PERFORMANCE QUALIFICATION PROTOCOL FOR MANUFACTURING & FILLING PROCESS OF METERED DOSE INHALERS (HFA)

1.0 OBJECTIVE OF VALIDATION:

To ensure that the suspension/solution homogeneity of Suspension/ Performance of Crimping Machine and Performance of Diaphragm Filler for Metered Dose Inhaler is maintained throughout the batch filling by estimation of content of active ingredient(s) per container and to estimate water content per container.

2.0 SCOPE OF VALIDATION:

Validation of homogeneity of Suspension / Performance of Crimping Machine and Performance of Diaphragm Filler of Metered Dose Inhaler.

3.0 JUSTIFICATION FOR SELECTION OF ITEM/EQUIPMENT/PROCESS/PRODUCT/ SYSTEM:

Justification for the selection should be recorded in the validation report.

4.0 SITE OF STUDY:

Aerosol Department:

Name of the Location should be recorded in the validation report.

5.0 RESPONSIBILITY:

Representatives from:

Production

Engineering

Safety

Quality Control

Quality Assurance

Name of the individuals should be recorded in the validation report.

6.0 DESCRIPTION OF EQUIPMENTS TO BE USED:

Equipment Name, Code No., Qualification date shall be recorded in the validation Report.

7.0 STANDARD OPERATING PROCEDURES/BMR/BPR/SPECIFICATIONS:

7.1 Batch manufacturing record for the product should be recorded in the validation report.

7.2 SOP for Operation of Mixing Vessel: SOP No.: (to be recorded in the validation report).

7.3 SOP for the Operation of Diaphragm Filler. SOP No.: (to be recorded in the validation report).

7.4 SOP for the operation of Crimping machine. SOP No.: (to be recorded in the validation report).

7.5 SOP for the weighing Balance. SOP No.: (to be recorded in the validation report).

7.6 Batch Manufacturing record. Manufacturing Code no and version no, to be recorded in the

validation report.

7.7 Specifications to be followed. Reference QC specification No. to be recorded in the validation report

8.0 CONTROLS:

8.1 **Calibration:** Calibration and Qualification details for process equipments shall be recorded in the validation report.

8.2 **Training:** Training status of the personnel involved in the validation exercise should be recorded in the validation report.

8.3 Precautions:

All safety precautions mentioned in individual SOPs of the equipments must be ensured during study.

8.4 Initial Checks:

8.4.1 Air pressure of Diaphragm pump/Lobe pump should be as per BMR and should be recorded in the validation report.

8.4.2 Air pressure of Diaphragm filler/Product filler should be as per BMR and should be recorded in the validation report.

8.4.3 Air pressure of Crimping machine should be as per BMR and should be recorded in the validation report.

8.5 VALIDATION PROCEDURE:

8.5.1 VALIDATION PROCEDURE FOR HOMOGENITY OF SUSPENSION:

8.5.1.1 Manufacture the batch as per the BMR

8.5.1.2 Calibrate balance as per SOP.

8.5.1.3 Set and operate product filler/ diaphragm filler as per SOP to deliver suspension (Quantity of Suspension as per BMR)

8.5.1.4 Send samples to QC for analysis from filling line as follows:

S.No.	Sample No.	Test to be performed
1.	Initial 3 successive containers	Estimation of Active Content per can
2.	2 successive containers after every 1/5th population of batch (1st , 2nd , 3rd and 4th intervals) i.e. 4x2= 8 containers	Estimation of Active Content per can
3.	5th interval (Final Stage) 3 successive containers	Estimation of Active content per can

S.No.	Sample No.	Test to be performed
4.	1 container each at Initial, middle and End stage of filling	Estimation of Water Content.
	Total	**17 containers**

8.5.2 Acceptance Criteria:

8.5.2.1 Content of Active ingredients and Water content upon testing as per quality control specification should be within the limits specified in the specification (Limits to be recorded in the report).

8.5.3 VALIDATION PROCEDURE FOR CRIMPING MACHINE:

8.5.3.1 Set and operate the product filler as per SOP.

8.5.3.2 Set and operate the Crimping machine as per SOP.

8.5.3.3 Calibrate the weighing machine as per SOP

8.5.3.4 Check the crimp height, crimp diameter and Total height of 50 containers as:

S.No.	Stage	Quantity of Sample
1.	Initial	17 containers
2.	Middle	16 containers
3.	End	17 containers

8.5.3.5 Check the fill weight of propellent-12 sequentially at the Initial, Middle and Final stage of Batch filling for 50 containers. Initially check the weight of crimped container with only suspension. Tare the weight, then reweigh the containers after filling with propellant. This is the weight of the propellant.

8.5.4 Acceptance Criteria:

8.5.4.1 The crimp height of the container should be within limit. (Limit specified in the BMR)

8.5.4.2 The Crimp Diameter of Container should be within limit. (Limit specified in the BMR)

8.5.4.3 The total height of container should be within limit. (Limit specified in the BMR)

8.5.4.4 The fill weight of Propellant should be within limit. (Limit specified in the BMR)

8.5.5 VALIDATION PROCEDURE FOR DIAPHRAGM FILLER:

8.5.5.1 Set the diaphragm filler as per SOP. (SOP no. to be mentioned in the validation report)

8.5.5.2 Throughout the batch filling operation collect 50 empty containers along with valves as :

S.No.	Stage	Quantity of Sample
1.	Initial	17 containers
2.	Middle	16 containers
3.	End	17 containers

8.5.5.3 Weigh the containers and record the same in the report (B)

8.5.5.4 Fill the containers with suspension and Crimp it as per the instructions given in the Batch Manufacturing Record.

8.5.5.5 Weigh the containers on the same balance and record it in the report (A)

8.5.5.5 Calculate the net weight of Suspension [C=A-B] and record the same in the validation report.

8.5.6 Acceptance Criteria

8.5.6.1 The fill weight of Suspension should be within the limit as specified in BMR.

9.0 SAMPLING AND TESTING PLAN:

Stage	Sampling Interval	Sample Quantity	Test
Homogeneity of suspension	Initial	3 filled cans	Content per can
	After _____ cans	2 filled cans	
	After _____ cans	2 filled cans	
	After _____ cans	2 filled cans	
	After _____ cans	2 filled cans	
	Final	3 filled cans	
Homogeneity of Suspension	Initial	1 filled can	Water Content
	Middle	1 filled can	
	Final	1 filled can	
Before Crimping of Aluminium containers	Initial	17 empty containers	Weight of Empty container and valve
	Middle	16 empty containers	
	End	17 empty containers	
After Crimping of Aluminium containers	Initial	17 empty containers	Crimp height, crimp diameter, Total height and weight loss after crimping
	Middle	16 empty containers	
	End	17 empty containers	
Filling of Suspension	Initial	17 empty containers	Fill weight of suspension
	Middle	16 empty containers	
	End	17 empty containers	

9.0 FREQUENCY:

Validation: On first three production batches.
Re-validation (Periodic): One batch every year.
Re-validation (After Major Change): Three consecutive batches.

10.0 RISK MANAGEMENT STUDIES:

Risk Management studies performed related to the activity should be recorded in the validation report.

11.0 RESULTS / OBSERVATIONS:

Record all the observations and results in the validation report.

12.0 SUMMARY OF VALIDATION ACTIVITY:

Summarize the findings of the validation study to draw an inference.

13.0 RECOMMENDATIONS:

Record the recommendations based on the interpretation of the results in the validation report.

14.0 TEAM APPROVAL:

The personnel who have performed the validation study, supervised the validation, completed the records, performed the testing of the product should approve the validation report.

15.0 REVIEW AND APPROVAL AND NOTIFICATION:

The validation report should be reviewed and finally approved by unit quality assurance Head and notified by unit head.

16.0 ATTACHMENTS:

All the attachments should be listed in the validation report

17.0 ABBREVIATION:

If any; state the full form of used short form in the validation report.