazone Sodium IP 1000 mg"** 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

Rutva J. Karkar

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ABSTRACT

Sanolet Life care 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)
- Standard Operating Procedure (SOP)

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 Kiranbhai Kanubhai Bunde, Tejaskumar Maganlal Padodara, Hiren Vasantlal Shah and Sachin Ishvarbhai Sardava.

DIFFERENT DEPARTMENTS OF COPMANY ARE:

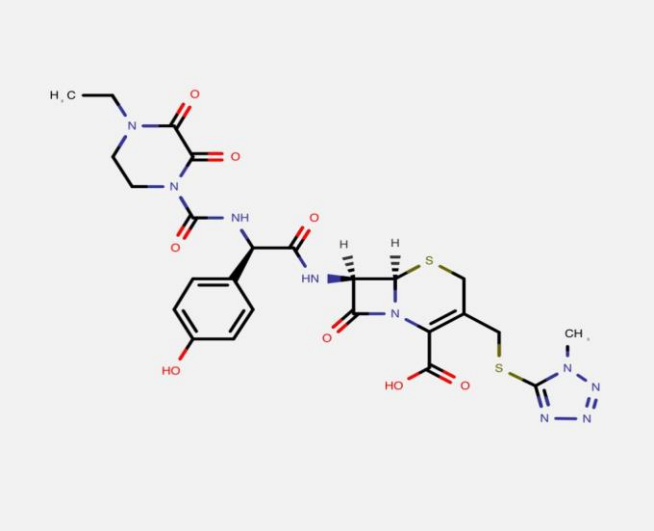
- ❖ Production Department
- ❖ QA Department
- ❖ QC Department
- ❖ Engineering Department

PRODUCT INFORMATION

Cefoperazone is used to treat bacterial infection in the different parts of the body. It works by killing bacteria or preventing their growth.

Cefoperazone Injection is a sterile solution of Cefoperazone Sodium and a suitable osmolality adjusting substance in Water for Injection. It may contain a suitable buffer. It contains the equivalent of not less than 90.0 per cent and not more than 120.0 percent of the labeled amount of cefoperazone.

Structure:



Chemical structure of cefoperazone

Chemical Formula:

$C_{25}H_{27}N_9O_8S_2$

Generic name:

- Cefoperazono
- Cefoperazonum

Pharmacodynamics:

Cefoperazone is a third-generation cephalosporin antibiotic. Cefoperazone exerts its bactericidal effect by inhibiting the bacterial cell wall synthesis.

Mechanism of action:

Like all beta-lactam antibiotics, cefoperazone binds to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the inhibition of the third and last stage of bacterial cell wall synthesis.

Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins.

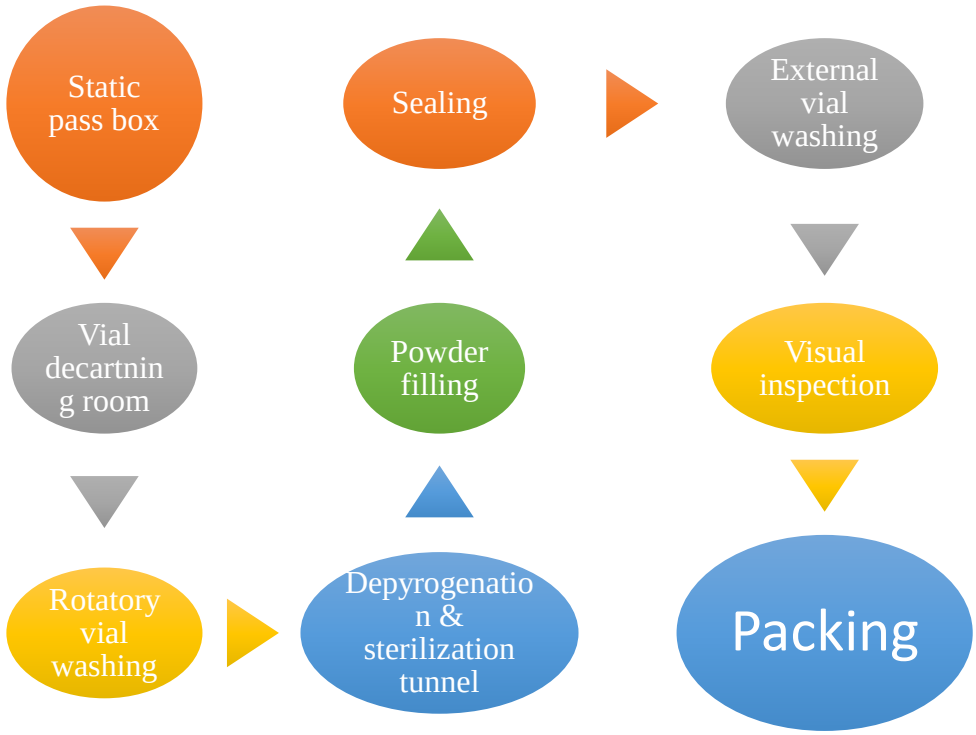
Toxicity:

Symptoms of overdose include blood in the urine, diarrhea, nausea, upper abdominal pain, and vomiting.

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: Cefoperazone sodium (IP) 1000 mg

Generic Name: Cefoperazone Sodium 1000mg for injection

Product Code: SC0015

Batch NO: 22DC124

Effective Date: 29/05/2022

Composition: Each vial contains: Sterile Cefoperazone Sodium IP 1000 gm

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.

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: 10000 vials

Mfg License No: G/28/1843

Superseded version NO:NA

Reason for change: new product

MFR NO: MFR/ SC0015/00

Actual Batch size:10000 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

iii. Control checks

- **a.** Working of AHU system
- **b.** Working of dehumidifier
- **c.** Fogging with disinfectant solution containing 11% H_2SO_4 & 0.01%$AgNO_3$

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: Cefoperazone sodium (IP) 1000 mg

Generic Name: Cefoperazone Sodium 1000mg for injection

BPR NO: BPR/SC0015/00

Batch NO: 22DC124

Effective Date: 29/05/2022

Composition: Each vial contains: Sterile Cefoperazone Sodium IP 1000 gm

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

Effective date: 29/05/2022

Effective Batch NO. NA

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Shelf Life: 24 months.

Standard Batch size: 10000 vials

Mfg License No: G/28/1843

Actual Batch size:10000 vial

Mfg Date: 01/2023

Exp. Date: 12/2024

Fill weight: As per calculation +_2%-

BMR Issued by (QA)

✓

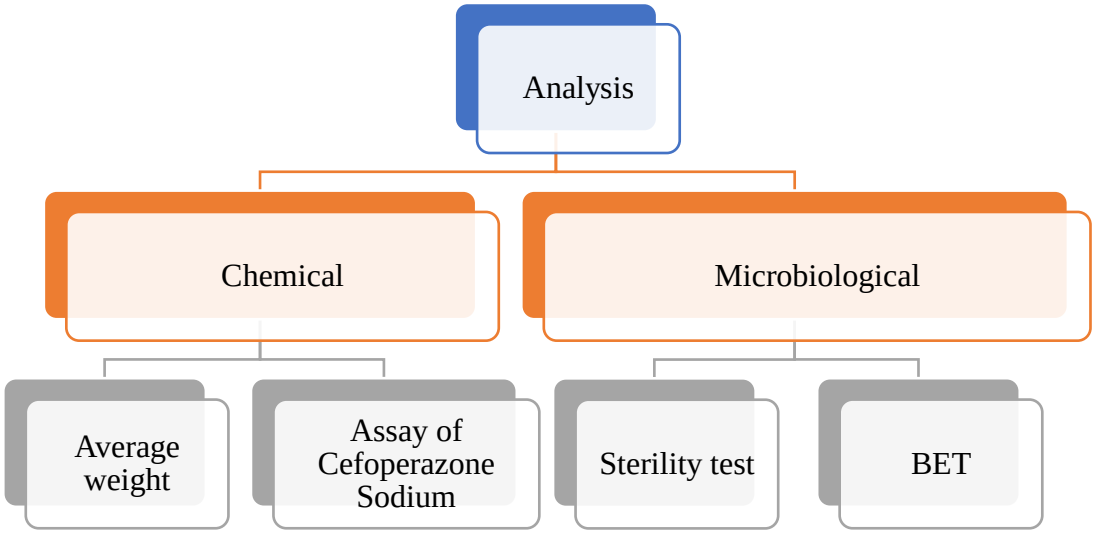
BMR Received by (Production):

✓

Batch Start Date & **Batch Completion date:**

QUALITY CONTROL DEPARTMEMNT

- ✓ 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

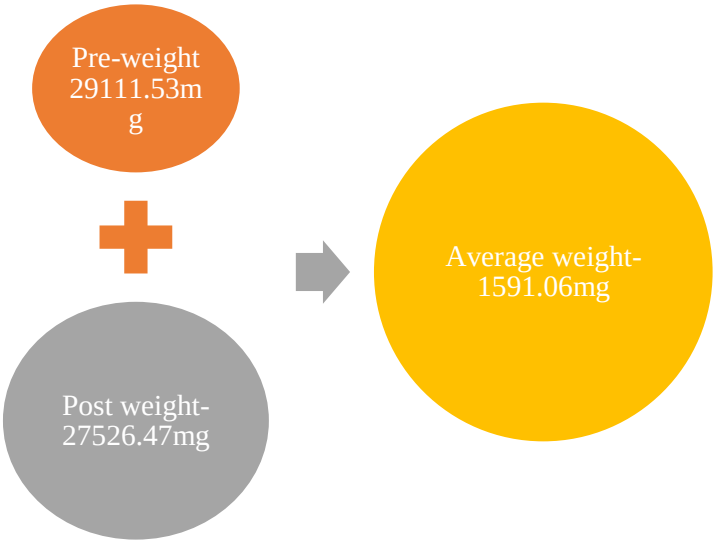
Take a vial & remove the seal

- 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 Cefoperazon Sodium:**

  - ✓ Cefoperazone is used to treat bacterial infection in the different parts of the body. It works by killing bacteria or preventing their growth.
  - ✓ Cefoperazone Injection is a sterile solution of Cefoperazone Sodium and a suitable osmolality adjusting substance in Water for Injection. It may contain a suitable buffer. It contains the equivalent of not less than 90.0 per cent and not more than 120.0 percent of the labeled amount of cefoperazone.

- **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 amebocyte 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 100µL of sample to the tubes.

3. Now add 100µL 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 remains intact the product is considered to contain endotoxin.

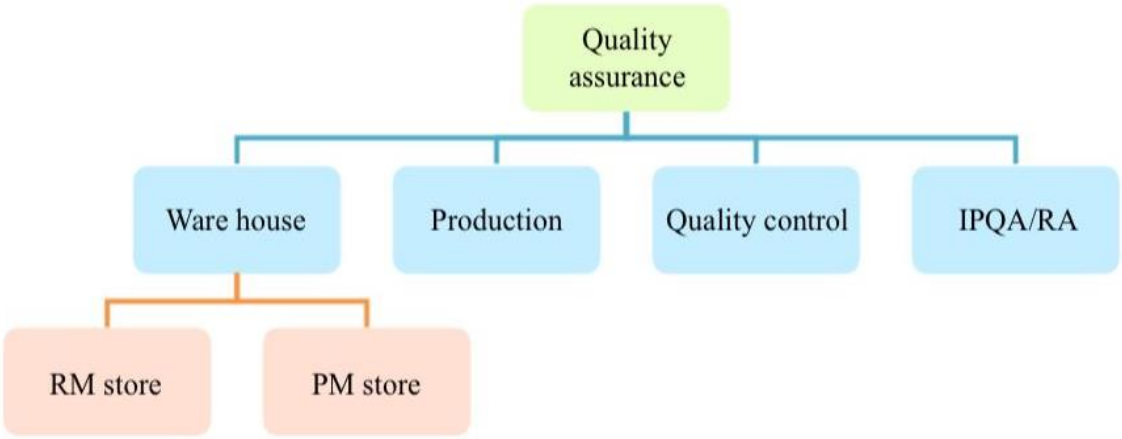
RESULT:

Endotoxin absent

Endotoxin present

QUALITY ASSURANCE DEPARTMENT (QA)w

- 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 DEPARTMNT

- Pharmaceutical engineering focuses on designing, building, and improving manufacturing facilities that produce drugs.
    1. Water System
    2. Air System

Determination of hardness of water

- **Principle**
    - ✓ 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 - 10 min
- 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 condition
- Shipper Box
- Plastic shrink

References

https://go.drugbank.com/

https://www.google.co.in/search?client=safari&channel=iphone_bm&sxsrf=APwXEddnyZShylf-7EM1nOQSFTZgUVdvSA:1681276863686&q=Cefoperazone+Injection&sa=X&ved=2ahUKEwjYkeqxzKP-AhVhSWwGHRc3DwQQ1QJ6BAhSEAE&biw=390&bih=745&dpr=3

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