VALIDATION PROTOCOL FOR MIXING AND LUBRICATION OF GRANULES IN FLUID BED EQUIPMENT

1. Objective:

To validate the process of Mixing and lubrication of granules so as to establish that the content uniformity of active ingredient is achieved, physical parameters like Tapped Density, Loss on Drying and Particle Size distribution are within the specified ranges.

2. Scope:

Applicable to Mixing and Lubrication of granules in Fluid Bed Equipment.

3. Justification:

Justification for selection of equipment, process and product to be mentioned in validation report.

4. Site of the Study:

Manufacturing Department.
Location: *To be recorded in Validation Report*

5. Responsibility:

Production	:
Engineering	:
Quality Control	:
Quality Assurance	:

(Individuals to be named in report)

6. Description of the Equipment to be used:

FLUID BED EQUIPMENT λ
CODE No. : *To be recorded in Validation Report*
CAPACITY : *To be recorded in Validation Report*

λ Date of Equipment Qualification to be recorded in the Report.

Sampling thief and Bulk sampler Code No. to be recorded in the Validation report.

7. Standard Operating Procedure (SOP) & Batch Manufacturing Record (BMR) to be followed:

i) SOP for operating Fluid Bed Equipment: To be recorded in Validation Report
ii) SOP for sampling with Sampling thief : To be recorded in Validation Report
iii) SOP for checking Loss on Drying (LOD): To be recorded in Validation Report
iv) SOP for Pour Bulk and Tapped density: To be recorded in Validation Report
v) SOP for water content (if applicable) : To be recorded in Validation Report
vi) SOP for Particle Size Distribution : To be recorded in Validation Report
vii) Batch Manufacturing Record: Formulation code and Manufacturing Code No. To be recorded in Validation Report.

8. Control:

8.1 Requirements:

I. Raw Material except A PI to be used should meet the requirement of Specification (Name of the raw Material, Quantity required, and Analytical Reference number should be recorded in Validation report).

ii. Validated Analytical Methods for estimation of active ingredient (Reference Analytical Validation protocol number / Reference Specification No. to be recorded in the report).

iii. Analytical Reference number for validation Technical Information Sheet

8.2 Calibration

Calibration of equipment and testing Apparatus *Calibration details to be recorded in the report.*

8.3 Training

Availability of training record of personnel involved in the validation exercise should be recorded in the Report.

8.4 Precautions

Safety aspects while operation of equipment and process must be ensured.

9. Validation Procedure:

***Mixing:**

i) Charge the sifted lubricants in the Fluid Bed equipment as per the sequence given in the Batch Manufacturing Record.

ii) Set the operating parameters as per BMR.

iii) Operate the FBE as per SOP.

iv) Sample approximately one to three unit doses in triplicate from 10 positions at various depths as shown in the sampling plan on Page 6 with the help of a sampling thief at mixing time specified in the BMR. Send these samples to Quality Control for analysis of content of Active Ingredient.

v) Check the appearance of Mix Blend after completion of mixing operation and record the same in report.

Lubrication:

i) Load the ingredients in the Fluid Bed equipment as per the sequence given in the Batch Manufacturing Record (BMR).

ii) Operate the Fluid Bed equipment as per SOP.

iii) Sample one to three unit doses in triplicate from 10 positions at various depths as shown in the sampling plan on Page 6 with the help of a sampling thief at Standard lubrication time as specified in the BMR. Send these samples to Quality Control for analysis of blend uniformity.

iv) Sample approximately 40 gm from top, middle, bottom position of the Fluid Bed Equipment at standard lubrication time. Make a composite sample of 120 gm.

100 gm for Particle size distribution
10 gm for pour bulk density and Tapped density.
2 to 3 gm for LOD
5 g for water content (QC analysis) (If applicable)

v) The results of content should be reported as Individual test results.

vi) % RSD should be calculated for the results of content. (To be done by Quality Control)

vii) Check the appearance of lubricated granules visually after lubrication operation and record the observations in the report.

10. Acceptance criteria:

The Optimal time decided should conform to the following:

i) Uniform distribution of the lubricated mix, when checked visually.

ii) Content of Active Ingredient upon testing at standard lubrication time as per Quality Control Specification should be within the limits.

iii) The Relative Standard Deviation (RSD) of blend uniformity at standard lubrication time (as given in BMR) should be less than 5.

iv) Results of physical parameters of the lubricated granules sampled at the standard time (as given in BMR).

11. Non-Compliance:

Details of deviations (including justification of acceptance if any) done to successfully carry out the validation exercise and any OOS results obtained should be recorded.

12. Type of Validation:

Concurrent validation / Re-validation

13. Frequency:

1) Concurrent validation: Three consecutive Successful validation exercises.

2) Re-validation (Periodic): One validation exercise should not exceed 5 years.

3) Revalidation (after major change): Three consecutive Successful validation exercises.

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14. Results / Observations:
Record the observations during the validation and results obtained from Quality Control Department in the Validation Report.

15. Summary of findings of validation (inference):
Summarize the findings of the Validation to draw an inference.

16. Recommendation (Including requirements of any additional documentation):
Record the recommendations based on the interpretation of the results of the Validation Report

17. Team approval:
The individuals who have performed the Validation, supervised the validation, completed the records, performed the testing of the product should approve the validation report.

18. Review (inclusive of follow up action, if any):
Unit Quality Assurance and Unit Head should review the Validation Report. The report should include any follow up action if required.

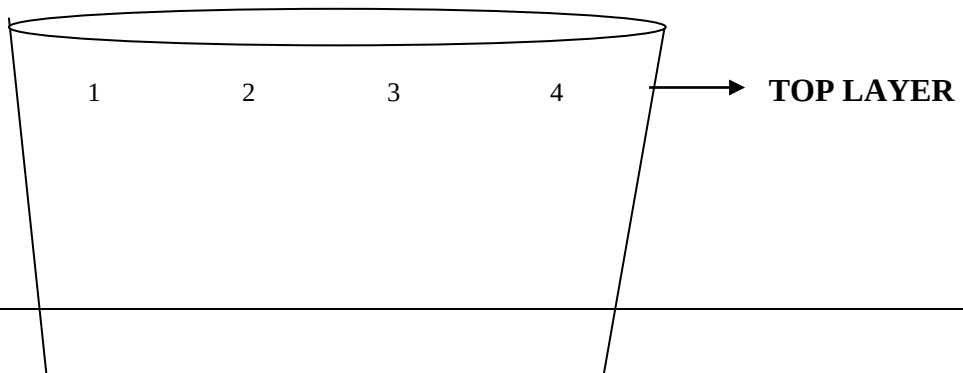
19. Approved by:
Unit Quality Assurance and Unit Head should finally approve validation Report.

20. Attachments:
Annexure (if any) attached to the Validation Report should be recorded.

21. Abbreviations:

Lt.	: Litres
No.	: Number
A.R.No.	: Analytical Reference Number
RSD	: Relative Standard Deviation
OOS	: Out of Specification
mg.	: Milligrams
QC	: Quality Control
LOD	: Loss on drying

SAMPLING POSITIONS FOR MIXING & LUBRICATION VALIDATION



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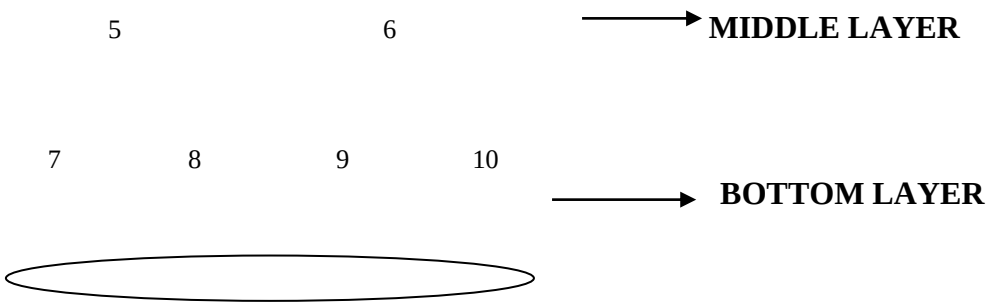

SAMPLING POSITIONS:

POSITION 1,2 ,3& 4: 0.5 Feet below from the top layer towards the periphery
POSITION 5 & 6: Half the depth of the total bed height
POSITION 7, 8, 9 & 10: 0.5 feet above from the bottom layer at the centre

Note: Samples to be drawn from Top, Middle and Bottom positions for Particle Size distribution.
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