# PROCESS VALIDATION

# DRAFT TEMPLATES

# PROTOCOL

# FOR

# COATED TABLETS

**TABLE OF CONTENTS**

# PROCESS VALIDATION PROTOCOL OF COATED TABLET

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 2 of 24 |



## 1.0 PROTOCOL APPROVAL:

# PROCESS VALIDATION PROTOCOL OF COATED TABLET

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 3 of 24 |

| | Department | Name | Signature | Date |
|---|---|---|---|---|
| Prepared By | Quality Assurance | | | |
| Reviewed By | Production | | | |
| | Quality Control | | | |
| | Engineering | | | |
| Approved By | Head-QA | | | |

## 2 . 0 INTRODUCTION:

Product shall be manufactured using the Wet Granulation Technology. The batches manufactured during the validation shall be setup for the stability study and other parameters monitored periodically and shall be reviewed by the validation Team.

## 3.0 OBJECTIVE:

The objective of this exercise is to develop a **PROCESS VALIDATION PROTOCOL** to validate the process and have documented evidence to ensure that critical process variables are checked during validation. Also to demonstrate the process capability of the product meets its predetermined specifications and quality attributes.

## 4.0 SCOPE:

This protocol for the Process validation of ***product name*** formulation defines the procedural aspects to be followed while carrying out Process validation activity that includes prerequisites before commencing the actual work like, Master formula and process, approved vendors and characteristics of raw materials. Also it defines the acceptance criteria, re-validation criteria and justification for critical process parameters.

## 5.0 VALIDATION CRITERIA:

- Process validation batch shall be manufactured as per process steps given in the Master Manufacturing Formula.
- The batches manufactured during process validation shall meet the criteria defined in product specification.

## 6.0 REVALIDATION CRITERIA:

The process shall be revalidated whenever there shall be changes in:

- Manufacturing process and the product formula.
- Manufacturing site or location.
- Change in critical equipment in manufacturing process
- Change in batch size

## 7.0 REASON FOR VALIDATION:

- The product ***Name*** will be manufactured as validation batch due to new product in ***Plant***,
- Transferred/ change in facility from another location of Pharmadevils.

## 8.0 PRODUCT PROFILE:

**Name of the product : ……**

**Label Claim** : Each enteric coated tablet contains:

API-1 (BP) ..... 12 mg

API-2 (IP) ……..…… 90 mg

API-3 (BP) ..... 100 mg

**Colours** : Sunset Yellow Supra

**Shelf Life** : 24 Months

**Appearance** : Reddish orange coloured, circular, biconvex, enteric coated tablets having plain surface on both sides.

**Storage Condition** : Store in cool and dry place. Protect from light.

## 9.0 MASTER FORMULA

**Batch size: 1000000 Tablets** **MMF No.: XX/YY/ZZ/AA-01**

| S.No. | Components | Specification | Weight/Tablet in mg |
|---|---|---|---|
| **Uncoated Tablets** | | | |

## PROCESS VALIDATION PROTOCOL OF COATED TABLET

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 6 of 24 |

| | | | |
|---|---|---|---|
| **Dry mixing** | | | |
| 1. | API-1 BP | BP | 100.00 |
| 2. | Croscarmellose sodium IP | IP | 51.00 |
| 3. | Microcrystalline cellulose IP (PH 112) | IP | 20.00 |
| 4. | Colloidal silicon dioxide IP | IP | 9.00 |
| **Binder Preparation** | | | |
| 5. | Povidone IP (K-30) | IP | 7.20 |
| 6. | Isopropyl alcohol IHS * | IHS | 210.00 |
| **Pre-Lubrication** | | | |
| 7. | API-3 BP | BP | 79.44 |
| 8. | API-2 IP | IHS | 62.7 |
| 9. | Croscarmellose sodium IP | IP | 34.00 |
| 10. | Colloidal silicon dioxide IP | IP | 1.00 |
| 11. | Polacrilin potassium USP | USP-NF | 23.70 |
| **Lubrication** | | | |
| 12. | Magnesium Stearate IP | IP | 4.40 |
| | | **Weight of uncoated tablet** | **XXX.00** |
| **Coating** | | | |
| **Seal Coating** | | | |
| 13. | Hydroxypropyl Methylcellulose (5 cps) IP | IP | 9.45 |
| 14. | Diethyl phthalate IP | IP | 0.95 |
| 15. | Isopropyl alcohol IHS* | IHS | 62.0 |
| 16. | Dichloromethane BP* | BP | 144.0 |
| | | **Weight build up** | **8.00** |
| **Enteric Coating** | | | |
| 17. | Methacrylic acid copolymer Type A USP-NF | USP-NF | 28.90 |
| 18. | Isopropyl alcohol IHS* | IHS | 240.00 |
| 19. | Acetone IP* | IHS | 180.00 |
| 20. | Talc IP | IP | 4.00 |
| 21. | Titanium dioxide IP | IP | 1.45 |
| 22. | Magnesium Stearate IP | IP | 1.00 |
| 23. | Sunset yellow Supra IHS | IHS | 2.90 |
| 24. | Purified water IHS/IP* | IHS/IP | 15.00 |

| | | | |
|---|---|---|---|
| 25. | Diethyl phthalate IP | IP | 4.65 |
| 26. | Isopropyl alcohol IHS* | IHS | 30.00 |
| | | **Weight build up** | **33.00** |
| | | **Total weight of Coated Tablet** | **XXX.00** |

* Not considered in final weight of tablet.

## 10.0 RISK ANALYSIS:

The product shall be manufactured in General block with batch size of 1000000 Tablets as a validation batch. product shall be manufacturing by using wet granulation. Raw materials of approved vendor source shall be sifted, dry mixed, granulated using binder solution and dried at 50 $^{O}$C ± 5 $^{O}$C. Dried granules are sized (Sifted and milled) and lubricated using Magnesium stearate. An Approved

lubricated granules will be compressed by using 11.5 mm diameter circular standard concave punches having plain surface on upper and lower punch.

- **Dispensing:**

  Dispensing of all raw material is done by using calibrated balance, all raw material are procured from approved vendor, there is no critical parameter identified for validation during dispensing stage.

- **Granulation:**

➢ **Sifting of raw material:** Sifting of raw material is done by specified sieve under supervision of the trained personnel. Sieve integrity is verified before and after processing.

➢ **Dry Mixing:** Dry mixing of the material is performed by laid down procedure and dry mixing uniformity was established during optimization of product, at dry mixing stage critical parameters are mixing time and speed of mixer is to be monitored. At the end of 10 minutes Samples from various locations shall be withdrawn and evaluated for mixing uniformity. Composite sample shall be withdrawn and evaluated for untapped bulk density, tapped bulk density, for record purpose as part of validation.

➢ **Binding:** At the time of binding manual monitoring is to be done for the defined mixing speed of agitator and chopper and end point of the granulation to be monitored by checking the mass intermittently for consistency and amperage load monitoring.

➢ **Drying:** At the Drying stage of the granules Inlet temperature to be monitored and sample to be withdrawn during drying and tested for LOD till the end of drying to find out rate of drying and at end of drying sample withdrawn from seven location of bowl for checking of drying uniformity for specified LOD by using IR moisture balance.

➢ **Sizing of Granules:** Sizing of granules is to be milled by using Multimill, Speed of the Multimill and direction of shafts is to be monitored and sample to be withdrawn at the end of the sizing operation for the monitoring of particle size distribution, untapped bulk density, tapped bulk density and LOD at 105 $^{o}$C on IRMB for record as part of validation.

➢ **Lubrication:** Critical Process variable to be monitor about speed of blender and mixing time of granules and sample to be withdrawn from ten location for verification of blend uniformity and also composite sample to be withdrawn for analysis particle size distribution, untapped bulk density, tapped bulk density and for complete analysis as per QC in process specification.

➢ **Compression:**

During compression stages physical parameter, assay and dissolution as per sample summary of tablet to be checked at different challenges, at maximum/minimum speed, at maximum/minimum hardness, at optimum speed and optimum hardness during – initial/ full of hopper stage, middle stage and end/ half of hopper stage of compression process. This process will cover critical process variables such as effect of speed and compression force. After completion of compression process composite sample to be withdrawn for analysis as per QC inprocess specification.

- **Coating:**

During coating stage all critical parameter like spray rate, pan rpm, inlet temperature, bed temperature, atomizing pressure, diameter of nozzle and peristaltic pump speed is to be monitored and sample to be withdrawn after end of the coating and tested for physical parameters. Composite sample to be withdrawn for complete analysis as per finished product specification including microbiological purity.

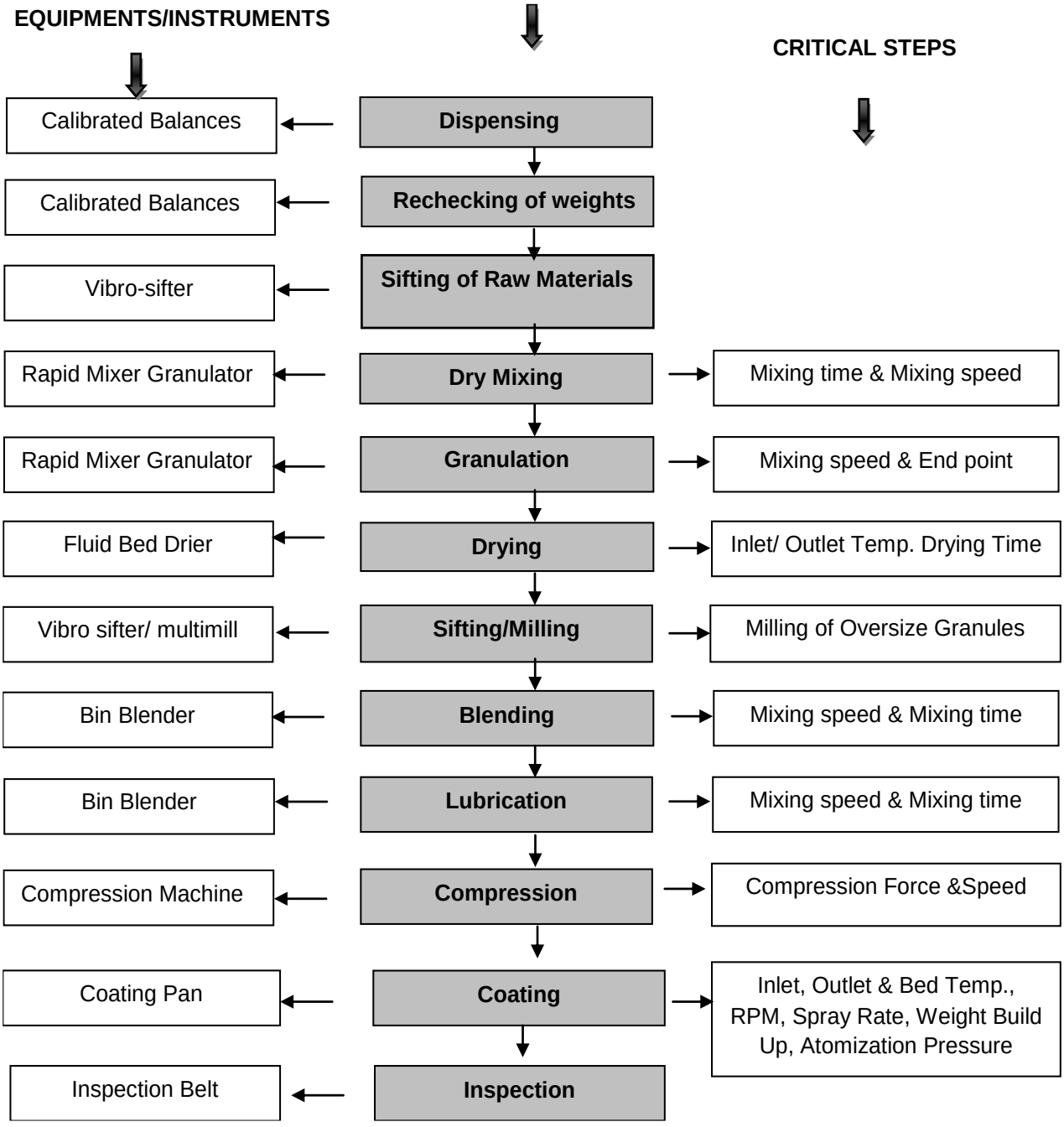
## 11.0 SAMPLING PROCEDURE:

- All validation samples except unit dose blend samples shall be placed in clean container and labeled.
- **Unit dose blend sample** shall be taken in accordance with SOP for **"Procedure for cleaning and operation of sampling thief".** The samples shall be placed in container or sampling poly bag and labeled.

## 12.0 FLOW DIAGRAM (PROCESS):

# PROCESS VALIDATION PROTOCOL OF COATED TABLET

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 10 of 24 |




## 13.0 MANUFACTURING PROCEDURE:

### 13.1 Sifting of raw material:

- Sift API-1 through s.s. sieve # 60 ASTM (250 µ) on a vibro sifter.
- Co-sift Microcrystalline cellulose (PH 112) and Colloidal silicon dioxide through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter.
- Sift Lactose Monohydrate through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter.

**13.2 Dry Mixing:**

- Transfer the material of step 10.1 to RMG and mix for 10 minutes at slow speed.

**13.3 Binder Preparation:**

- Dissolve Povidone (K-30) in Isopropyl alcohol under stirring to form a clear solution.

**13.4 Granulation:**

- Add the binder solution obtained in step 10.3 to the dry mix of step 10.2 and granulate to obtain dough mass of required consistency. Continue mixing till the desired dough mass is obtained. If required add additional quantity of Isopropyl alcohol to get the desired dough mass and note down the same.

**13.5 Drying:**

- Air-dry the granules in FBD for 30 minutes. Reshuffle the granules.
- Air-dry the granules in FBD for 10 minutes. Reshuffle the granules.
- Dry the granules at an inlet temperature of 50 $^{O}$C ± 5 $^{O}$C, till the desired LOD (Limit: 3.0 % - 4.0 % w/w at 105 $^{O}$C on IRMB) is achieved.

**13.6 Sifting and Milling:**

- Sift the dried granules through sieve # 24 on a vibro sifter.
- Mill the granules retained on # 24 through 1.5 mm screen fitted on multimill; at medium speed knives forward direction and pass the granules through # 24.

**13.7 Pre-Lubrication:**

- Co-sift API-2 and API-3 geometrically through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter.
- Co-sift the materials of step 10.7.1 with the dried granules of step 10.6 geometrically through s.s. sieve # 24 on a vibro sifter.
- Sift Croscarmellose sodium through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter.
- Sift Colloidal silicon dioxide through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter.
- Sift Polacrilin potassium through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter.
- Transfer the sifted materials of step 10.7.2, 10.7.3, 10.7.4 and 10.7.5 into the blender and mix for 15 minutes.

**13.8 Lubrication:**

- Sift Magnesium stearate through s.s. sieve # 60 ASTM (250 µ) on a vibro sifter.
- Transfer the sifted Magnesium stearate to the blender and mix for 3 minutes.

**13.9 Blend Analysis:**

- Intimate the Quality Control department for analysis of blend as per current in process specifications.

**13.10 Compression:**

- Compress the approved blend on rotary compression machine as per in process specification.

**13.11 Coating :**

**13.11.1 Seal Coating**

- Disperse Hydroxypropyl methylcellulose in Isopropyl alcohol under stirring and add Dichloromethane under stirring to get clear solution.
- Add Diethyl phthalate to step 10.11.1 under stirring. Filter the coating solution through muslin cloth.
- Load the approved uncoated tablets into baffles coating pan. Warm the tablets at temperature of 45 $^{O}$C – 50 $^{O}$C for 10 minutes. Set the seal coating parameters as per specification.
- Spray the seal coating solution over the bed of tablets to achieve the desired weight gain is achieved. Dry the tablets for 5 minutes.

**13.11.2 Enteric Coating**

- Dissolve Methacrylic Acid Copolymer Type A (Drugcoat L-100) in the mixture of Isopropyl alcohol and Acetone under stirring for 5 minutes.
- Add Diethyl phthalate into the bulk of step 10.11.5.
- Sift Talc, Titanium dioxide and magnesium stearate through s.s. sieve # 40 ASTM (425 µ) on a vibro sifter. Make the slurry of the sifted material in Isopropyl alcohol.
- Dissolve Sunset yellow Supra in Purified water and add it to the slurry of step 10.11.7 and pass the slurry through colloidal mill for 20 minutes.
- Filter the slurry through nylon cloth and add to step 10.11.5 under stirring. Continue stirring for 20 minutes. Filter the coating solution through nylon cloth.
- Set the coating parameters as per specification.
- Spray the enteric coating solution over the bed of seal coated tablets. Continue spraying till the desired weight gain is achieved.

- Dry the tablets at inlet temperature 30 OC – 35 OC for 30 minutes.
- Cool the tablets to room temperature before unloading.

**13.12 Finished Product Analysis:**

- Intimate the Q.C. for analysis of finished product as per current Finished Product Specifications.

**14.0 CALIBRATION / QUALIFICATION:**

All equipment utilized in conducting the Validation activity shall be within calibration / qualification. Calibration/qualification shall be conducted in-house in accordance with approved SOPs or by an external body. All standards used in calibration shall be traceable to a national standard and shall remain within calibration for the duration of the Validation exercise.

**15.0 SAMPLE SUMMARY:**

| Stage | Location | Sample Size | Sample Type | Frequency | Tests | Acceptance Criteria |
|---|---|---|---|---|---|---|
| $Dry Mixing | 10 position from RMG | Draw samples equivalent to between 1-3 unit dose (XX mg to XX mg)* | Unit dose sample | After 10 minutes of dry mixing | Mixing Uniformity** | As per specification / To record |
| | Composite sample from the Top, middle and bottom | Approximately 20 gm * | Composite sample | | Untapped bulk density Tapped bulk density | |

# PROCESS VALIDATION PROTOCOL OF COATED TABLET

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 14 of 24 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | level of RMG | | | | | |
| $Drying | Fluid bed drier | Approximately 2 gm | Composite sample | During drying operation | LOD at 105° C/ IR Balance | Till the desired LOD achieved as per BMR |
| | | Approximately 2 gm each | 6 locations | At the end of drying | LOD | As per BMR |
| $ Milled granules | Blender | Approximately 50 g * | Composite | At the end of milling operation | LOD<br>Particle Size Distribution (20#,40#,60#,80#and 100#)<br>Untapped Bulk Density<br>Tapped Bulk Density | As per BMR<br>To record<br>To record<br>To record |
| Pre-lubrication | 10 position from Blender | Draw samples equivalent to between 1-3 unit dose (XX mg to XX mg) * | Unit dose sample | After 10 minutes of pre-lubrication | Blend Uniformity** | As per specification / To record |
| lubrication | 10 position from Blender | Draw samples equivalent to between 1-3 unit dose (XX mg to XX mg) * | Unit dose sample | After 3 minutes of lubrication | Blend Uniformity | As per specification |
| | Composite sample from the top, middle and bottom level of Blender | 50 g* | Composite | | 1) Particle size distribution* (20,40,60,80 & 100#)<br>2) Untapped bulk density*,<br>3) Tapped bulk density*<br>4) LOD* | For record<br>For record<br>For record |
| | | | | | 5) For complete analysis | As per blend specification |

Average weight during lubrication : 400.0 mg

* Sample shall be withdrawn and sent to QC along with test requisition.

** Duplicate sample to be retained by QA for reference purpose till testing.

$ Sample from each lot.

For unit dose sampling during Lubrication stage use 1.0 CC covette.

Sample shall be withdrawn at the depth of Approx 20 % from top layer of blend using sampling thief and about Approx .0.6 feet from wall of the Bin Blender.

Sample shall be withdrawn at the depth of Approx 50 % from top layer of blend using sampling thief and about Approx. 0.6 feet from wall of the Bin Blender.

Sample shall be withdrawn at the depth of Approx 80 % from top layer of blend using sampling thief and about approx. 0.6 feet from wall of the Bin Blender.

| Stage | Location | Sample Size | Sample Type | Frequency | Tests | Acceptance Criteria |
|---|---|---|---|---|---|---|
| **Compression #** | Direct from Compression Machine | 100** Tablets | Individual Tablets | 1) At maximum hardness<br>2) At minimum hardness | 1) Appearance*<br>2) Group Weight<br>3) Avg. Weight<br>4) Uniformity of weight<br>5) Thickness<br>6) Hardness<br>7) Disintegration | As per Specification |

# PROCESS VALIDATION PROTOCOL OF COATED TABLET

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 15 of 24 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | time<br>8) Friability | |
| | | | | | Capability index | NLT 1.33 |
| | | 100+(20*)** Tablets | | 3) At maximum speed<br>4) At minimum speed<br>5) At optimum speed & hardness<br>a) Initial stage/ Full Hopper<br>b) Middle stage<br>c) End stage/ Half Hopper | 1) Appearance*<br>2) Group Weight<br>3) Avg. Weight<br>4) Uniformity of weight<br>5) Thickness<br>6) Hardness<br>7) Disintegration time<br>8) Friability<br>9) Assay* | As per Specification |
| | | | | | Capability index | NLT 1.33 |
| | | 100 Tablets | Individual Tablets | At regular interval as per BMR | 1) Appearance<br>2) Group Weight<br>3) Avg. Weight<br>4) Uniformity of weight<br>5) Thickness<br>6) Hardness<br>7) Disintegration time<br>8) Friability | As per Specification (To be recorded in BMR) |
| | Pooled Tablet Container | 100 Tablets* | Composite sample | End of Compression | For complete analysis* | As per QC specification |
| **Coating** | Coating pan | 20 Tablets | Composite sample | At the end of Coating | 1) Appearance<br>2) Group Weight<br>3) Avg. Weight<br>4) Uniformity of weight<br>5) Thickness<br>6) Disintegration time | As per Specification |
| | | | | | Capability index | NLT 1.33 |
| | Pooled tablet's container | 100 Tablets* | Composite sample | At the end of Coating | For complete analysis* | As per finish product specification |
| | | 10 g Tablets@ | | | For Microbial analysis* | As per specification |

* Sample shall be withdrawn and sent to QC along with test requisition.
** Duplicate sample to be retained by QA for reference purpose till testing.
*** Results to be recorded in PVR.
@ For Microbial analysis.
# Samples to be collected from L.H.S and R.H.S separately and sent to QC as per sample summery.

.

## 16.0 RAW MATERIALS RATIONALE:

The raw materials shall be tested to ensure that the materials are of the acceptable quality prior to their use in the manufacturing. All the API and excipients shall be tested as per the respective Pharmacopoeial monograph. The details of reference monographs, vendor and analytical reference number are to be written in validation report.

## 17.0 SPECIFICATIONS:

**Specifications for Uncoated Tablets: (As per BMR/MMF*)**

| Sr. No. | Parameter | Specification |
|---|---|---|
| **1.** | Appearance | Light yellow circular, biconvex uncoated tablet having plain surface on both sides. |
| **2.** | Weight of 20 tablets | 8.0 g ± 2.5% |
| **3.** | Average weight | 400.0 mg ± 2.5 % |
| **4.** | Uniformity of weight | 400.0 mg ± 5.0 % |
| **5.** | Thickness | 4.4 ± 0.30 mm |
| **6.** | Hardness | NLT 6 $kg/cm^2$ |
| **7.** | Friability | NMT 1.0 % w/w |
| **8.** | Disintegration time | NMT 15 minutes |

**Specifications for Coated Tablets: (As per BMR/MMF*)**

| Sr. No. | Parameter | Specification |
|---|---|---|
| **1.** | Appearance | Reddish orange coloured, circular, biconvex, enteric coated tablets having plain surface on both sides. |
| **2.** | Weight of 20 tablets | 9.020 g □ 2.5 % |
| **3.** | Average weight | 451.0 mg ± 2.5 % |
| **4.** | Uniformity of weight | 451.0 mg □ 5.0 % |
| **7.** | Thickness | 4.6 ± 0.30 mm |
| **8.** | Disintegration time | As per IP monograph for enteric coated tablets. |

**Note:-**

- Uncontrolled Copy of Raw material specification attached*:_____
- Uncontrolled Copy of Inprocess specification for Lubricated blend and core tablets attached*:_____
- Uncontrolled Copy of Finished product specification attached*:_____

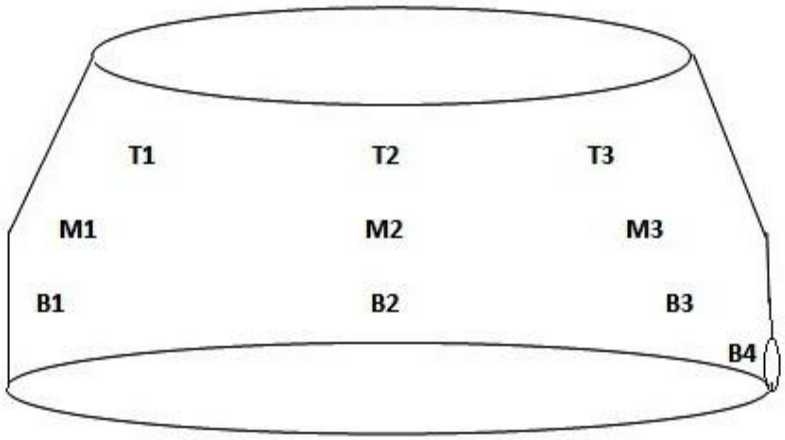
- **DRY MIXING:**

  As specified in the BMR, dry mix the material for 10 minutes. Withdraw about 20 gm of sample after 10 minutes of dry mixing as specified in BMR, from the centre position of Top, middle and bottom layer of dry mixed granules in rapid mixer granulator for determination as test given in sample summary.

**PROCESS VALIDATION PROTOCOL OF COATED TABLET**

| | |
|---|---|
| **Batch Size:** 1000000 Tablets | **BMR No.:** XXX/PRO/BMR/ZZ-00 |
| **Protocol No.:** XXX/BBB/PPV/ZZ-00 | **Page No.:** 18 of 24 |

**DIAGRAM AND SAMPLING LOCATION FOR R.M.G :**




T1 = Top left T2 = Top middle T3 = Top right

M1 = Middle left M2 = Middle centre M3 = Middle right

B1 = Bottom left B2 = Bottom middle B3 = Bottom right

B4 = Discharge chute

- **DRYING:**

Dry the granules at inlet temperature defined in BMR. Withdraw the composite sample during drying to till the end of drying to get the desired LOD and after the completion of drying withdraw samples from seven locations to determine the uniformity of drying in FBD as defined in sample summary.

**DIAGRAM OF FLUID BED DRYER BOWL WITH SAMPLING POINTS:**

**Where,**

| | | | | | |
|---|---|---|---|---|---|
| **T1** | = | Top Left | **M2** | = | Middle Right |
| **T2** | = | Top Right | **B1** | = | Bottom Left |
| **M1** | = | Middle Left | **B2** | = | Bottom Right |

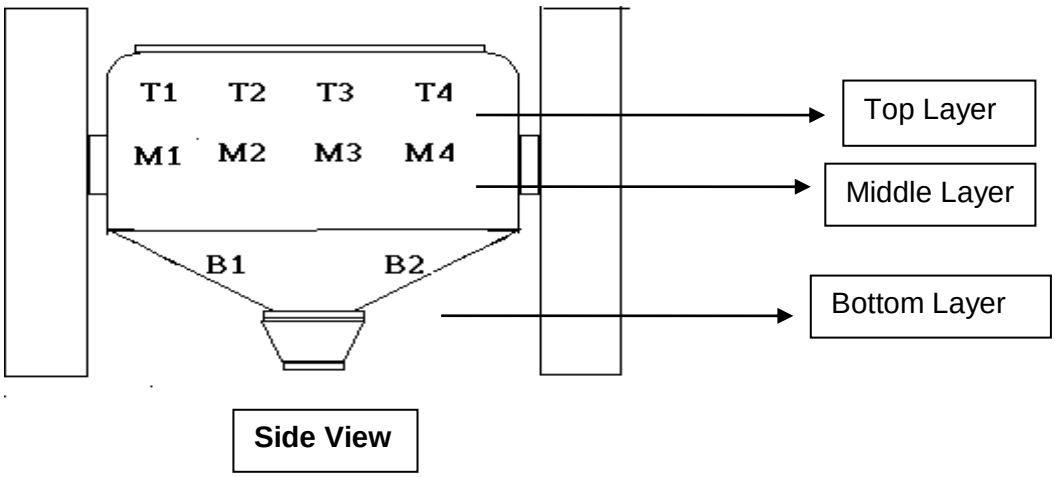
❖ **LUBRICATION:**

As specified in the BMR, blend the material for 20 minutes for pre-lubrication. Withdraw the samples equivalent to between 1 – 3 unit dose (395.60 – 1216.80) mg, in duplicate separately from 10 locations as per defined sampling location; determine the blend uniformity of granules.

As specified in the BMR, blend the material for 03 minutes for lubrication. Withdraw the samples equivalent to between 1 – 3 unit dose (400.0 – 1230.0) mg, in duplicate separately from 10 locations as per defined sampling location; determine the blend uniformity of granules.

Withdraw about 50 gm of sample after 03 minutes of blending as specified in BMR, from the centre position of Top, middle and bottom layer of blend in Bin bender for determination of test given in sample summary.

**DIAGRAM OF BIN BLENDER WITH SAMPLING LOCATIONS:**




**Side View**

**Where,**

| | | | | | |
|---|---|---|---|---|---|
| **T1** | = | Top Left | **M2** | = | Middle Front |
| **T2** | = | Top Front | **M3** | = | Middle Rear |
| **T3** | = | Top Rear | **M4** | = | Middle Right |
| **T4** | = | Top Right | **B1** | = | Bottom Left |
| **M1** | = | Middle Left | **B2** | = | Bottom Right |

❖ **COMPRESSION:**

On release of the lubricated granules by QA, the granules are taken up for compression. During tablet compression stage, the homogeneous granules are compressed on a tableting machine. To validate the tableting process for ***product***, the compression machine is run on maximum / minimum hardness, maximum / minimum speed and on optimum hardness / speed - at initial run, middle run, end of the run. Samples are collected for analysis as defined in the sample summary. The in-process testing shall be carried out at regular intervals during the machine run. These validation samples shall be tested as per the sample summary, to meet the acceptance criteria specified therein.

- **PROCEDURE**

Appropriately label the sample containers and collect samples as follows:

Set the machine, and adjust the compression parameters. After stabilization of the compression machine, the parameters mentioned below are checked and recorded in the respective BMR and report.

| | **Parameters of Evaluation** | | |
|---|---|---|---|
| 1. | Appearance | 5. | Disintegration Time |
| 2. | Hardness | 6 | Group Weight |
| 3. | Thickness | 7. | Average Weight |
| 4. | Friability | 8. | Uniformity of Weight |

**After the start of compression operation, set the compression machine -**

**AT OPTIMUM HARDNESS AND MAXIMUM SPEED:**

Set the compression machine at optimum hardness and maximum limit of speed and collect the tablets as per the sample summary. Maximum speed to be recorded in validation report.

**AT OPTIMUM HARDNESS AND MINIMUM SPEED:**

Set the compression machine at optimum hardness and minimum limit of speed and collect the tablets as per the sample summary. Minimum speed to be recorded in validation report.

**AT OPTIMUM SPEED AND MAXIMUM HARDNESS:**

Set the compression machine at optimum speed and higher limit of hardness range and collect the tablets as per the sample summary. Target hardness and thickness to be recorded in validation report.

**AT OPTIMUM SPEED AND MINIMUM HARDNESS:**

Set the compression machine at optimum speed and lower limit of hardness range and collect the tablets as per the sample summary. Target hardness and thickness to be recorded in validation report.

**OPTIMUM RUN:**

Set the compression machine at optimum speed / hardness and collect the tablets as per the sample summary Optimum speed to be recorded in validation report.

**AT INITIAL /FULL HOPPER RUN**

**MIDDLE RUN**

**END/HALF HOPPER OF RUN**

Collect tablets at regular intervals till the end of the compression cycle as per the Batch Manufacturing Record and sample summary. Record the sample details in validation report and Batch Manufacturing Record. About 100 tablets in a container labelled, as ‘POOLED SAMPLE’ shall be collected

throughout the compression operation. The tablet for Inprocess analysis shall be taken from the pooled sample for Inprocess Product Analysis as per specification.

❖ **COATING:**

On release of the Compressed Tablets by QA, the core Tablets are taken up for coating. During tablet coating stage, Tablets are coated in a autocoater to validate the Coating process for Product. Samples are collected for analysis as defined in the sample summary. These validation samples shall be tested as per the sample summary, to meet the acceptance criteria specified therein.

**PROCEDURE:**

Set the Inlet Temperature, and adjust the operational parameters as defined in BMR. After completion of Coating, the parameters mentioned below are checked and recorded in the respective BMR and report.

**Parameters of Evaluation**

| | | | |
|---|---|---|---|
| 1. | Appearance | 4. | Disintegration Time |
| 2. | Group Weight | 5. | Average weight |
| 3. | Thickness | 6. | Uniformity of weight |

**At completion of coating**

- Samples shall be collected for analysis of physical parameters mentioned above.
- About 100 tablets and 10 gram tablets in a container labelled, as 'POOLED SAMPLE' shall be collected throughout the coating operation. The tablet for final product analysis including microbial analysis shall be taken from the pooled sample for Finished Product Analysis as per specification.

## 18.0 DESTRUCTION OF REMAINING VALIDATION SAMPLES:

All remaining samples of the validation batch shall be destroyed as per respective SOP, details to be recorded in validation report.

## 19.0 SUMMARY, CONCLUSION AND APPROVAL:

Record the summary of the validation study with special emphasis on physical parameter, chemical parameter and evaluation of data obtained in validation report. Details of out of specification / deviation if any should be recorded in validation report. Record the recommendations or suggestions

based on the implementations of the results in validation report. It should include the approval of quality assurance, quality control and production head.

## 20.0 ABBREVIATIONS:

QA : Quality Assurance
QC : Quality Control
OOS : Out of Specification
SOP : Standard Operating Procedure
LOD : Loss on Drying
BMR : Batch Manufacturing Record
MMF : Master Manufacturing Formula
A.R. No. : Analytical Report Number
NLT : Not Less Than
NMT : Not More Than
FBD : Fluid Bed Dryer
RMG : Rapid Mixer Granulator
PVR : Process validation report
ASTM : American Society for Testing and Materials
IRMB : Infra Red Moisture Balance
API : Active Pharmaceutical Ingredient

## REVISION CARD

| S.No. | PPV No. | RPV No. | Reason for Revision | Change Control No. |
|---|---|---|---|---|
| 1 | | | New | ----- |