STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Yield deviation at different stages of processing	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 PURPOSE

To define a procedure for in process checks to be performed during manufacturing and packing of pharmaceutical products to ensure that all the critical parameters are within the specified limits or standards.

2.0 SCOPE

2.1 This procedure applies for in process checks to be performed during manufacturing and packing of pharmaceutical products at .....

Note: This SOP is applicable for Tablet and Hard gelatin Capsule formulations.

3.0 REFERENCE(S) & ATTACHMENTS

3.1 References

3.1.1 Indian Pharmacopoeia

3.1.2 United States Pharmacopoeia

3.1.3 In House

3.2 Attachments

3.2.1 Nil

4.0 DEFINITION & ABBREVIATION(S)

4.1 Definitions

4.1.1 **In process check:** These are the check points carried out during processing of a product at some predefined interval of time to ensure whether the product being processed meets the desired specification. Environmental monitoring of an area is also considered as an in process check.

4.1.2 **Inprocess Defects:**

Capping: Capping means separation of top or bottom portion of a tablet from the main body horizontally & comes as a cap.

Lamination: Separation of a tablet in to two or more layers.

Picking: Sticking of a tablet portion & being removed by the punch face.

Sticking: Adherence of tablet material to the die wall.

Blistering: Local detachment of film from the substrate forming blister.

Mottling: Unequal distribution of colour on a tablet.

Orange peel/ Roughness: A defect where the surface of the film becomes rough & non glossy.

Dent: A defect where cap or body part of a capsule being pressed inside.

Telescopic: A defect where either of the cap or body overlaps on each other.

Absence of printing on blister or strip: Absence of Printing information is observed on blister/strip.

4.2 Abbreviations

4.2.1 IPQA : In-process Quality Assurance

4.2.2 SOP : Standard Operating Procedures

4.2.3 PPQ: Process Performance Qualification

5.0 RESPONSIBILITY:

5.1 Production and IPQA staff:

5.1.1 Performing the in-process checks during manufacturing.

5.2 Quality Assurance Head:

5.2.1 To ensure implementation of the defined procedure.

5.3 Plant Head:

5.3.1 To ensure implementation of the defined procedure.

6.0 Distribution:

I. Quality Assurance
II. Production

7.0 PROCEDURE:

7.1 Frequency and limits of in-process checks shall be as per BMR/ BPR of individual product.

7.2 Start up inprocess check will be done by IPQA person after the satisfactory inprocess check done by production person & the same activity will be recorded in respective BMR/BPR.

7.3 In -process check frequency for development and Process Performance Qualification (PPQ) batches preferably shall be twice with respect to routine commercial batches e.g. if in-process check frequency is every one hour for commercial batch then frequency for in-process checks shall be every 30 minutes for development and PPQ batches.

7.4 IPQA/production person shall ensure environmental conditions and other specified requirements are maintained throughout the activity.

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Yield deviation at different stages of processing	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

7.5 IN-PROCESS CHECKS IN TABLETS:

7.5.1 IN-PROCESS CHECKS DURING GRANULATION

Parameters	Sample type	Quantity	Frequency
Loss on drying (Powders/ Granules):	Composite	2-3 gm	After completion of drying
Appearance/Description for blend (for colour, odour & lump formation)	Composite*	20 gm	After lubrication

* If there is only one container containing the blend, then sample shall be drawn from initial, middle & bottom of the container & composite sample will be prepared. If more than one container are there containing the blend, then sample will be collected from each container & composite sample will be prepared.

7.5.2 IN-PROCESS CHECKS DURING TABLET COMPRESSION

Parameters	Sample Type	Quantity	Frequency
Appearance / Description for tablets (for defects like surface finish crumbling, mottling, chipping, swelling, powder on the tablets embossing (if any) stickiness, capping, lamination, sticking, burring and picking)	Directly from the compression machine.	At the beginning and every start up: Total no. of stations + *additional no. of tablets & 20 Nos. thereafter from each side of the machine.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Dimension	Directly from the compression machine.	Equal to total no. of stations from each side of the machine.	At the beginning, every start up of machine
Average Weight	Directly from the compression machine.	20 Nos.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Uniformity of weight	Directly from the compression machine.	At the beginning and every start up: Total no. of stations + *additional no.	At the beginning & as per frequency mentioned in BMR thereafter**, every

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Yield deviation at different stages of processing	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

Parameters	Sample Type	Quantity	Frequency
		of tablets & 20 Nos. thereafter from each side of the machine.	start up of machine
Thickness	Directly from the compression machine.	At the beginning and every start up: Total no. of stations and 10 Nos. thereafter from each side of the machine.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Hardness	Directly from the compression machine.	10 Nos. from each side of the machine.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Friability test	Directly from the compression machine.	Tablets with a unit mass equal to or less than 650 mg, take a sample of whole tablets corresponding to 6.5 g. For tablets with a unit mass of more than 650 mg, take a sample of 10 whole tablets. Take sample from each side of the machine.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Disintegration time	Directly from the compression machine.	06 Nos. from each side of the machine.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine

*additional no. of tablets depends on the no. of stations of the compression machine.

For example:

*Additional tablets for a 45/ 55/75 station machine shall be 5 nos. and for a 26/36 station machine shall be 4 nos. to make a next round figure i.e. 50, 60 and 80 no. of sample in case of 45, 55 and 75 station machine respectively and 30 and 40 no. of sample in case of 26 and 36 station machine respectively.

** For a batch which runs less than 4 hours, the frequency of inprocess check will be initial, middle & end of processing. For a batch which runs more than 4 hours, the frequency of in process check will be every 2 hours till end of processing.

7.5.3 IN-PROCESS CHECKS DURING TABLET COATING

Parameters	Sample Type	Quantity	Frequency
Appearance/Description for tablets (for defects like surface finish, crumbling, mottling, chipping, swelling, peeling, bridging, deposition in embossing (if any), stickiness, twining) etc.	Composite	20 Nos.	At the end of coating
Dimension	Composite	20 Nos.	At the end of coating
Average Weight	Composite	20 Nos.	At the end of coating
Uniformity of weight	Composite	20 Nos.	At the end of coating
Thickness	Composite	20 Nos.	At the end of coating
Disintegration time***	Composite	06 Nos.	At the end of coating

*** For enteric coated tablets, check the disintegration time using 0.1 M Hydrochloric acid & pH 6.8 buffer.

7.6 IN-PROCESS CHECKS IN HARD GELATIN CAPSULES:

7.6.1 IN-PROCESS CHECKS DURING BLEND:

Parameters	Sample type	Quantity	Frequency
Loss on drying (Powders / Granules):	Composite	2-3 gm	After completion of drying
Appearance / Description for blend (for colour, odour & lump formation)	Composite*	20 gm	After lubrication

* If there is only one container containing the blend, then sample shall be drawn from initial, middle & bottom of the container & composite sample will be prepared. If more than one container are there containing the blend, then sample will be collected from each container & composite sample will be prepared.

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Yield deviation at different stages of processing	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

7.6.2 IN-PROCESS CHECKS DURING HARD GELATIN CAPSULE FILLING

Parameters	Sample type	Quantity	Frequency
Appearance/Description for capsules (for defects like dented capsules, empty capsules, capsules with V-notch, printing quality, crust/lump formation in the blend, powder leaking from the locking end, powder on capsules, Chipping of sides of capsules)	Directly from the capsule filling machine	Nos. equal to the No. of stations at the beginning & 20 nos. thereafter as per frequency	At the beginning & as per frequency mentioned in BMR thereafter**, every startup of machine
Lock Length	Directly from the capsule filling machine	Nos. equal to the No. of stations at the beginning & 20 nos. thereafter as per frequency	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Average weight of filled capsules	Directly from the capsule filling machine	20 nos.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Uniformity of weight	Directly from the capsule filling machine	Nos. equal to the No. of stations at the beginning & 20 nos. thereafter as per frequency	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine
Disintegration	Directly from the capsule filling machine	06 nos.	At the beginning & as per frequency mentioned in BMR thereafter**, every start up of machine

** For a batch which runs less than 4 hours, the frequency of inprocess check will be initial, middle & end of processing. For a batch which runs more than 4 hours, the frequency of inprocess check will be every 2 hours till end of processing.

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Yield deviation at different stages of processing	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

7.7 IN-PROCESS CHECKS DURING PRIMARY PACKING (BLISTER/STRIP PACKING) IN TABLETS AND CAPSULES

Parameters	Details to be checked	Quantity
Appearance of tablets	Broken / capped/ laminated / chipped / discoloured / black particles / foreign particle / distorted or de-shaped	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.
Appearance of Capsules	Chipped / broken / deformed / dented capsules/ V notched capsules /Capsules with foreign material /capsules with oil stain & Improper lock length	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.
Foil shifting	Foil shifting reduces the sealing width of strips and to be observed carefully.	-----
Batch coding details on foil	Check the batch details as per BPR and observe the correctness of coding details, legibility of coding details, missing of letters or smudging / lifting of ink.	Collect the number of strips equivalent to the no. of stereos on the overprinting roller.
Empty Pockets/Cut pocket	Check each individual pocket of strip for the presence of tablet / capsule and integrity of pocket.	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.
Proper forming of blister	The blister shall be fully formed as per the shape of the cavity of forming roller. Each strip is to be carefully observed for any irregularity in the shape of blisters.	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.
Proper cutting of the strips / blisters	Examine the strips for proper cutting. Check the horizontal & vertical cutting.	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.
Appearance of the strip	Check the strips for poor knurling, de-lamination, hologram creasing on foil (if applicable) and also faulty printing such as ink lining; ink patches, Smudging of ink and poor legibility of printed letters.	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.
Leak test	Perform leak test as per the respective SOP.	Collect the number of strips equivalent to the no. sealed on one complete rotation of the sealing roller surface.

7.8 IN-PROCESS CHECKS DURING SECONDARY PACKAGING IN TABLETS AND CAPSULES

Parameters	Details to be checked
Batch details on carton/ cache cover	Check the batch details as per BPR and also observe for legibility of letters, missing of letters or smudging of ink etc.
Proper gluing of side seam/bottom lock of carton/catch cover	The sealing of side seam and lock bottom flaps of carton / cache cover should be intact and shall not show any opening.
Number of strips in one carton / cache cover as per required pack profile	Check each carton or catch cover for the total number of strips and verify the results with pack profile mentioned in BPR.
Number of unit cartons in one outer shipper (Corrugated box) as per required pack size	Count the number of unit cartons in one outer shipper and verify with the pack size mentioned in the BPR and outer shipper.
Presence of package insert / Patient information leaflets	Before final closing of carton / unit carton, ensure the presence of package insert in each carton / unit carton, wherever applicable.
Proper insertion of tuck-in flaps	Check whether the tuck-in flaps of the cartons are properly inserted and locked with the supporting flaps or not.

7.9 IN-PROCESS TERTIARY PACKAGING CHECKS

Parameters	Details to be checked
No. of bottles/cartons/shrink packed units in one shipper (corrugated box).	Count the no. of bottles/cartons/shrink packed units in one shipper.
Overprinting on corrugated boxes	Check the overprinting details on the shipper
Pasting of BOPP tape	Check the pasting of BOPP tape on corrugated box for peeling-off of tape or opening of seal etc.
Gross weight of shipper	Check and record for gross weight of shipper
Loose Shipper	Check the loose shipper for number of bottles/cartons/Shrink packed units. The label of loose shipper shall be signed by production and cross verified by QA for loose quantity. The gross weight of the loose shipper shall be written in the shipper.

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Yield deviation at different stages of processing	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

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