VALIDATION PROTOCOL FOR LUBRICATION OF POWDER/GRANULES IN IPC BLENDER/OCTAGONAL BLENDER

1.0 Objective:

To demonstrate that the critical operations involved in the lubrication process of powder/ granules in the IPC/Octagonal blender are capable of consistently producing batches which meets the limits of acceptance criteria.

2.0 Scope:

Applicable for lubrication of powder/ granules in the IPC/ Octagonal Blender.

3.0 Justification for selection of Item/Equipment/Process/Product/System:

(To be recorded in the validation report)

4.0 Site of Validation:

Department: (To be recorded in the validation report)
Location: (To be recorded in the validation report)

5.0 Validation team:

Production
Engineering
Quality Control
Quality Assurance
(Individuals to be named in the validation report)

6.0 Manufacturing process:

The current master batch manufacturing record (MBMR) will be used to manufacture the batches. Instructions are specified in the MBMR. Product name, manufacturing code, version No., batch Size/ nos., equipment name, code No. and date of validation to be recorded in validation report.

7.0 Standard operating procedure:

7.1 SOP for operation of IPC blender/ octagonal blender.
SOP No.:(To be recorded in the validation report)

7.2 SOP for sampling with sampling thief
SOP No.:(To be recorded in the validation report)

7.3 SOP for determination of Loss on Drying
SOP No.:(To be recorded in the validation report)

7.4 SOP for determination of Bulk Density/ Tapped Density
SOP No.:(To be recorded in the validation report)

7.5 SOP for determination of particle size distribution.
SOP No.:(To be recorded in the validation report)

7.6 SOP for weighing balance.
SOP No.:(To be recorded in the validation report)

7.7 All the critical operations, process parameters specified in the batch manufacturing record will be monitored and results will be recorded in the batch record.

8.0 Controls:

8.1 Calibration/ Qualification:
Calibrated/ qualified testing apparatus/ equipments shall be used
(Details shall be recorded in the validation report.)

8.2 Precautions:
Safety aspects during operation of equipment and process shall be ensured.

8.3 Training:
Trained personnel shall perform the validation
(Details of training shall be recorded in the validation report)

9.0 Number of batches to be monitored:
Number of batches to be validated to be recorded in the validation report.

10.0 Validated analytical methods/ specifications:
Validated analytical methods of intermediates/ finished products for estimation of active ingredient (Reference analytical method validation protocol number/ specification number to be recorded in the validation report.)

11.0 Active Pharmaceutical ingredient :
Active pharmaceutical ingredient: Name of API to be recorded in the validation report

Pharmaceutical grade (if applicable): Pharmaceutical grade to be recorded in the validation report.

Manufacturer/ item code : Manufacturer name and item code shall be recorded in the validation report

Tests*	Reference A.R. No	Source Data	Acceptance Criteria
Assay	Record in report	Quality control testing	As per API specification
Water content	Record in report	Quality control testing	As per API specification
Loss on drying (LOD)	Record in report	Quality control testing	As per API specification

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Tests*	Reference A.R. No	Source Data	Acceptance Criteria
Bulk density	Record in report	Quality control testing	As per API specification
Tapped density	Record in report	Quality control testing	As per API specification
Particle size analysis	Record in report	Quality control testing	As per API specification

* Tests as per applicable
Reference A.R. No. and specification number to be recorded in the validation report.

12.0 Validation procedure for Lubrication process:

12.1 Load the ingredients in the IPC/Octagonal blender as per the sequence given in the Batch Manufacturing Record (BMR).

12.2 Operate the IPC/Octagonal blender as per Standard Operating Procedure (SOP).

12.3 Calculate the depth of the sampling layers of IPC/Octagonal blender and record the report in the report.

12.4 Blend and lubricate the powder/ granules as per time and speed of IPC/Octagonal blender specified in Batch Manufacturing Record (BMR) and withdraw the sample after lubrication equivalent to between 1- 3 unit doses in triplicate quantity from different positions of IPC/Octagonal blender as shown in the sampling plan and from sampling positions an pages 5 to 11 of 11with the help of qualified cleaned sampling thief.

12.5 Sampling thief, sampling bullet and bulk sampler: Code No. to be recorded in the validation report.

12.6 Send the above removed samples to quality control for the determination of blend uniformity of powder/ granules and results shall be recorded in validation report.

Tests	Source of data	Acceptance Criteria
Blend Uniformity	Quality control testing	As per specification

12.7 Draw about 70g of samples after lubrication as per the standard time specified in the BMR from centre of Top , Middle and Bottom positions of IPC/Octagonal Blender as per sampling plan on page 6 of 11 , (Approximately 210g) and determine the physical and chemical tests given in the below table.

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*Tests	Source of data	Acceptance Criteria
Description of blend	Quality Control Testing	As per specification
Blend Uniformity	Quality Control Testing	As per specification
Water Content (%w/w)	Quality Control Testing	As per BMR/ Specification
Loss on drying (LOD) (% w/w)	In-Process Testing	As per BMR
Bulk Density (g/ml)	In-Process Testing	As per BMR
% fines below 60# (% w/w)	In-Process Testing	As per BMR
* Particle size distribution (By sieve analysis) Above 20#, 40#, 60#, 80#, 100# and below 100#) (%w/w)	In-Process Testing	As per BMR

* Tests as applicable

Note: 1. Sieve integrity shall be checked before and after particle size distribution and details to be recorded in validation report.

2. Acceptance criteria and reference quality control specification No. shall be recorded and verified by quality assurance in validation report.

12.8 Unload the Lubricated blend in the clean intermediate product container (IPC)/ SS bins / SS containers (if required). Withdraw samples equivalent to and between 1- 3 unit doses in triplicate from Top, Middle and Bottom layers from each of the IPC / SS bins/ SS containers as per the sampling plan on Page 8 to 10 of 11. Keep the samples as reserve sample. Carry out the analysis if the results of the Blend uniformity are not within the acceptance criteria.

Tests	Source of data	Acceptance Criteria
Blend Uniformity	Quality control testing	As per specification

Note: The RSD of blend uniformity study should not exceed 5%. However, if RSD is more than 4% and less than 5%, subject the blend sample of IPC SS bins/SS containers withdrawn as reserve sample for analysis. Balance sample to be destroyed after compilation of validation report.

12.9 Calculate the unaccountable loss after particle size distribution and report in the validation report.

% Quantity of sample retained over individual sieve = B/A x 100
Where, Quantity of sample taken = A

Quantity retained over individual sieve = B
Quantity passing through 60# (C) = Quantity retained above 80# +above 100# + below 100#
=_____g

% fines below 60# = C/Ax 100=_____g / A x 100 = XX.XX%

Total quantity retained on each sieve (D)= Above 20# + above 40# + above 60# + above 80# + above 100# + below 100#

=_____g

Unaccountable loss (if applicable) = A – D

=_____g

12.10 SAMPLING AND TESTING PLAN:

Stage	Sampling Location	Sample size	Sampled By	*Test
Lubrication	10 different positions from IPC/Octagonal blender after Lubrication. (As per BMR)	Withdraw samples equivalent to and between 1- 3 unit dose in triplicate	Validation Team	Blend Uniformity
	Composite samples from Top, middle and Bottom level of IPC/ Octagonal blender	Approximately 150g	Validation Team	1. Description 2. Water content 3. Loss on drying 4. Bulk Density 5. Tapped density 6. Particle size distribution 7. % fine below 60#
	From IPC/ SS bins / SS containers as per Sampling Plan	Withdraw samples equivalent to and between 1-3 unit dose in triplicate	Validation Team	Blend Uniformity

***** Tests as applicable.

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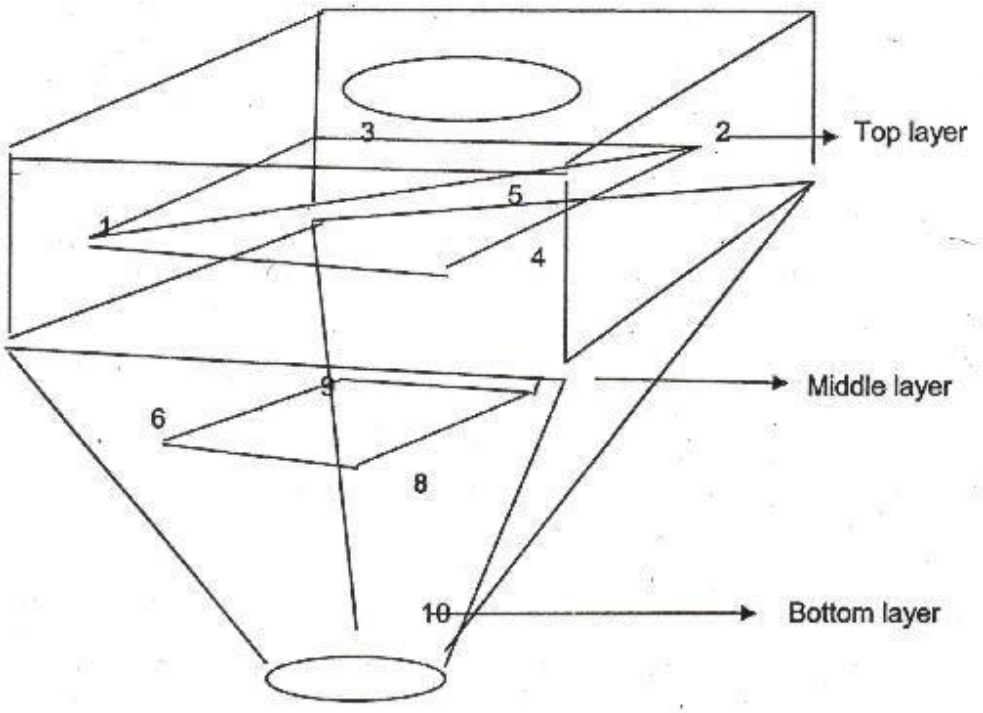
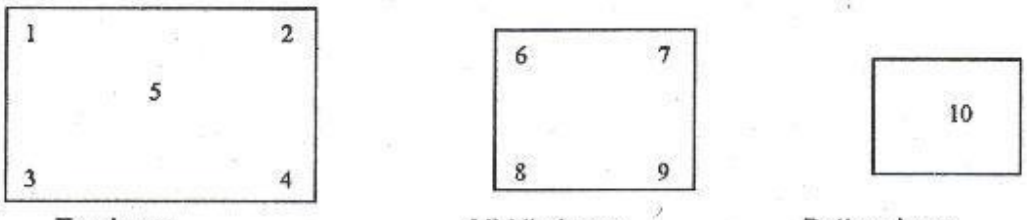
12.11 SAMPLING POSITIONS:

SAMPLING POSITIONS AFTER LUBRICATION FROM IPC BLENDER





Where Serial Nos. 1-10 indicates sampling positions

Where ⟶ indicates sampling layers

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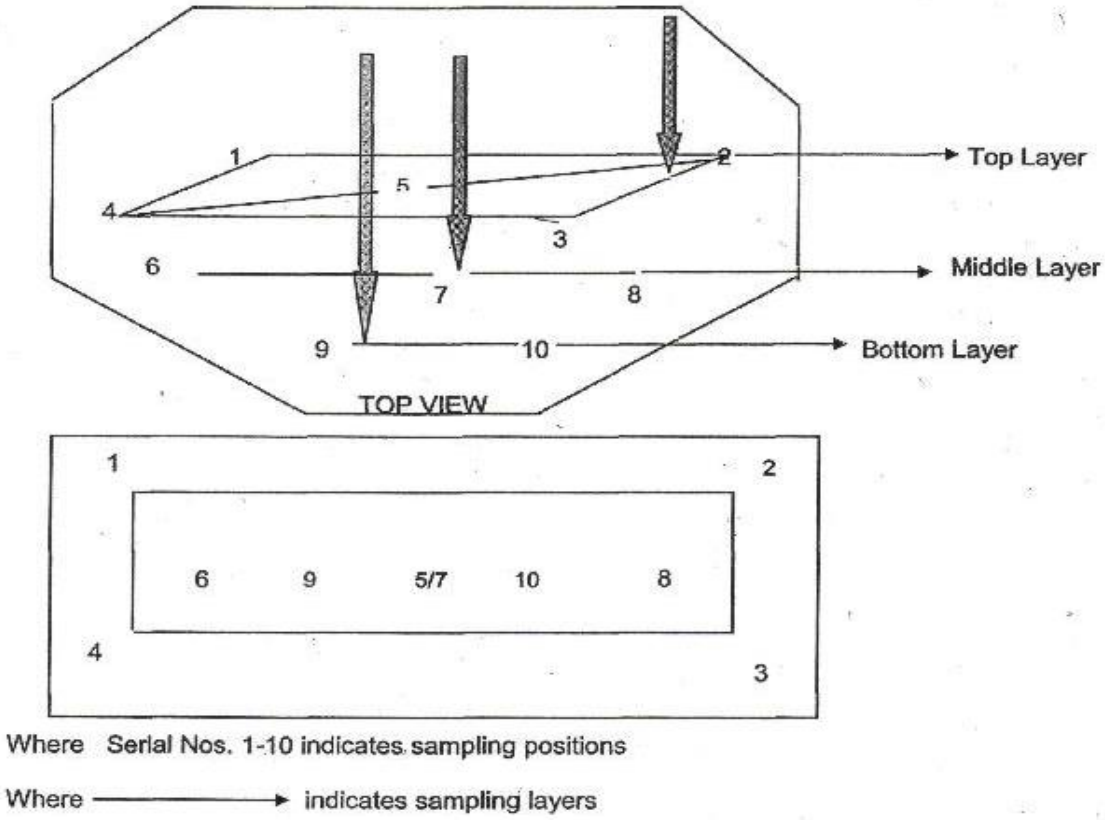
SAMPLING POSITION AFTER LUBRICATION FROM OCTAGONAL BLENDER



Where Serial Nos. 1-10 indicates sampling positions

Where ⟶ indicates sampling layers

SAMPLING POSITIONS OF INTERMEDIATE PRODUCT CONTAINER:

Samples are to be drawn from container as shown in following diagrams:

1. In case of only one container sampling to be done from 10 positions shown in diagram A.
2. In case of two to three containers, samplings to be done from 5 positions as shown in diagram B.
3. In case of four or more containers, samplings to be done from 3 positions as shown in diagram C

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SAMPLING POSITIONS OF IPC CONTAINER
DIAGRAM A

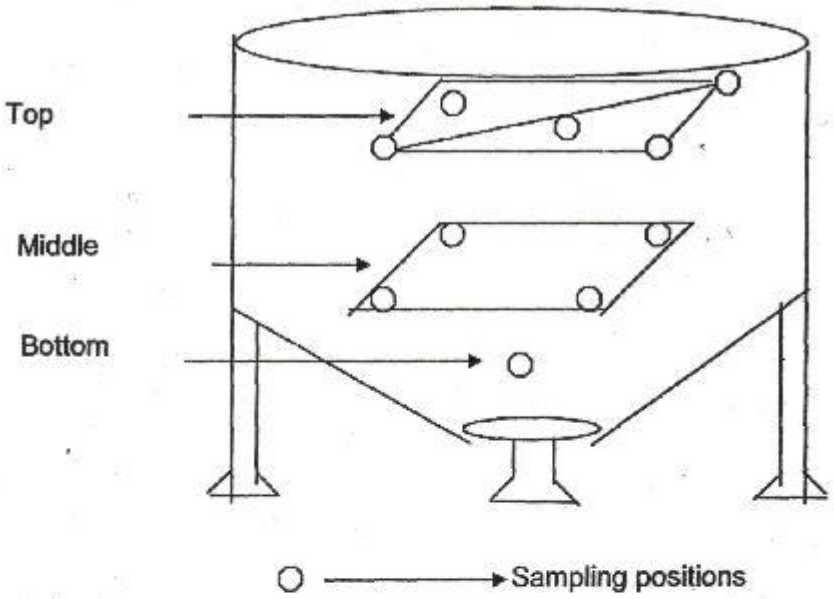

DIAGRAM B

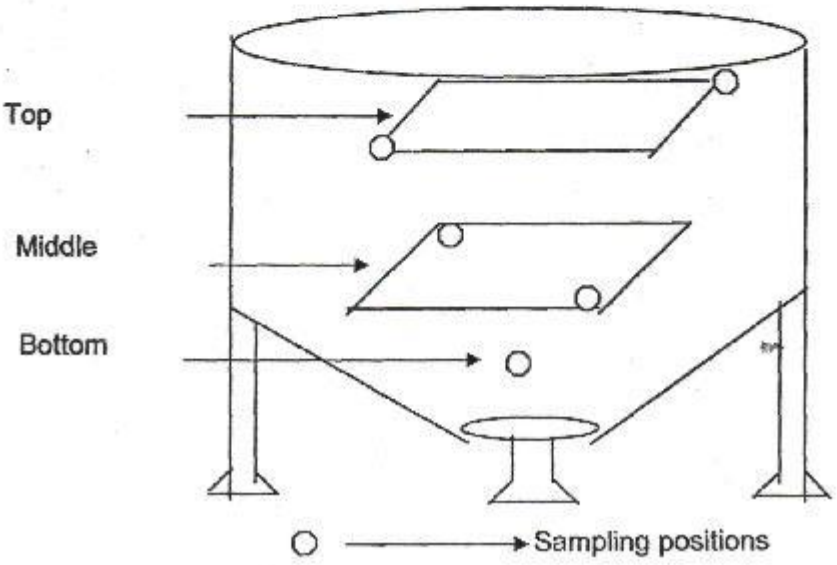

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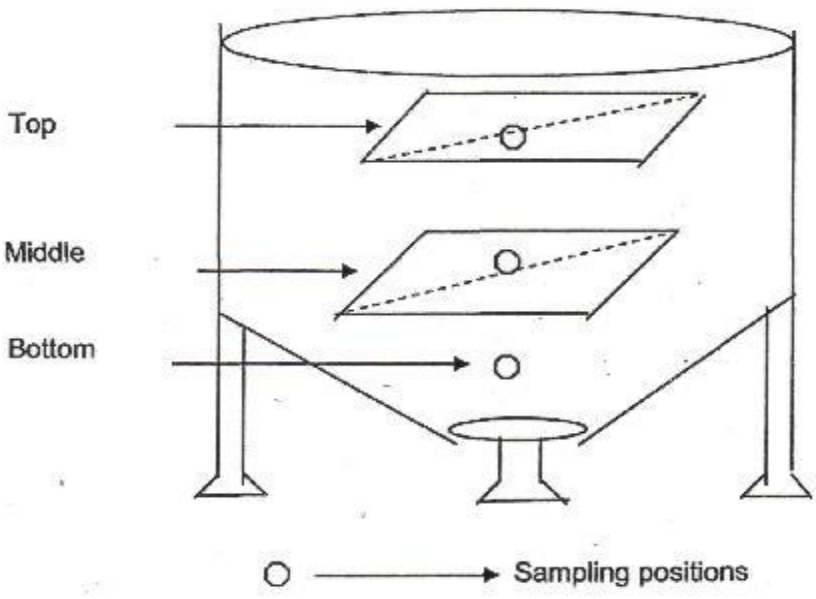
DIAGRAM C



SAMPLING POSITIONS OF STAINLESS STEEL BIN (S.S. BIN):

Samples are to be drawn from S.S. bin as per shown in the following diagram

1. In case of only one S.S. bin, sampling to be done from 10 positions as shown in diagram A.
2. In case of two or three S.S. bin, sampling to be done from 5 positions as shown in diagrams B.

In case of four or more S.S. bin, sampling to be done from 5 positions as shown in diagram c

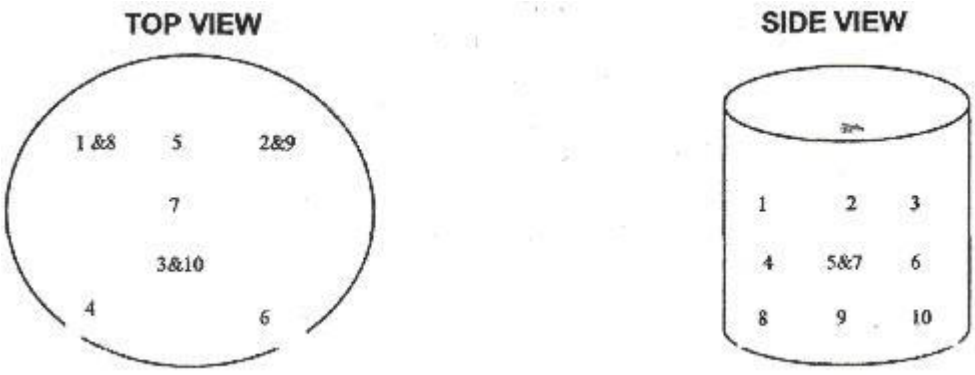


Diagram A

VALIDATION PROTOCOL FOR LUBRICATION OF POWDER/GRANULES IN IPC BLENDER/OCTAGONAL BLENDER

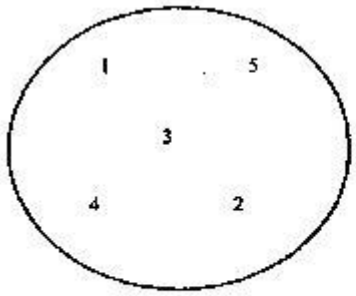
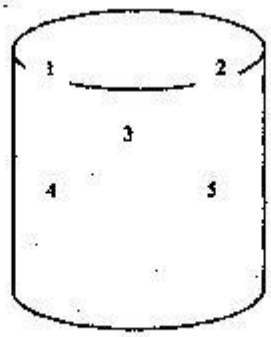


DIAGRAM B



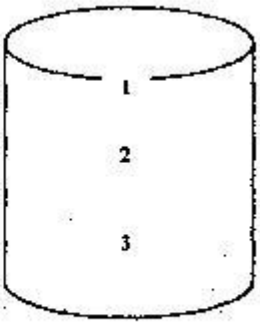


DIAGRAM C

13.0 Details of non compliances:

Details of deviations (including justification of acceptance if any) done to successfully carry out the exercise and out of specification results obtained shall be recorded. (Attach the details in the validation report).

14.0 Type of validation:

Type of validation to be recorded in the validation report (i.e. concurrent validation).

15.0 Frequency:

1) Concurrent validation: Three consecutive successful validation exercises.

2) Revalidation:

I) Periodic verification of validation: One verification exercise every three years
II) After major change: Three consecutive successful validation Exercises

16.0 Risk management study:

Record the details of risk management study in the validation report.

17.0 Results / Observations:

Record the observations and results in the validation report.

18.0 Summary of the validation :

Summary of the findings shall be recorded in the validation report.

19.0 Recommendations:

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

20.0 Team Approval:

The filled report shall be checked and finally approved by the team.

21.0 Review and Approval:

The report shall be reviewed and finally approved by unit quality assurance and unit head. The report shall include any follow-up action if required.

22.0 Attachments:

Attachments (if any) to be attached to the validation report shall be recorded.

23.0 Destruction of remaining samples:

All remaining samples of the batch are destroyed as per respective SOP.

24.0 Abbreviations:

No./ Nos.	:	Number/Numbers
MBMR	:	Master Batch Manufacturing Record
%w/w	:	Percent weight by weight
IPC	:	Intermediate product container
BMR	:	Batch Manufacturing Record
%	:	Percentage
RSD	:	Relative Standard Deviation
g	:	gram
LOD	:	Loss on drying
g/ml	:	gram per millilitre
ml	:	millilitre
A.R. No.	:	Analytical reference number
SOP		standard operating procedure
API	:	Active pharmaceutical ingredient
SS	:	Stainless steel
i.e.	:	that is