PROTOCOL CUM REPORT FOR POWDER ESCAPE STUDY IN BLENDING AREA

TABLE OF CONTENTS

1.0 DOCUMENT PREPARATION AND APPROVAL:

Preparation and Approval of this Powder escape Study protocol cum report will be joint responsibility of the following functional area. Any modification in this document shall be documented and approved.

Prepared By

Name	Designation	Department	Signature	Date

Reviewed By

Name	Designation	Department	Signature	Date

Approved By

Name	Designation	Department	Signature	Date

2.0 INTRODUCTION:

This guidance describes the importance of implementing appropriate steps for determination of Cross Contamination from blending area to Corridor of production area, as there is no Air lock between the corridor and the blending room.

3.0 OVERVIEW:

3.1. OBJECTIVE:

The objective of this containment-monitoring program to establish documented evidence, based on sound scientific principles that no cross contamination is occurring between the Blending area & corridor of production area.

3.2. SCOPE:

This protocol will address containment monitoring program relating to the validation of Blending area used for Blending of products to prevent cross contamination to corridor of manufacturing area.

3.3. RESPONSIBILITIES:

Depending upon validation requirements, validation team comprising of personnel with required expertise from QA, Production, QC, Engineering (as applicable) shall be involved. The following are some of the major responsibilities of members of the Validation team.

- **QUALITY ASSURANCE DEPARTMENT:**

- Preparation of the validation documents (Protocol & Report).
- To approve the protocol to ensure compliance with regulatory and cGMP rules prior to Execution.
- To check for “completeness and correctness” of the execution of the activities, reports and documentation.
- To co-ordinate the validation activities with appropriate individuals and departments.
- To review and approve the report to give final approval.

➢ **PRODUCTION DEPARTMENT:**

- To execute validation in accordance with the protocol.
- To train the supervisors and operators for the area and equipment cleaning.
- To check the report prior to QA approval.

➢ **QUALITY CONTROL DEPARTMENT:**

- To co-ordinate for the preparation of the documents for the validation activities related to the respective department.
- To co-ordinate the validation in accordance with the protocol and report preparation.
- To co-ordinate the activities with appropriate individuals and departments.
- To review the resolution of the discrepancies, ensure discrepancies are resolved as agreed and review the execution.
- To check for "completeness and correctness" of the execution of the activities, reports and documentation.
- To check the report prior to QA approval.

➢ **ENGINEERING DEPARTMENT:**

- To co-ordinate for the validation performed with respect to Maintenance requirements.

3.4. REVALIDATION:

Revalidation shall be considered in case of:

- Any change in existing facility design of Blending room and corridor of production, which may a source for cross contamination.
- Any major modification in the respective area utilities e.g. (AHU).
- Any Infrastructural changes in the respective Area.

4.0 EXECUTION OF PLANNING:

4.1. Theory:

The acceptable approach for containment monitoring is to carry out air sampling and swab sample analysis for detection and qualification of trace levels of active drug in the adjoining

areas of blending area to production corridor. Trace level in swab and air samples determine by using HPLC (High performance Liquid chromatography).

4.2. Risk Assessment for Cross Contamination:

- All material from the granulation to blending area are being transferred in well closed container.
- Before the transfer of the material in to the bin blender, person involved in this area wear the secondary gowning.
- During the process, which does not take much time, involved person, does not go outside the room until process is completed so there is no chance of any contamination.
- After the completion of final blending process material transfer in to the double poly bag and tied with nylon tie and put it into the container's and close with its lid and transfer to the blend quarantine area.
- After the completion of the blending and transfer procedure , de- gowning is done and put it in to the used garments means secondary gown used once in process are not reused. For new process, use fresh, gown each time prior to execution.
- Proper air changes per hour in area and different pressure maintained between the blend area and passage.
- Passage adjacent to blend area is the classified and maintained properly.
- Blending activity is performed in closed condition /equipments.
- In-process container is used with lid after material take in and takeout.
- An electromagnetic lock is installed in blending area door so that door is always be magnetically locked apart from the door closure. Electromagnetic lock act as secondary control to keep the door close always.

4.3. PRE-VALIDATION STUDY (VALIDATION APPROACH):

- Standard cleaning procedure for cleaning and sanitization of area.
- Validated appropriate sampling and testing methodology for determination of residues.
- Selection of worst-case location for sampling.

4.4. VALIDATION RUNS:

The successful run the products in blending area and sampling will be performed at worst-case selected location of corridor area to determine the product residues contamination.

- Sampling and testing
- Collection of data
- Reporting of the results
- Evaluation of the results

5.0 VALIDATION METHODOLOGY:

Determine the worst area location of corridor area where more probability of cross contamination with drug particles from blending area. .

- Clean the blending area & corridor area as per standard cleaning procedure.
- Perform the blending of product in blending area.
- Perform the swab / air sampling from the selected location and the sample send to QC/ external lab for analysis.

5.1. Approach for Study:

- Approach for conducting the study for monitoring of residue shall be based on the high toxicity worst case of Molecule (API).
- Swab and air sampling shall be performed during operation and after completion of operation in blending area.

5.2. Sampling Method:

Two sampling methods are applicable to determine the contamination level in production corridor.

- Direct surface sampling (Swab sampling)
- Air sampling.

5.2.1. Direct Surface Sampling (Swab Analysis):

This method is utilized to directly evaluate the reachable product traces on the surface of corridor floor. The 'hard to clean areas' shall be directly sampled. The swabs used for sampling should be physically compatible with the drug residue, in that they should not interfere with the drug residue, should not cause degradation and should allow extraction of the compound for analysis.

A. Preparation of swabbing solution:

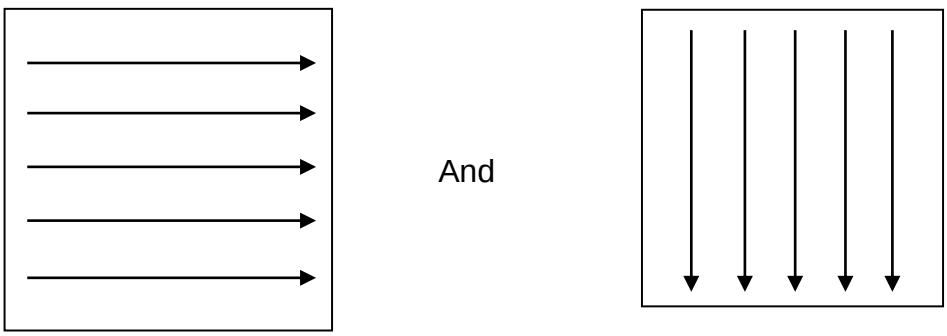
Solvent Mixture: 60 Volumes of acetonitrile and 40 volumes of water.

- Sampling shall be done using swab stick
- During sampling the person shall perform sampling shall wear gloves.
- Take 4 ml of Acetonitrile: water (60:40) solution in a test tube
- Dip the Swab in Acetonitrile: water (60:40) solution to moisten the swab.

B. Swab Sampling Technique:

Sampling patterns: Wipe the defined area in both the directions as shown in the figure. Apply only one time. Do not rub the surface in to & fro movement. Refer the typical diagram to collect the sample-using swab. Swab approximate 25 cm² surface area of equipment as per below diagram.

(Direction of swabbing strokes)



- Required numbers of swabs shall be applied in this manner at defined locations as mentioned in 5.3

- Swab the specified area and store in a test tube containing 4 ml Acetonitrile and water (60:40). Stopper the test tube. Put the identification tag on the sampled test tube.
- Submit the swab sample to QC for analysis.
- Analysis the sample by using analytical testing method for determination of traces of residue.
- Repeat the procedure for each sampling point location.

Acceptance Criteria:

The amount of residue detected in sampling area should be less than 10 ppm

5.2.2. Air Sampling Study:

- The suspended particles are collected using air sampler A extractive sampling method, whereby a small stream of representative sample is drawn to determine contaminant concentration.
- Take the air sampler and sampling accessories, perforated plate, whatman filter paper (size 90 mm) , Petri plate , diluents etc. to the area where sampling is to be conducted.
- Moist the whatman filter paper in diluents and keep it in a 90 mm Petri plate.
- Remove the aspirating head of air sampler, carefully insert Petri plate with filter paper and affix the plate in grip. Carefully replace the aspirating head.
- Position the air sampler on floor on location.
- Start the air sampler as per SOP “operation and procedure for environmental monitoring by active air sampling method” SOP current revision)
- Press the start button to start air sampling and sample the 1000 Ltr Air.
- Sample the 1000-litre air.
- After sampling of 1000-litre air sampler will stop automatically.
- Remove the Petri plate and labeled the Petri plate with sampling point name
- Submit the sample to QC for analysis. Analyze the sample by using the analytical testing method for determination of traces of drug residue.
- Repeat the procedure for each sampling point.

Acceptance Criteria:

The amount of residue detected in sampling area should be less than 10 ppm

5.3. Sampling location

5.3.1. Sampling location For Swab sampling and air sampling:

Area	Location	No. of Sample	Sampling point name
Corridor	Door outside	01	B1
	Floor near to the Door Opening to the blending area	01	B2
	Granulation I Material air lock	01	B3
	Near to granulation II Material Air lock door	01	B4
	Near to bulk quarantine door	01	B5
	Near return riser of corridor	01	B6

6.0 OBSERVATION & RESULTS :

6.1. Pre-validation Study Observation:

S.No.	Sop Title	SOP No.	Effective date
1.	Operation and procedure for environmental monitoring by active air sampling method"		
2.	Swab sampling		
3.	General procedure for cleaning of production area		
Checked By: QA (Sign & Date)			

6.2. Sampling details:

S.No.	Sampling location	Sampling method	Sampling Date	Sampling done By	Sampling method	Sampling Date	Sampling done By
1.	Door outside	Swab sampling			Air sampling		
2.	Floor near to the Door Opening to the blending area	Swab sampling			Air sampling		
3.	Granulation I Material airlock	Swab sampling			Air sampling		
4.	Near to granulation II Material Air lock door	Swab sampling			Air sampling		
5.	Near to bulk quarantine door	Swab sampling			Air sampling		
6.	Near return riser of corridor	Swab sampling			Air sampling		

6.3. Drug Residue Analysis Report:

6.3.1. Results of Swab Sampling:

S.No.	Sampling location	Sampling code	Sampling method	Results
1.	Door outside	B1	Swab sampling	
2.	Floor near to the Door Opening to the blending area	B2	Swab sampling	
3.	Granulation I Material air lock	B3	Swab sampling	
4.	Near to granulation II Material Air lock door	B4	Swab sampling	
5.	Near to bulk quarantine door	B5	Swab sampling	
6.	Near return riser Of corridor	B6	Swab sampling	

6.3.2.Results of Air Sampling

S.No.	Sampling location	Sampling code	Sampling method	Results
1.	Door outside	B1	Air Sampling	
2.	Floor near to the Door Opening to the blending area	B2	Air Sampling	
3.	Granulation I Material air lock	B3	Air Sampling	
4.	Near to granulation II Material Air lock door	B4	Air Sampling	
5.	Near to bulk quarantine door	B5	Air Sampling	
6.	Near return riser Of corridor	B6	Air Sampling	

7.0 DEVIATIONS:

If any deviation is observed from the approved protocol during execution the same shall be investigated and documented as defined in the SOP-Current Version for deviation.

If appropriate, corrective and/or preventive actions shall be taken to correct the problem.

Any deviation(s) from the approved protocol: Yes ☐ No ☐

If Yes, Elaborate:

8.0 SUMMARY:

CONCLUSION:

9.0 ABBREVIATIONS:

Abbreviation	Expansion
MACO	Maximum allowable carry over
Ltr.	Litre.

10.0 DOCUMENT COMPILATION AND POST APPROVAL:

Compiled By

Name	Designation	Department	Signature	Date

Reviewed By

Name	Designation	Department	Signature	Date

Approved By

Name	Designation	Department	Signature	Date