PROTOCOL CUM REPORT FOR CEPHALOSPORIN FREE ENVIRONMENT

Protocol cum Report for Cephalosporin free Environment

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2.0 PRE- APPROVAL:

Prepared By	**Name**	**Signature**	**Date**
Quality Assurance			
Reviewed By	**Name**	**Signature**	**Date**
Quality Control			
Plant Head			
Approved By	**Name**	**Signature**	**Date**
Head- Quality Assurance			

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3.0 OBJECTIVE:

To provide documentary evidence and prove that the Controlled manufacturing environment area is free from cephalosporin contamination or cephalosporin residue, this protocol supports to assure that the surrounding area is free from cephalosporin contamination.

4.0 SCOPE:

The protocol shall be applicable for validation to determine environment should be free from Cephalosporin residue.

5.0 RESPONSIBILITY:

The validation group comprising of a representative from each of the following departments have been responsible for the overall compliance of this protocol:

Department	Responsibilities
Quality Control / Quality Assurance	• Preparation and Review of protocol and report • To perform swab sampling as per approved protocol • To perform air sampling and testing as per approved protocol
Head – Quality Control	• To review the sampling plan and the analysis report.
Head – Quality Assurance	• To approve the validation protocol and report

6.0 VALIDATION APPROACH:

This validation study is applicable to provide the documentary evidence that during manufacturing of cephalosporin containing products in cephalosporin area, no any residues/traces of cephalosporin found in the surrounding environment, which may be means of exhaust of air through air handling system or man and material movement. The study shall be designed to carry all the risk factors which shall contaminate the surrounding environment. Swab sampling and air sampling of floor/area shall be carried out as per below listed sampling location.

Swab sampling and air sampling shall be carried out as per relevant standard operating procedure. Samples shall be collected and evaluated for cephalosporin residue.

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7.0 Sampling Locations:

S.No.	**Sampling Location:** General Block & Outside of Cephalosporin area	Type
1.	Men entry area in Cephalosporin block	Air
2.	Men entry gate in Cephalosporin block (Floor)	Swab
3.	Material entry area in Cephalosporin block	Air
4.	Raw Material/ Packing Material Receiving are in general block (Floor)	Swab
5.	Exhaust of Auto-coater Cephalosporin block	Air
6.	Service area of cephalosporin block	Air
7.	Men entry general block (Floor)	Swab
8.	Material entry area in General block	Air
9.	Service area of General Block (AHU air inlet side)	Air
10.	Canteen	Air
11.	Security Cabin	Air
12.	Quality Assurance/ Quality Control Lab (Entry)	Air

8.0 Sampling Material and Equipment:

8.1 Active air Sampler

8.2 Swab Stick

8.3 Test Tube

8.4 Petri dishes

9.0 Sampling Procedure:

9.1 Air Sampling Procedure:

9.1.1 Ensure the functioning of air sampler.

9.1.2 Place the relevant mobile phase (to be used for as carrier in chromatography)in a petriplate and put the pteri-dish in air sampler

9.1.3 Put the air sampler at respective location and switch ON the sampler to suck the air.

9.1.4 Allow at least 1000 Litres air to pass on the dish.

9.1.5 Transfer the dish to quality control lab for testing of cephalosporin molecule.

9.2 Swab Sampling Procedure

9.2.1 Take swab sticks moistened with purified water and test tubes containing relevant diluents medium required as per respective standard testing procedure.

9.2.2 Keep the swab sampling plate having area 5 x 5 cm at the sampling point.

9.2.3 Do the swab sampling by rotating the swab in such a way that it should cover 5 X 5 cm areas both horizontally and vertically

9.2.4 After sampling put the swab in respective marked (location) test tubes containing diluents.

9.2.5 Transfer the sample to QC with proper labelling for analysis.

10.0 Testing Procedure:

For testing procedure follow below standard testing procedure. Carry out the test as per below test procedure

Carry out analysis by HPLC as given below:

Standard preparation:

Weigh accurately Cefixime trihydrate WS eq. to 50 mg of Cefixime and transfer in 100.0 ml volumetric flask add 75.0 ml pH 7.0 phosphate buffer to dissolve the standard and make up the volume to 100.0 ml with pH 7.0 phosphate buffer. Pipette out 2.0 ml of resulting solution in 100.0 ml volumetric flask add sufficient pH 7.0 phosphate buffer to produce 100.0 ml. Pipette out 10.0 ml of resulting solution in 100.0 ml volumetric flask add sufficient pH 7.0 phosphate buffer to produce 100.0 ml.

Sample preparation:

Transfer the filter paper in to 25 ml glass beaker having 10 mL of pH 7.0 Phosphate buffer and sonicate for 10 minutes.

Preparation of Mobile phase:

Prepare a suitable filtered and degassed mixture of Tetrabutylammonium hydroxide solutionand acetonitrile (3:1)

Tetrabulylammonium hydroxide solution- Dilute 25 ml of 0.4 M tetrabutylammonium hydroxide solution with water to obtain 1000 ml of solution, and adjust with 1.5 M phosphoric acid to a pH of 6.5.

Monobasic potassium phosphate solution- Dissolve 6.8 g of monobasic potassium phosphate in water to make 500 ml of solution.

Diluent:

pH 7.0 Phosphate Buffer- Dissolve 7.1 g of anhydrous dibasic sodium phosphate in water to make 500 mL of solution. Adjust a volume of this solution with a sufficient volume of Monobasic potassium phosphate solution to a pH of 7.0.

Chromatographic Conditions

• Column : Princeton 100 Sphere C18 (12.5 X 4.6 X 5µ)Packing L1

- Flow Rate :1.0 ml/min.(Adjust flow rate so that the retention time of Cefixime is about 10 min)
- Injection Volume: 10 µL
- Wavelength : 254 nm
- Column Temperature: 40°C

Procedure:

Filter through a 0.2µm pore size nylon membrane and separately injects 10µl of the standard preparation and sample preparation into the chromatography system, record the chromatograph and the measure the response for the major peaks. Calculate the results by comparison.

System Suitability Criteria:

The test is not valid unless the relative standard deviation for replicate injections is not morethan2.0%.Column efficiency is not less than 4000 theoretical plates.
The tailing factor is not less than 0.9 and not more than 2.0.

Sequence of injections: Inject the solution as per the sequence of injection given below:

Sequence of Injection	No. of Injection
Blank	1
Standard Solution	5
Sample Solution	1

11.0 Observations:

All the observations shall be enclosed along with the report of this protocol with Annexure. Prepare the validation summary report and enclose the graph of analysis.

12.0 Acceptance Criteria:

The traces of cephalosporin may be not more than Limit of Detection.

13.0 Revalidation Criteria:

Once in a year.

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14. Summary Report & Conclusion:

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15. Post Approval:

Prepared By	**Name**	**Signature**	**Date**
Quality Assurance			
Reviewed By	**Name**	**Signature**	**Date**
Head- Quality Control			
Plant Head			
Approved By	**Name**	**Signature**	**Date**
Head- Quality Assurance			

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Annexure – I
Activity Log in General Block during validation

S.No.	Product	Batch Number	Activity	Stage

Performed By:
(QC Officer)

Checked By:
(Head – QC)

Approved By:
(Head- QA)

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Annexure – II

Activity Log in Cephalosporin Block during validation

S.No.	Product	Batch Number	Activity	Stage

Performed By:
(QC Officer)

Checked By:
(Head – QC)

Approved By:
(Head- QA)

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Annexure – III

Analytical Report

S.No.	**Sampling Location:** General Block & Outside of Cephalosporin area	Result (ppm)
1.	Men entry area in Cephalosporin block	
2.	Men entry gate in Cephalosporin block (Floor)	
3.	Material entry area in Cephalosporin block	
4.	Raw Material/ Packing Material Receiving area general block (Floor)	
5.	Exhaust of Autocoater Cephalosporin block	
6.	Service area of cephalosporin block	
7.	Men entry general block (Floor)	
8.	Material entry area in General block	
9.	Service area of General Block (AHU air inlet side)	
10.	Canteen	
11.	Security Cabin	
12.	Quality Assurance/ Quality Control Lab (Entry)	