VALIDATION PROTOCOL FOR COMPRESSION OF GRANULES

1. Objective:

To validate the Compression of lubricated granules in Compression machine by:

1.1 Ensuring uniformity of tablet quality throughout the batch.

1.2 Ensuring that the machine produces tablets, which are within the range of predetermined standards when the machine is set at speeds above and below the standard speed. (Machine is set above/below the standard speed for challenge purpose).

1.3 Ensuring that the tablet parameters are within the limits when the hardness is set at upper and lower sides of the standard specification and machine is run at standard speed. (Hardness set at upper/lower sides of standard specification for challenge purpose).

1.4 Ensuring that Assay, Dissolution & Content uniformity (if applicable) are within the limits at initial, middle & end of the optimum compression run.

2. Scope:

Applicable to Compression of lubricated granules on Compression Machine.

3. Principle:

Compaction of material between adjustable cavities through external pressure to get a prescribed shape and size of the tablet.

4. Site of the Study:

Hormone Department.

5. Responsibility:

Production :

Engineering :

Quality Control :

Quality Assurance :

(Individuals to be named in the report)

6. Description of the Equipment to be used:

Equipment: COMPRESSION MACHINE. λ

Type and Code No.: To be recorded in report.

λ Date of equipment Qualification done to be recorded in report.

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

i) SOP for operating Compression machine: To be recorded in the report.

ii) SOP for testing Friability: To be recorded in the report.

iii) SOP for determination of Disintegration Time: To be recorded in the report.

iv) SOP for determination of Thickness: To be recorded in the report

v) SOP for determination of Hardness: To be recorded in the report

vi) Batch Manufacturing Record: Manufacturing & Formulation Code number to be recorded in Report.

8. Controls:

8.1 Calibration:

Calibration details of equipments to be recorded in the report.

8.2 Training:

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

8.3 Precautions:

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

8.4 Requirement:

Analytical method for estimation of Active Ingredient/s: (Reference Analytical validation protocol No./Reference Specification No. to be recorded in the report.)

9. Validation Procedure:

A. Operate the machine as per SOP at standard speed.

i) Perform the following tests on tablets collected in the bowl on one or both sides of the compression machine.

i. Physical appearance of tablets
ii. Embossing/Debossing
iii. Breakline/Scoring on tablets
iv. Capping of tablets
v. Sticking/Picking on tablets
vi. Lamination on tablets
vii. Granules Flow
viii. Mottling
ix. Chipping of tablets
x. Rat hole effect in Hopper (visual checking)
xi. Segregation of granules in feed frame / Force feeder (Visual checking)
xii. Vibrations of machine
xiii. Group weight of 20 tablets

Frequency: Initial and every 30 minutes.

ii) Collect "Y" number of tablets for 1 round of compression cycle run from one or both sides of the compression machine incase of double rotary machine and perform the following tests.

a) Individual weight variation on "X" number of tablets.
b) Thickness of 10 tablets.
c) Hardness of 10 tablets.
d) Friability of “XX” tablets (Where “XX” is no. of tablet as per BMR)
e) Disintegration test on six tablets (Three tablets each from both sides for double rotatory machine) Dispersion time on 2 tablets (if applicable).

Frequency: Initial, after every 2 hour and at the end of compression run.

Note: If optimum compression run is less than or equal to 2 hours at the standard speed all the above mentioned tests to be performed at initial, middle and end of interval of total run.

(Note: If challenge studies not performed due to smaller batch size then justification to be attached with the validation report.

(Note**:** Where "Y" = number of tablets depends upon number of stations(X) + number of tablets for Disintegration test and Friability.)

(Note: Where X= Number of tablets to be collected depending on Number of stations)

For 26/27 stations machine, X=30 tablets
For 36 stations machine, X=40 tablets
For 45 stations machine, X=50 tablets

B. Following studies to be done at the start of the last IPC or towards the end of the batch.

i. Set the machine speed at lower & higher speed.

Set the machine speed,

At standard speed + 200 Tablets Per Minutes (TPM) for 26/27 station compression run

At standard speed - 200 Tablets Per Minutes (TPM) for 26/27 station compression run

At standard speed + 400 Tablets Per Minutes (TPM) for 36/45 station compression run

At standard speed – 400 Tablets Per Minutes (TPM) for 36/45 station compression run

At standard speed + 100 Tablets Per Minutes (TPM) for double layer tablets

At standard speed – 100 Tablets Per Minutes (TPM) for double layer tablets

Collect "Y" number of tablets for 1 round of compression cycle run from one or both sides of the compression machine incase of double rotary machine and perform the following tests.

a) Physical appearance of tablets

b) Embossing/Debossing
c) Breakline/Scoring on tablets
d) Chipping of tablets
e) Sticking/Picking on tablets
f) Lamination
g) Mottling
h) Capping of tablets
i) Rat hole effect in Hopper
j) Segregation of granules in feed frame/forced feeder (Visual checking)
k) Vibrations of machine
l) Individual weight variation on "X" number of tablets
m) Thickness of 10 tablets
n) Hardness of 10 tablets
o) Disintegration test on six tablets (Three tablets each from both sides for double rotatory machine) Dispersion time on 2 tablets (if applicable).
p) Friability of “XX” tablets. (Where “XX” is no. of tablet as per BMR)

(Note**:** Where "Y" = number of tablets depends upon number of stations X + number of tablets for Disintegration time, Friability).

For 26/27 stations machine, X=30 tablets
For 36 stations machine, X=40 tablets
For 45 stations machine, X=50 tablets

ii) Following tests to be done at lower & higher Hardness range.

1. Operate the machine as per SOP at Standard speed.
2. Collect "Y" number of tablets from one or both sides by setting the compression machine at upper and lower limits of hardness and perform the following tests.

a) Physical appearance of tablets
b) Embossing/Debossing
c) Breakline/Scoring on tablets
d) Chipping of tablets
e) Sticking/Picking on tablets
f) Lamination
g) Mottling
h) Capping of tablets
i) Rat hole effect in Hopper
j) Segregation of granules in feed frame (Visual checking)
k) Vibrations of machine

l) Individual weight variation on "X" number of tablets

m) Thickness of 10 tablets

n) Hardness of 10 tablets

o) Disintegration test on six tablets (Three tablets each from both sides for double rotatory machine) Dispersion time on 2 tablets (if applicable).

p) Friability of “XX” tablets. (Where “XX” is no. of tablet as per BMR)

(**Note:** Where "Y" = number of tablets depends upon number of stations X+number of tablets for Disintegration time, Friability.)

For 26/27 stations machine, X=30 tablets

For 36 stations machine, X=40 tablets

For 45 stations machine, X=50 tablets

Note: Tablets compressed for above validation i.e. running at upper and lower limits of hardness to be kept as "Rejects".

If challenge studies not performed due to smaller batch size then justification to be attached with the validation report.

10. Acceptance criteria:

The observations made during the validation study should meet the acceptance criteria given under observation and results in the Validation report and the Quality Control Specifications.

11. Details of Deviations:

Details of deviations (including justification of acceptance) done to successfully carry out the validation exercise and any OOS results obtained should be checked. (Attach the details in the Validation report).

12. Type of Validation:

Concurrent validation/ Re-validation

13. Frequency:

i. Concurrent validation : Three successful validation exercises.

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

iii. Revalidation (any major change): Three successful validation Exercises.

14. Results/Observations:

Record the observations during the study and results obtained from Quality Control Department in the Validation Report.

15. Summary of validation activity:

Summarize the findings of the Validation Study to draw an inference.

16. Recommendation:

Record the recommendations based on the interpretation of the results of the Validation Report

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

18. Review:
The Validation Report should be reviewed by Unit Quality Assurance and Unit Head. The report should include any follow up action if required.

19. Approved by:
Validation Report should be finally approved by Unit Quality Assurance and Unit Head.

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

21. Abbreviations:

OOS	: Out of specification
IPC	: Intermediate Product Container
BMR	: Batch Manufacturing Record
T.I Sheet	: Technical Information Sheet
SOP	: Standard Operating Procedure
A.R No.	: Analytical Reference Number