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| --- | --- | --- | --- | --- | --- | --- |
| **Product Details** | |  | **Details of BMR** | | | |
| Location: | Block :II (Granulation – Area) | Issuance | No. of Pages | Issued By (QA) | Received By  (PD) |
| Label claim | NA | First Issue (A) |  |  |  |
| Market | EUROPE | Additional Issue (B) |  |  |  |
| Ref. MFC No. | VGC/TA/EU/001-00 |  |  |  |
| Batch Size | 80.625 Kg | Total Pages |  |  |  |
| Shelf Life | 2 Years | Manufacturing Date (MM/YYYY) |  | Expiry Date (MM/YYYY) |  |
| Product Code | 3011555 | Allotted By (PD)  Signature & Date |  | Checked By (QA)  Signature & Date |  |
| Supersede MPR | NA | **Review of Executed BMR** | | | |
| Storage Conditions | Store at 20°C - 25°C (68°F - 77°F) | Reviewed by (Sign & Date) | PD |  | |
| QA |  | |

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|  | **Prepared By** | **Approved By** | | | | **Authorized By** |
| **Department** | **QA** | **Production** | **R&D / Tech. Transfer** | **Regulatory Affairs** | **In-charge - QA** | **Head - QA** |
| **Name** |  |  |  |  |  |  |
| **Designation** |  |  |  |  |  |  |
| **Signature** |  |  |  |  |  |  |
| **Date** |  |  |  |  |  |  |

**MANUFACTURING FORMULA**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Material Code** | **Material Name & Specification** | **Vendor Details** | **UOM** | **Quantity / Unit** | **UOM** | **Quantity / Batch** |
| **¥ Dry Mix:** | | | | | | | |
| 1 | 4023393 | Valganciclovir Hydrochloride, IH \*\* | Hetero Drugs Limited, Unit IX, Plot No. 1, Hetero Infrastructure Ltd.-SEZ,N. Narasapuram (Vil), Nakkapalli (Mandal), Visakhapatnam (Dist), 531081, A.P, India | mg | 496.300 | Kg | 62.038 |
| 2 | 1000599 | Cellulose, Microcrystalline,Ph.Eur (Avicel PH101) # | DuPont Nutrition | mg | 94.350 | Kg | 11.794 |
| 3 | 1000231 | Crospovidone, Ph.Eur(Kollidon CL) | BASF | mg | 3.450 | Kg | 0.431 |
| **¥ Granulation:** | | | | | | | |
| 4 | 1001245 | Povidone, Ph.Eur (Kollidon 30) | BASF | mg | 12.000 | Kg | 1.500 |
| 5 | 3001093 | Purified Water, IHS/USP/Ph.Eur @ | -------- | mg | 60.000 | Kg | 7.500 |
| 6 | 3001093 | Purified water, IHS/USP/Ph.Eur @ (additional quantity)$ | -------- | Mg | 14.400 | Kg | 1.800 |
| **Extra Granular Ingredients (Pre Lubrication):** | | | | | | | |
| 7 | 1000599 | Cellulose, Microcrystalline, Ph.Eur (Avicel PH101) | DuPont Nutrition | mg | 15.000 | Kg | 1.875 |
| 8 | 1000231 | Crospovidone, Ph.Eur  (Kollidon CL) | BASF | mg | 15.900 | Kg | 1.987 |

**MANUFACTURING FORMULA (Contd…..):**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Material Code** | **Material Name & Specification** | **Vendor Details** | **UOM** | **Quantity / Unit** | **UOM** | **Quantity / Batch** |
| **Extra granular Ingredient (Lubrication):** | | | | | | | |
| 9 | 1002613 | Stearic Acid, Ph.Eur(Speziol® L2SM GF Pharma) | BASF | mg | 8.000 | Kg | 1.000 |
| **Core tablet Mass:** | | | | **mg** | **645.000** | **Kg** | **80.625** |
| \*\* This quantity is to be based on 100% m/m assay.  # Qty. of intra granular portion of Cellulose, Microcrystalline, Ph.Eur (Avicel PH101) to be adjusted to get a constant tablet mass based on actual assay and % m/m Water content of Valganciclovir Hydrochloride.  @ Purified Water shall be dispensed by production personnel.It will not appear in the final product except in traces.  $ Additional quantity of Purified water to be added in incremental quantity until to get the desired granular consistency is formed.  **Note: Weigh the Purified Water as per least count of the weighing balance.**  **¥ Dispensing shall be done in 2 lots.** | | | | | | | |

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| **Assay Based calculations for Valganciclovir Hydrochloride, IH: (Single A.R. No.)**  Theoretical Qty. x 100 x 100\_x 1000000 \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Formula – 1 =  (Assay on anhydrous & Solvent free basis) x (100 – % m/m water content) x (1000000 – Residual Solvents (ppm))  **Assay Based calculations for Valganciclovir Hydrochloride, IH: (Multiple A.R. No.):**  Qty. available x (Assay on anhydrous & Solvent free basis) x (100 – % m/m water content) x (1000000 – Residual Solvents (ppm))  Formula – 2 =  100 x 100 x 1000000  ­­\_\_\_\_\_\_\_\_\_\_\_\_­­­­­\_\_\_\_\_\_\_\_\_ Balance Qty. x 100 x 100\_x 1000000 \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Formula – 3 =  (Assay on anhydrous & Solvent free basis) x (100 - % m/m water content) x (1000000 – Residual Solvents (ppm))  Theoretical Quantity of Valganciclovir Hydrochloride, IH = 62.038 Kg. |

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| **Valganciclovir Hydrochloride, IH** | | | | | | **Calculated by (WH)**  **(Sign & Date)** | **Verified by (QA)**  **(Sign & Date)** |
| **Lot No.** | **A.R. No.** | **% m/m water content by KF** | **Assay on Anhydrous basis & Solvent free basis** | **Residual Solvents (ppm)** | **Quantity (Kg)** |
| **I** |  |  |  |  |  |  |  |
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| **II** |  |  |  |  |  |  |  |
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| **Assay Based calculations (Lot-I):** |
| **Assay Based calculations (Lot-II):** |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Name of Ingredient** | **UOM** |  | **Lot-I** | | **Lot-II** | **Total (Kg)** |
| **1.0** | **Compensation of Cellulose, Microcrystalline Ph.Eur (Avicel PH101):** | | | | | | |
| 1.1 | Valganciclovir Hydrochloride IH | Kg | Std.Qty.-A | 31.019 | | 31.019 | 62.038 |
| Issued. Qty.-B |  | |  |  |
| 1.2 | Cellulose, microcrystalline Ph.Eur (Avicel PH 101) | Kg | Std.Qty.-C | 5.897 | | 5.897 | 11.794 |
| 1.3 | To be dispensed quantity of Cellulose, Microcrystalline, Ph.Eur (Avicel PH101) | Kg | (A+C) – B |  | |  |  |
| **Calculated By (WH – Sign & Date)** | | | | |  |  |  |
| **Checked By (QA– Sign & Date)** | | | | |  |  |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Dispensing Instructions**:   * 1. Follow the gowning procedures as per **SOP NO. WH012**   2. Wear safety nose masks and gloves to avoid contact with skin.   3. Dispense only in the dispensing area.   4. Dispense only approved materials for production.   5. Check and ensure that all balances are calibrated before use.   6. Check the raw materials for Name, Material codes, Appearance (Visual check), Quantity, A.R. No. and Expiry /retesting date (if any) etc.,   7. Check for assay in case of active ingredients and dispense the quantity as mentioned in Assay based calculation sheet.   8. Weigh each raw material in properly tared containers, polybags and label them accordingly.   9. Select the balance for dispensing materials based on the operating range displayed on the balance.  |  |  |  | | --- | --- | --- | | **List of abbreviation:** | | | | IH/IHS | : | In House Specification LOD : Loss on Drying | | NMT | : | Not More Than WC : Water column | | NLT | : | Not Less Than Pa : Pascal | | USP | : | United States Pharmacopoeia mm : millimeter | | mg | : | Milligram Kg : Kilogram | | SOP | : | Standard Operating Procedure QA : Quality Assurance | | HEPA | : | High Efficiency Particulate Air No. : Number | | cGMP | : | current Good Manufacturing Practices Qty. : Quantity | | RH | : | Relative Humidity PD : Production | | A.R. | : | Analytical Reference ADU : Air Displacement Unit | | NA | : | Not Applicable WH : Ware House | | %m/m | : | Percentage mass by mass ID : Identity | | Ph.Eur | : | European Pharmacopoeia UOM : Units of measure | | RPM | : | Rotation per minute | | ºC | : | Degree centigrade | |

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| **Dispensing Area cGMP Check List:** | | | | |
| **Check the following** | | | **Active Dispensing** | |
| **ROOM No.:\_\_\_\_\_\_\_\_\_\_\_** | |
| **Status** | |
| Area and dispensing booth cleanliness | | |  | |
| Previous product/Batch No. | | |  | |
| Removal of previous product material | | |  | |
| Balance calibration records | | |  | |
| Differential pressure of room **(Start of the activity) (\_\_\_\_\_\_\_\_\_ mm of WC)** | | | Men Entry: | Material Entry: |
| Differential pressure of room **(End of the activity)( \_\_\_\_\_\_\_\_\_ mm of WC)** | | | Men Entry: | Material Entry: |
| Temperature (0C) and relative humidity (%) (Start of the activity)(NMT 25oC & RH NMT 40%) | | |  | |
| Temperature (0C) and relative humidity (%) (End of the activity)(NMT 25oC & RH NMT 40%) | | |  | |
| Differential pressure of Dispensing Booth | **HEPA filter** | **Pa – Pa** |  | |
| **Intermediate filter** | **Pa – Pa** |  | |
| **Pre filters** | **Pa – Pa** |  | |
| **Checked by (Warehouse) (Sign & Date)** | | |  | |
| **Verified by (QA) (Sign & Date)** | | |  | |

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| **Dispensing Area cGMP Check List:** | | | | |
| **Check the following** | | | **In-active Dispensing** | |
| **ROOM No.:\_\_\_\_\_\_\_\_\_\_\_** | |
| **Status** | |
| Area and dispensing booth cleanliness | | |  | |
| Previous product/Batch No. | | |  | |
| Removal of previous product material | | |  | |
| Balance calibration records | | |  | |
| Differential pressure of room **(Start of the activity) (\_\_\_\_\_\_\_\_\_ mm of WC)** | | | Men Entry: | Material Entry: |
| Differential pressure of room **(End of the activity)( \_\_\_\_\_\_\_\_\_ mm of WC)** | | | Men Entry: | Material Entry: |
| Temperature (0C) and relative humidity (%) (Start of the activity)(NMT 25oC & RH NMT 55%) | | |  | |
| Temperature (0C) and relative humidity (%) (End of the activity)(NMT 25oC & RH NMT 55%) | | |  | |
| Differential pressure of Dispensing Booth | **HEPA filter** | **Pa – Pa** |  | |
| **Intermediate filter** | **Pa – Pa** |  | |
| **Pre filters** | **Pa – Pa** |  | |
| **Checked by (Warehouse) (Sign & Date)** | | |  | |
| **Verified by (QA) (Sign & Date)** | | |  | |

**2.0 Weighing Record:**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Name of ingredient** | | Batch No. / **GRN No.** | **A.R. No.** | | **Container**  **No.** | **Gross**  **Weight (kg)** | | **Tare**  **Weight (kg)** | **Net**  **Weight (kg)** |
| **1** | Valganciclovir Hydrochloride, IH  **(\_\_\_\_\_\_\_\_Kg) (Lot – I)** | |  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
| **Total Net mass ⇒** | | | | | | |  |
| Valganciclovir Hydrochloride, IH  **(\_\_\_\_\_\_\_\_Kg) (Lot – II)** | |  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
| **Total Net mass ⇒** | | | | | | |  |
| **2.** | Cellulose , Microcrystalline Ph.Eur  (Avicel PH 101)  **(\_\_\_\_\_\_\_\_Kg) (Lot – I)** | |  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
| **Total Net mass ⇒** | | | | | | |  |
| Cellulose , Microcrystalline Ph.Eur  (Avicel PH 101)  **(\_\_\_\_\_\_\_\_Kg) (Lot – II)** | |  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
|  |  | |  |  | |  |  |
| **Total Net mass ⇒** | | | | | | |  |
| **Refer Attached Printout (Attached / Not Attached).** | | | | | | | | | | |
| **Activity** | | **Weighing Balance ID** | | | **Done By (Sign & Date)** | | | **Verified By (QA). (Sign & Date)** | | |
| **Dispensing (WH)** | |  | | |  | | |  | | |
| **Cross Verification (PD)** | |  | | |  | | |  | | |

**2.0 Weighing Record (Cont.…):**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Name of ingredient** | | Batch No. / **GRN No.** | **A.R. No.** | **Container**  **No.** | **Gross**  **Weight (kg)** | | **Tare**  **Weight (kg)** | **Net**  **Weight (kg)** |
| **3.** | Crospovidone, Ph.Eur (Kollidon CL)    **(0.215 Kg) (Lot – I)** | |  |  |  |  | |  |  |
|  |  |  |  | |  |  |
|  |  |  |  | |  |  |
| **Total Net mass ⇒** | | | | | |  |
| Crospovidone, Ph.Eur (Kollidon CL)  **(0.216 Kg) (Lot – II)** | |  |  |  |  | |  |  |
|  |  |  |  | |  |  |
|  |  |  |  | |  |  |
| **Total Net mass ⇒** | | | | | |  |
| **4.** | Povidone, Ph.Eur (Kollidon 30)  **(0.750 Kg) (Lot – I)** | |  |  |  |  | |  |  |
|  |  |  |  | |  |  |
|  |  |  |  | |  |  |
| **Total Net mass ⇒** | | | | | |  |
| Povidone, Ph.Eur (Kollidon 30)  **(0.750 Kg) (Lot – II)** | |  |  |  |  | |  |  |
|  |  |  |  | |  |  |
|  |  |  |  | |  |  |
| **Total Net mass ⇒** | | | | | |  |
| **Refer Attached Printout (Attached / Not Attached).** | | | | | | | | | |
| **Activity** | | **Weighing Balance ID** | | | **Done By (Sign & Date)** | | **Verified By (QA) (Sign & Date)** | | |
| **Dispensing (WH)** | |  | | |  | |  | | |
| **Cross Verification (PD)** | |  | | |  | |  | | |

**2.0 Weighing Record (Cont.…):**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Name of ingredient** | | Batch No. / **GRN No.** | **A.R. No.** | | **Container**  **No.** | **Gross**  **Weight (kg)** | **Tare**  **Weight (kg)** | **Net**  **Weight (kg)** |
| **5** | Cellulose, Microcrystalline Ph.Eur (Avicel PH101)  **1.875 Kg** | |  |  | |  |  |  |  |
|  |  | |  |  |  |  |
|  |  | |  |  |  |  |
| **Total Net mass ⇒** | | | | | |  |
| **6** | Crospovidone, Ph.Eur (Kollidon CL)  **1.987 Kg** | |  |  | |  |  |  |  |
|  |  | |  |  |  |  |
|  |  | |  |  |  |  |
| **Total Net mass ⇒** | | | | | |  |
| **7** | Stearic Acid, Ph.Eur (Speziol® L2SM GF Pharma)  **1.000 Kg** | |  |  |  | |  |  |  |
|  |  |  | |  |  |  |
|  |  |  | |  |  |  |
| **Total Net mass ⇒** | | | | | |  |
| **Refer Attached Printout (Attached / Not Attached).** | | | | | | | | | |
| **Activity** | | **Weighing Balance ID** | | | | **Done By (Sign & Date)** | | **Verified By (QA) (Sign & Date)** | |
| **Dispensing (WH)** | |  | | | |  | |  | |
| **Cross Verification (PD)** | |  | | | |  | |  | |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **GRANULATION:**  **General & Safety precautions:**   1. Follow gowning procedure as per **SOP NO. PD002 and PD003**. 2. Snood for entire face covering. 3. Wear safety masks and gloves to avoid contact with skin. 4. Avoid skin contact while handling and processing bulk active drug substance. 5. Air stream helmets. 6. Goggles for eye protection if required. 7. Nose mask for respiratory protection (3M mask). 8. Ensure earthing of the machine. 9. Do not put your hands inside the bowl when blades are moving.  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **SUMMARY OF EQUIPMENTS USED IN MANUFACTURING** | | | | | | | **Name of the equipment** | **Equipment No.** | **Model / Type** | **Capacity / size** | **Manufacturer’s details** | **Operation SOP No. & Cleaning SOP No.** | | Vibratory sifter | PDE – 1088 | SAI-750 | 30” | Tapasya | PD329† | | Vibratory sifter | PDE – 1096 | GMP | 30” | Sams | PD045†/ PD046† | | Vibratory sifter | PDE – 1037 | GMP | 30” | Sam’s | | Vibratory sifter | PDE-1098/ PDE-1099 | GMP, FLP | 30” | Sam’s | PD045†/ PD046† | | Vibratory sifter | PDE – 1001 | VSFT 750, GMP | 30” | Gansons | PD221† | | Rapid mixer granulator | PDE - 1003 | HSMG-250L | 250 L | Gansons | PD223† | | Fluid bed dryer | PDE – 1004 | GFBD-250 L | 250 L | Gansons | PD225† | | Portable stirrer | PDE-1152 | GMP | 50 L | Nava Bharath Pharma Technologies | PD354† | | Portable stirrer | PDE-1153 | GMP | 100 L | Nava Bharath Pharma  Technologies | PD354† | | Mobile cone mill cum multi mill | PDE – 1024/  PDE-1038 | SAI-CM-500 | 500 Kg/hr | Tapasya | PD216† | | Pillar type bin blender | PDE – 1007 | Gansons bin blender system is GMP compliance | 250 L | Gansons | PD227† | | Pillar type bin blender | PDE-1513 | BB-500/750L | 250L | GEM Pharma | PD467† |   **† Current effective version to be referred.** | | | | | | |
| **Activity** | **Date** | **Time** | **Differential pressure**  **(\_\_\_\_\_\_\_\_\_ mm of WC)** | **Temperature**  **(NMT 25°C)** | **% Relative Humidity (NMT 40% RH)** | **Done By**  **(Sign & Date)** |
| Start of Activity |  |  |  |  |  |  |
| End of Activity |  |  |  |  |  |  |
| Start of Activity |  |  |  |  |  |  |
| End of Activity |  |  |  |  |  |  |
| Start of Activity |  |  |  |  |  |  |
| End of Activity |  |  |  |  |  |  |
| **Manufacturing Area cGMP Check List:**  Inspect the working area and equipment for cleanliness before use and ensure that the status tags are properly filled in.    **Area Clearance:**   |  |  | | --- | --- | | **Check the following** | **Status** | | Room Name & No. |  | | Previous Product & Batch No. |  | | Type of Area cleaning | **Type A /  Type B** | | Area Cleanliness | **Satisfactory / Not Satisfactory** |   **Note: Enter √ mark on the Type A /  Type B and Satisfactory / Not Satisfactory**  **Inspected By (PD) (Sign & Date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Checked By (PD) (Sign & Date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** | | | | | | |

**Equipment Clearance:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Equipment Name** | **Equipment No.** | **Previous Product** | **Batch No.** | **Strength/Batch/ Product/**  **Colour change over** | **Type of cleaning** |
| Vibratory sifter | PDE – 1088 |  |  |  |  |
| Vibratory sifter | PDE – 1096 |  |  |  |  |
| Vibratory sifter | PDE – 1037 |  |  |  |  |
| Vibratory sifter | PDE-1098/ PDE-1099 |  |  |  |  |
| Vibratory sifter | PDE – 1001 |  |  |  |  |
| Rapid mixer granulator | PDE – 1003 |  |  |  |  |
| Fluid bed dryer | PDE – 1004 |  |  |  |  |
| Portable stirrer | PDE-1152 |  |  |  |  |
| Portable stirrer | PDE-1153 |  |  |  |  |
| Mobile cone mill cum multi mill | PDE – 1024/  PDE-1038 |  |  |  |  |
| Mechanical Stirrer | PDA- |  |  |  |  |
| **Checked By (PD)(Sign & Date):\_\_\_\_\_\_\_\_\_\_\_\_\_ Approved By (QA)(Sign & Date)\_\_\_\_\_\_\_\_\_\_\_\_\_\_** | | | | | |

|  |  |
| --- | --- |
| **Step No.** | **Process Instructions** |
| **3.0** | **Sifting:** |
| 3.1 | Check the integrity of the Sieve before and after use Record the observations in the given table **(Sieve Integrity Check).** |
| 3.2 | Check the Integrity of the All gaskets for the first campaign batch and last campaign batch. Record the observations in the given table  **(Gasket Integrity Check).** |
| 3.3 | Sift **Cellulose, Microcrystalline (Avicel PH101)** and **Crospovidone, (Kollidon CL)** together through mesh **# 30** fitted  On vibratory sifter. Collect the sifted materials into a suitable container / double lined polyethylene bag. |
| 3.4 | Sift **Valganciclovir Hydrochloride**, andthematerials ofStep No **3.3** together through mesh **# 20** fitted on vibratory sifter. Collect the sifted materials into a suitable container / double lined polyethylene bag. |
| |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **3.1** | **Sieve Integrity Check** | | | | | | **Sieve No.** | **Sieve Code No.** | **Sieve Integrity before use** | **Checked By**  **(Sign & Date)** | **Sieve Integrity after use** | **Checked By**  **(Sign & Date)** | | **# 30** |  | S  / NS  |  | S  / NS  |  | | **# 20** |  | S  / NS  |  | S  / NS  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | | **3.2** | **\*Gasket Integrity Check** | | | | | **Gasket Integrity Before use**  **Campaign first Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | **Checked By (Sign & Date)** | **Gasket Integrity after use**  **Campaign last Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | **Checked By (Sign & Date)** | | S / NS / NA  | |  | S / NS / NA  |  | | **\*Note: Gasket Integrity shall be checked for the 1st Batch of campaign and end of the campaign.** | | | | |   **Note: Enter √ mark on the S-Satisfactory / NS-Not Satisfactory;NA-Not applicable**   | **Process Details** | Lot-I | Lot-II | | --- | --- | --- | | Start of activity by Name |  |  | | Start Time |  |  | | Sign & Date |  |  | | Sifter ID No. |  |  | | End of activity by Name |  |  | | End Time |  |  | | Sign & Date |  |  | | **Checked By (Sign & Date)** |  |  | | |

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| **Step No.** | **Process Instructions** |
| **4.0** | **DRY MIXING:** |
| 4.1 | Check the integrity of the RMG filter bag integrity and screen integrity before and after use. Record the observations in the given table  **(RMG Filter Bag and Screen Integrity Check).** |
| 4.2 | Check the Integrity of the All gaskets for the first campaign batch and last campaign batch. Record the observations in the given table  **(Gasket Integrity Check).** |
| 4.3 | Transfer the sifted materials of Step No.**3.4** into Rapid mixer Granulator. |
| 4.4 | Mix for **10 minutes** with **impeller at slow speed (75 RPM) and chopper off** and record the amperage reading of impeller motor**.** |
| 4.5 | Withdraw the in – process sample - by QA as per **SOP QA023†, † Current effective version to be referred.** |
| **5.0** | **PREPARATION OF GRANULATING SOLUTION:** |
| 5.1 | Take purified water in S.S container equipped with a propeller stirrer. |
| 5.2 | Add **Povidone, (Kollidon 30)** slowly to Purified water of step No. **5.1** while stirring, Increase the speed of stirrer if necessary. Continue stirring till to get a clear solution. |
| **6.0** | **WET GRANULATION:** |
| 6.1 | Granulate the dry mix of Step No. **4.4** by adding granulating solution of step No. **5.2** **for 2 minutes** while mixingwith **impeller at fast speed (120 RPM) and chopper at** **fast speed** and record the amperage readings of impeller motor and chopper motor. |
| 6.1 (A) | **Note:** Hand squeeze the powder mix collected from four different locations in granulator and then check whether the powder mix adequately  moistened (Wetted or not Wetted) |
| 6.2 | Based on granulation consistency add additional quantity of Purified water **(0.900 Kg per each Lot) for 1 minute** while mixing with **impeller at** **fast speed (120 RPM) and chopper at** **fast speed** andrecord the amperage reading of impeller motor and chopper motor. |
| 6.2 (A) | **Note:** Hand squeeze the powder mix collected from four different locations in granulator and then check whether the powder mix adequately  moistened (Wetted or not Wetted) |
| 6.3 | Knead the wet mass **for 1 minute** with **impeller at** **fast speed (120 RPM) and** **chopper** **at** **fast speed** check for complete formation of granules and record the amperage readings of impeller and chopper motor. |
| 6.4 | End point is determined by the physical observation of wet mass. The wet mass is observed for end point where the formation of discrete  Granules take place. |
| **Note : Impeller amperage limit 014 – 016 AMP** |
| 6.5 | Withdraw the in – process sample - by QA as per **SOP QA023†** |

**† Current effective version to be referred.**

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| **Step No.** | **Process Instructions** |
| **7.0** | **WET MASS DISCHARGE:** |
| 7.1 | Check the FBD Bowl Sieve Integrity before and after use. Unloading the wet mass into bowls |
| 7.2 | Discharge the wet mass while mixing **Impeller at slow speed (20-75 RPM)** into Fluid Bed Dryer Bowl through Co-mill fitted with **8.0 mm** screen. |

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| **4.0** | **DRY MIXING** | | | | | | | | | |
| **4.1** | **RMG Filter Bag and RMG Screen Integrity Check** | | | | | | | | | |
| **RMG Filter Bag**  **integrity** | | | **RMG Filter Bag No.** | | **RMG Filter Bag Integrity before use** | | **Checked By**  **(Sign & Date)** | **RMG Filter Bag Integrity after use** | | **Checked By**  **(Sign & Date)** |
|  | | S  / NS  | |  | S  / NS  | |  |
| **Screen**  **integrity** | | | **8.0 mm Screen**  **Code No.** | | **Screen Integrity before use** | | **Checked By**  **(Sign & Date)** | **Screen Integrity**  **after use** | | **Checked By**  **(Sign & Date)** |
|  | | S / NS  | |  | S  / NS  | |  |
| **4.2** | | **\*Gasket Integrity Check** | | | | | | | | |
| **Gasket Integrity Before use**  **Campaign first Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | | **Checked By(Sign & Date)** | | **Gasket Integrity after use**  **Campaign last Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | **Checked By(Sign & Date)** | |
| S / NS / NA  | | | |  | | S / NS / NA  | | |  | |
| **\*Note: Gasket Integrity shall be checked for the 1st Batch of campaign and end of the campaign.** | | | | | | | | | | |

**Note: Put ‘√’ mark** **S – Satisfactory/** **NS – Not Satisfactory;** **NA-Not applicable**

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| **Step No.** | | **Process Instructions** | | | |
| **4.0** | **DRY MIXING (Cont.…)** | | | Lot-I | Lot-II |
| **Equipment No.** | | | |  |  |
| **Activity Start By** | | | Time |  |  |
| Name |  |  |
| Sign & Date |  |  |
| 4.3 | Loading of sifted material into RMG | | **Start time** |  |  |
| **Sign & Date** |  |  |
| **End time** |  |  |
| **Sign & Date** |  |  |
| 4.4 | **Mixing set time (10 Minutes)** | | |  |  |
| **Impeller slow speed** **(75 RPM)** | | |  |  |
| **Impeller Amperage (AMP)** | | |  |  |
| **Activity End By** | | | Time |  |  |
| Name |  |  |
| Sign & Date |  |  |
| 4.5 | **Sampled By (QA)** | | Sample (Qty) |  |  |
| Name |  |  |
| Sign & Date |  |  |

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| **Step No.** | **Process Instructions** | | | | | | | |
| **5.0 PREPARATION OF GRANULATING SOLUTION** | | | | | **Weighing Record** | | | |
| **Weighing Balance ID No.** | | | | |  | | | |
| **5.1** | **Name of ingredient** | **A.R. No.** | **Container No.** | **Gross Weight (kg)** | | **Tare Weight (kg)** | **Net Weight (kg)** | **Collected By (Sign & Date)** |
| Purified water, IHS/USP/Ph.Eur  **3.750 kg (Lot-I)** |  |  |  | |  |  |  |
|  |  |  | |  |  |  |
|  |  |  | |  |  |  |
| Purified water, IHS/USP/Ph.Eur  **3.750 kg (Lot-II)** |  |  |  | |  |  |  |
|  |  |  | |  |  |  |
|  |  |  | |  |  |  |
| **5.1 (A)** | Purified water, IHS/USP/Ph.Eur  (additional quantity)  **0.900 Kg (Lot-I)** |  |  |  | |  |  |  |
|  |  |  | |  |  |  |
|  |  |  | |  |  |  |
| Purified water, IHS/USP/Ph.Eur  (additional quantity)  **0.900 kg (Lot-II)** |  |  |  | |  |  |  |
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| **Step No.** | **Process Instructions** | | Lot-I | Lot-II |
| **5.0** | **Granulating Solution Preparation** | |  |  |
| **Activity Start By** | | Time |  |  |
| Name |  |  |
| Sign & Date |  |  |
| **5.1** | Take purified water in S.S vessel container equipped with a propeller stirrer. | | | |
| **5.2** | Add Povidone, (Kollidon 30) slowly to Purified water of step No. 5.1 while stirring, Increase the speed of stirrer if necessary. Continue stirring till to get a clear solution. | | | |
| **Activity End By** | | Time |  |  |
| Name |  |  |
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| **Step No.** | **Process Instructions** | | | |
| **6.0** | **WET GRANULATION** | | Lot-I | Lot-II |
| **Activity Start By** | | Name |  |  |
| Sign & Date |  |  |
| Time |  |  |
| **6.1** | Granulate the dry mix by adding granulating solution | Total Mixing set time **(for 2 minutes)** |  |  |
| Impeller at fast Speed **(120 RPM)** |  |  |
| chopper at fast speed |  |  |
| Impeller AMP |  |  |
| Chopper AMP |  |  |
| **6.1 (A)** | Whether the powder mix adequately moistened (Wetted) or not. | | Yes /No  | Yes /No  |
| **6.2** | **Weighing balance ID No** | |  |  |
| Based on granulation consistency add additional quantity of purified water **(0.900 Kg per each Lot)** | Mixing time **(for 1 Minute)** |  |  |
| Impeller at fast speed **(120 RPM)** |  |  |
| Chopper at fast speed |  |  |
| Chopper AMP |  |  |
| Impeller AMP |  |  |
| Quantity of Purified water added (Kg) |  |  |
| **6.2 (A)** | Whether the powder mix adequately moistened (Wetted) or not. | | Yes /No  | Yes /No  |
| **6.3** | Knead the wet mass | Mixing time (**for 1 minute**) |  |  |
| Impeller at fast speed **(120 RPM)** |  |  |
| Chopper fast speed |  |  |
| Impeller AMP |  |  |
| Chopper AMP |  |  |

**Note: Put ‘√’ mark as applicable; Yes / No **

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| **Step No.** | **Process Instructions** | | | | | | | |
| **6.0** | **WET GRANULATION (Cont….)** | | | | | Lot-I | Lot-II | |
| **6.4** | End point by physical observation | | | | | Confirmed/ Not Confirmed | Confirmed/ Not Confirmed | |
| End point by physical observation made by | | | Name | |  | |  |
| Time | |  | |  |
| Sign & Date | |  | |  |
| **Note : Impeller amperage limit 014 – 016 AMP** | | | | | | | | |
| **6.5** | Sampled By (QA) | | Sampled Qty | | |  |  | | |
| Name | | |  |  | | |
| Sign & Date | | |  |  | | |
| **7.0** | Wet Mass Discharge | | | | | | | | |
| 7.1 | FBD Bowls Sieve Integrity Check (before use) | | | | | S / NS  | S / NS  | | |
| **Checked by (Sign & Date)** | | | | |  |  | | |
| 7.2 | Discharge the wet mass while mixing **Impeller at slow speed (20-75 RPM)** into Fluid Bed Dryer Bowl through Co-mill fitted with **8.0 mm** screen. | | | | **Impeller RPM** | Done / Not Done | Done / Not Done | | |
|  |  | | |
| **End of Activity by** | | **Name** | | | |  |  | | |
| **Time** | | | |  |  | | |
| **Sign & Date** | | | |  |  | | |
| **Checked by** | | **Sign & Date** | | | |  |  | | |
| **Note: Put ‘√’ mark as applicable; S – Satisfactory; NS – Not Satisfactory Done / Not Done ; Confirmed/ Not Confirmed** | | | | | | | | | |

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| **Step No.** | **Process Instructions** |
| 8.0 | **DRYING** |
| 8.1 | Check the integrity of the finger bags before and after use. Record the observations in the given table **(FBD Finger Bag Integrity Check).** |
| 8.2 | Check the Integrity of the All gaskets for the first campaign batch and last campaign batch. Record the observations in the given table  **(Gasket Integrity Check).** |
| 8.3 | Verify the Air Pressure before start of the drying activity. **(Air Pressure Check )** |
| 8.4 | Dry the wet mass of Step No. **7.2** at an inlet air temperature **Not more than** **600C** in fluid bed dryer till to get **LOD in the range of 3.0 to 4.0%** **m/m** at **1050C** by auto mode using suitable moisture analyzer. Check and record the LOD of the granules. |
| 8.5 | Record the inlet temperature, Bed temperature and outlet temperature for **every 15 minutes or as and when required**. Rake the granules intermittently as and when required. Record the operation details in the following table **(Drying Monitoring Record).** |
| Withdraw the in – process sample – by QA as per **SOP QA023†,**  **† Current effective version to be referred.** |
| **9.0** | **Sifting And Milling of Dried Granules** |
| 9.1 | Check the integrity of the sieve before and after use. Record the observations in the given table **(Sieve Integrity Check).** |
| 9.2 | Check the screen integrity before and after milling. Record the observations in the given table **(Screen Integrity Check).** |
| 9.3 | Check the Integrity of the All gaskets for the first campaign batch and last campaign batch. Record the observations in the given table  **(Gasket Integrity Check).** |
| 9.4 | Sift the dried granules of Step No. **8.4** through mesh **# 24** and mill the retentions using mobile cone mill cum multi mill fitted with **1.5 mm screen** at **slow speed/Knives forward direction.** |
| 9.5 | Sift the milled granules of Step No. **9.4** through mesh **# 24** and mill the retentions (if any) using mobile cone mill cum multi mill fitted with **1.5 mm screen** at **medium speed/ Knives forward direction.** |
| 9.6 | If required repeat the Step No.**9.5** till all granules passed through mesh **# 24**.Collect the sifted granules into a suitable container / double lined polyethylene bag. |
| 9.7 | Record the Net mass of sifted and milled granules. |

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| **8.1** | **FBD Finger Bag integrity Check** | | | | | | | | | | | | |
| **Finger Bag integrity** | | | | **Finger Bag No.** | | | **Finger Bag integrity before use** | | **Checked By**  **(Sign & Date)** | | **Finger Bag integrity after use** | | **Checked By**  **(Sign & Date)** |
|  | | | S  / NS  | |  | | S  / NS  | |  |
| **8.2** | | **\*Gasket Integrity Check** | | | | | | | | | | | |
| **Gasket Integrity Before use**  **Campaign first Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | | | | **Checked By (Sign & Date)** | | **Gasket Integrity after use**  **Campaign last Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | | **Checked By (Sign & Date)** | |
| S / NS / NA  | | | | | |  | | S / NS / NA  | | | |  | |
| **\*Note: Gasket Integrity shall be checked for the 1st Batch of campaign and end of the campaign.** | | | | | | | | | | | | | |
| **8.3** | | | **Air Pressure Check** | | | | | | | | | | |
| **Lot No.** | | | | | **Lot -I** | | | | | **Lot -II** | | | |
| **Air Pressure before Use** | | | | | S / NS  | | | | | S / NS  | | | |
| **Checked By (Sign & Date)** | | | | |  | | | | |  | | | |
| **Note: Put ‘√’ mark** **S – Satisfactory/** **NS – Not Satisfactory;****NA-Not applicable** | | | | | | | | | | | | | |

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| **8.4 Drying Monitoring Record: (Lot – I)** | | | | | | | | | | | | | | | | | |
| Start by (Name, Sign & date) | | | | | | | |  | | | | |  | | | | |
| Equipment No. | | | | | | | |  | | | | | | | | | |
| Moisture analyzer ID No. | | | | | | | |  | | | | | | | | | |
| Activity | Time | | Temperature (ºC) | | | Drying time  (Min) | LOD (%) | Activity | Time | | | Temperature (ºC) | | | | Drying time  (Min) | LOD (%) |
| Start | End | Inlet | Bed | Out let | Start | End | | Inlet | | Bed | Out let |
| Drying Cycle-1 |  |  |  |  |  |  |  | Drying Cycle-12 |  |  | |  | |  |  |  |  |
| Drying Cycle-2 |  |  |  |  |  |  |  | Drying Cycle-13 |  |  | |  | |  |  |  |  |
| Drying Cycle-3 |  |  |  |  |  |  |  | Drying Cycle-14 |  |  | |  | |  |  |  |  |
| Drying Cycle-4 |  |  |  |  |  |  |  | Drying Cycle-15 |  |  | |  | |  |  |  |  |
| Drying Cycle-5 |  |  |  |  |  |  |  | Drying Cycle-16 |  |  | |  | |  |  |  |  |
| Drying Cycle-6 |  |  |  |  |  |  |  | Drying Cycle-17 |  |  | |  | |  |  |  |  |
| Drying Cycle-7 |  |  |  |  |  |  |  | Drying Cycle-18 |  |  | |  | |  |  |  |  |
| Drying Cycle-8 |  |  |  |  |  |  |  | Drying Cycle-19 |  |  | |  | |  |  |  |  |
| Drying Cycle-9 |  |  |  |  |  |  |  | Drying Cycle-20 |  |  | |  | |  |  |  |  |
| Drying Cycle-10 |  |  |  |  |  |  |  | Drying Cycle-21 |  |  | |  | |  |  |  |  |
| Drying Cycle-11 |  |  |  |  |  |  |  | Drying Cycle-22 |  |  | |  | |  |  |  |  |
| **Refer Printout Attached / Not Attached** | | | | | | | | | | | | | | | | | |
| Total Drying Time (Min) : | | | | |  | | | Sample Qty: | | |  | | | | | | |
| **End of Activity By**  **(Sign & Date)** | |  | | | | | | **Sampled By (QA)(Sign & Date)** | | |  | | | | | | |
| **8.4 Drying Monitoring Record: (Lot – II)** | | | | | | | | | | | | | | | | | |
| Start by (Name, Sign & date) | | | | | | | |  | | | | |  | | | | |
| Equipment No. | | | | | | | |  | | | | | | | | | |
| Moisture analyzer ID No. | | | | | | | |  | | | | | | | | | |
| Activity | Time | | Temperature (ºC) | | | Drying time  (Min) | LOD (%) | Activity | Time | | | Temperature (ºC) | | | | Drying time  (Min) | LOD (%) |
| Start | End | Inlet | Bed | Out let | Start | End | | Inlet | | Bed | Out let |
| Drying Cycle-1 |  |  |  |  |  |  |  | Drying Cycle-12 |  |  | |  | |  |  |  |  |
| Drying Cycle-2 |  |  |  |  |  |  |  | Drying Cycle-13 |  |  | |  | |  |  |  |  |
| Drying Cycle-3 |  |  |  |  |  |  |  | Drying Cycle-14 |  |  | |  | |  |  |  |  |
| Drying Cycle-4 |  |  |  |  |  |  |  | Drying Cycle-15 |  |  | |  | |  |  |  |  |
| Drying Cycle-5 |  |  |  |  |  |  |  | Drying Cycle-16 |  |  | |  | |  |  |  |  |
| Drying Cycle-6 |  |  |  |  |  |  |  | Drying Cycle-17 |  |  | |  | |  |  |  |  |
| Drying Cycle-7 |  |  |  |  |  |  |  | Drying Cycle-18 |  |  | |  | |  |  |  |  |
| Drying Cycle-8 |  |  |  |  |  |  |  | Drying Cycle-19 |  |  | |  | |  |  |  |  |
| Drying Cycle-9 |  |  |  |  |  |  |  | Drying Cycle-20 |  |  | |  | |  |  |  |  |
| Drying Cycle-10 |  |  |  |  |  |  |  | Drying Cycle-21 |  |  | |  | |  |  |  |  |
| Drying Cycle-11 |  |  |  |  |  |  |  | Drying Cycle-22 |  |  | |  | |  |  |  |  |
| **Refer Printout Attached / Not Attached** | | | | | | | | | | | | | | | | | |
| Total Drying Time (Min) : | | | | |  | | | Sample Qty: | | |  | | | | | | |
| **End of Activity By**  **(Sign & Date)** | |  | | | | | | **Sampled By (QA)(Sign & Date)** | | |  | | | | | | |

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| **Step No.** | **Process Instructions** | | **Lot-I** | **Lot-II** |
| **9.0** | **Sifting And Milling of Dried Granules** | | | |
| **Start of activity By** | | **Name** |  |  |
| **Sign & Date** |  |  |
| **Time** |  |  |
| Mobile cone mill cum multi mill ID | | |  |  |
| Sifter ID No. | | |  |  |

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| **Sieve Integrity Check** | | | | | | | | | |
| 9.1 | **Sieve No.** | **Sieve Code No.** | | | **Sieve Integrity before use** | **Checked By (Sign& Date)** | **Sieve Integrity after use** | | **Checked By**  **(Sign & Date)** |
| **# 24** |  | | | S  / NS  |  | S  / NS  | |  |
| **Screen Integrity Check** | | | | | | | | | |
| 9.2 | **Screen No.** | **Screen Code No.** | | | **Screen Integrity before use** | **Checked By (Sign& Date)** | **Screen Integrity after use** | | **Checked By**  **(Sign & Date)** |
| **1.5 mm** |  | | | S  / NS  |  | S  / NS  | |  |
| 9.3 | **\*Gasket Integrity Check** | | | | | | | | |
| **Gasket Integrity Before use**  **Campaign first Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | **Checked By(Sign & Date)** | **Gasket Integrity after use**  **Campaign last Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | | **Checked By(Sign & Date)** | |
| S / NS / NA  | | |  | S / NS / NA  | | | |  | |
| **\*Note: Gasket Integrity shall be checked for the 1st Batch of campaign and end of the campaign.** | | | | | | | | | |

**Note: Enter √ mark on the S-Satisfactory / NS-Not Satisfactory;NA-Not applicable**

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| **Step No.** | **Process Instructions** | | | **Lot-I** | **Lot-II** |
| **9.0** | **Sifting And Milling of Dried Granules (Cont…..)** | | | | |
| 9.4 | Sift the dried granules Step No.**8.4** through mesh **#24** | | | Yes / No | Yes / No |
| Mill the retentions milling speed at **slow speed /Knives forward direction** | | |  |  |
| 9.5 | Sift the milled granules of Step No.**9.4** through mesh **#24** | | | Yes / No | Yes / No |
| Mill the retentions (if any) milling speed at **medium speed /Knives forward direction** | | |  |  |
| 9.6 | If required repeat Step No.**9.5** | | Sift the milled granules through mesh **#24** | Yes / No | Yes / No |
| Mill the retentions (if any) milling speed at **medium speed /Knives forward direction** |  |  |
| Ensure all granules pass through #24. | Yes / No | Yes / No |
| 9.7 | Record the Net mass of sifted and milled granules | | |  |  |
| **End of Activity By** | | **Time** | |  |  |
| **Name** | |  |  |
| **Sign & Date** | |  |  |

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| FBD Bowls Sieve Integrity Check (After use) | S  / NS  | S  / NS  |
| **Checked By (Sign & Date)** |  |  |

**Note: Put ‘√’ mark as applicable;**  **S – Satisfactory;**  **NS – Not Satisfactory; Yes / No**

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| **9.7** | **Weigh the sifted & milled granules and record the mass in following table** | | | | | | | **Weighing Balance ID No.: PDE-** | | | | |
| **Container No./**  **Bin No.** | **Gross Weight (Kg)** | **Tare Weight**  **(Kg)** | **Net Weight(Kg)** | **Done By**  **(Sign&Date)** |  | **Container No./**  **Bin No.** | | **Gross Weight (Kg)** | **Tare Weight**  **(Kg)** | **Net Weight(Kg)** | **Done By**  **(Sign&Date)** |
| **Lot - I** | | | | | **Lot - II** | | | | | |
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| **9.7.1** | **Total Net mass of sifted & milled granules: Lot-I (\_\_\_\_\_\_\_ Kg) +**  **Lot-II (\_\_\_\_\_\_\_\_ Kg) = \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Kg** | | | | | | **Checked By (Sign & Date):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** | | | | | |

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| **10.0** | **BLEND QUANTITY COMPENSATION CALCULATION:** |
| 10.1 | **% Yield Calculation for Sifted and milled granules:**  % yield calculation for sifted and milled granules = Observed Mass of sifted and milled granules\_\_\_\_ ­­­\_\_\_\_\_\_\_\_\_ \_\_\_\_\_ %  =  x 100  =  x 100  Theoretical Mass of sifted and milled granules (Kg) 75.763 Kg  **NOTE: If the yield of sifted and milled** **granules is less than 95%, then extra granular materials to be compensated.**   * **Theoretical mass of Sifted and Milled Granules (P): 75.763 Kg** * **Practical mass of Sifted and Milled Granules (Q) = \_\_\_\_\_\_\_\_\_\_\_ Kg**  |  |  |  |  |  | | --- | --- | --- | --- | --- | | **S. No.** | **Extra granular Agent** | **Theoretical Batch Quantity (Kg) (R)** | **Compensated Batch Quantity (Kg) [ Q x R/P ]** | **Done by (PD)**  **(Sign & Date)** | | 1. | Cellulose, Microcrystalline, Ph.Eur (Avicel PH101) | 1.875 |  |  | | 2. | Crospovidone, Ph.Eur  (Kollidon CL) | 1.987 |  |  | | 3. | Stearic Acid, Ph.Eur (Speziol L2SM GF Pharma) | 1.000 |  |  |   **Checked by (PD) (Sign & date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Verified by (QA) (Sign & date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |

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| **Step No.** | **Process Instructions** |
| **11.0** | **SIFTING OF EXTRA GRANULAR MATERIALS:** |
| 11.1 | Check the integrity of the Sieve before and after use Record the observations in the given table **(Sieve Integrity Check).** |
| 11.2 | Check the Integrity of the All gaskets for the first campaign batch and last campaign batch. Record the observations in the given table  **(Gasket Integrity Check).** |
| 11.3 | Sift **Cellulose, Microcrystalline (Avicel PH101)** and **Crospovidone (Kollidon CL)** togetherthrough mesh **# 30** fitted on vibratory sifter. Collect the sifted material into a suitable container / double lined polyethylene bag. |
| 11.4 | Sift **Stearic Acid, (Speziol**® **L2SM GF Pharma),** through mesh **# 40** fitted on vibratory sifter. Collect the sifted material into a suitable container / double lined polyethylene bag. |
| |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **11.1** | **Sieve Integrity Check** | | | | | | | | | **Sieve No.** | **Sieve Code No.** | | **Sieve Integrity before use** | | **Checked By**  **(Sign & Date)** | **Sieve Integrity after use** | | **Checked By**  **(Sign & Date)** | | **# 30** |  | | S  / NS  | |  | S  / NS  | |  | | **#40** |  | | S  / NS  | |  | S  / NS  | |  | | **11.2** | **\*Gasket Integrity Check** | | | | | | | | | **Gasket Integrity Before use**  **Campaign first Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | **Checked By(Sign & Date)** | | **Gasket Integrity after use**  **Campaign last Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | | **Checked By(Sign & Date)** | | | S / NS / NA  | |  | | S / NS / NA  | | |  | | | **\*Note: Gasket Integrity shall be checked for the 1st Batch of campaign and end of the campaign.** | | | | | | | | |   **Note: Enter √ mark on the S-Satisfactory / NS-Not Satisfactory;NA-Not applicable**   | **Process Details** | | | | | --- | --- | --- | --- | | Start of activity By Name |  | Sign & Date: | | | Start Time |  | | | | Sifter ID No. |  | | | | End of activity By Name |  | | Sign & Date: | | End Time |  | | | | **Checked By (Sign & Date)** |  | | | | |

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| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Activity** | **Date** | **Time** | **Differential pressure**  **(\_\_\_\_\_\_\_ mm of WC)** | **Temperature**  **(NMT 25°C)** | **% Relative Humidity (NMT 40% RH)** | **Done By**  **(Sign& Date)** | | Start of Activity |  |  |  |  |  |  | | End of Activity |  |  |  |  |  |  | | Start of Activity |  |  |  |  |  |  | | End of Activity |  |  |  |  |  |  |   **Area Clearance:** Inspect the working area and equipment for cleanliness before use and ensure that the status tags are properly filled in   |  |  | | --- | --- | | **Check the following** | **Status** | | Room Name & No. |  | | Previous Product & Batch No. |  | | Type of Area cleaning | **Type-A / Type-B** | | Area Cleanliness | **Satisfactory / Not Satisfactory** |   **Note: Enter √ mark on the Type A /  Type B and Satisfactory / Not Satisfactory**  **Inspected By (PD) (Sign& Date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Checked By (PD) (Sign& Date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**  **Equipment Clearance:**  **Checked By (PD) (Sign & Date): \_\_\_\_\_\_\_\_\_\_\_\_\_ Approved By (QA) (Sign & Date): \_\_\_\_\_\_\_\_\_\_\_\_**   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Equipment Name** | **Equipment No.** | **Previous Product** | **Batch No.** | **Strength/Batch/ Product/ Colour change over** | **Type of cleaning** | | Pillar type bin blender | PDE - 1007 |  |  |  |  | | Pillar type bin blender | PDE–1513 |  |  |  |  | | 250 L Bin | PDA- |  |  |  |  | |

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| **Step No.** | **Process Instructions** |
| **12.0** | **Blending:** |
| 12.1 | Check the Integrity of the All gaskets for the first campaign batch and last campaign batch. Record the observations in the given table  **(Gasket Integrity Check).** |

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| 12.1 | **\*Gasket Integrity Check** | | | |
| **Gasket Integrity Before use**  **Campaign first Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | | **Checked By (Sign & Date)** | **Gasket Integrity After use**  **Campaign Last Batch No.\_\_\_\_\_\_\_\_\_\_\_\_** | **Checked By (Sign & Date)** |
| S / NS / NA  | |  | S / NS / NA  |  |
| **\*Note: Gasket Integrity shall be checked for the 1st Batch of campaign and end of the campaign.** | | | | |
| **Note: Enter √ mark on the S-Satisfactory / NS-Not Satisfactory/NA-Not applicable** | | | | |

**12.2 Loading of sifted and milled granules into Pillar type bin blender (250L)**

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| **Lot-I** | **Container No./Bin No.** | **Loaded into Blender By (Sign & Date)** | **Lot-II** | **Container No./Bin No.** | **Loaded into Blender By (Sign & Date)** |
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| **Step No.** | **Process Instructions** |
| **13.0** | **PRE-LUBRICATION:** |
| 13.1 | Add the sifted material of Step No. **11.3** to the loaded Materials of Step No **12.2** into Pillar type bin blender(250 L). |
| 13.2 | Blend for **10 minutes** at blender Speed **10 RPM** |
| 13.3 | Withdraw the in – process sample - by QA as per **SOP QA023†** |
| **14.0** | **LUBRICATION:** |
| 14.1 | Add sifted material of Step No.**11.4** to the blend of Step No.**13.2**. |
| 14.2 | Blend for **5 minutes** at blender **speed10 RPM** |
| 14.3 | Withdraw the in – process sample - by QA as per **SOP QA023†** |
| 14.4 | Unload the material into suitable in process containers. |
| 14.5 | Withdraw the in – process sample --- by QA as per **SOP QA023†**   * **For blend analysis approximately 25g & for Blend Uniformity (1X-3X) 645 mg-1935 mg (Recommended sampling die size: 3.0 CC)** * **For Validation batches, Sampling Shall be done as per the validation protocol** |
| 14.6 | Close the containers tightly. Record the details in given table |

**† Current effective version to be referred.**

| **Step No.** | **Process Instructions** | **Observations** | |
| --- | --- | --- | --- |
| Activity Start By (Name, Sign & Date) | |  |  |
| Activity Start Time | |  | |
| Equipment ID | |  | |
| **13.0** | **Pre Lubrication** | | |
| 13.1 | Add the sifted material of Step No. **11.3** to the loaded Materials of step No **12.2** | Yes  / No  | |
| 13.2 | Set Blending Time **(10 minutes) & Set RPM (10)** | Blending Time: \_\_\_\_\_\_\_minutes and RPM:\_\_\_\_\_\_\_ | |
| Blending | Start Time:\_\_\_\_\_\_\_\_\_\_\_\_\_ End Time:\_\_\_\_\_\_\_\_\_\_\_\_ | |
| 13.3 | Sampling (Applicable  / Not Applicable ) | Sampling thief ID Number: \_\_\_\_\_\_\_\_\_\_\_\_ | |
| Sample Quantity : \_\_\_\_\_\_\_\_\_\_\_\_\_ | |
| Sampled By (QA) (Sign& Date): | |
| **14.0** | **Lubrication** | | |
| 14.1 | Add sifted material of Step No.**11.4** to the blend of Step No.**13.2.** | Yes  / No  | |
| 14.2 | Set Blending Time **(5 minutes) & Set RPM (10)** | Blending Time: \_\_\_\_\_\_\_minutes and RPM:\_\_\_\_\_\_\_ | |
| Blending | Start Time:\_\_\_\_\_\_\_\_\_\_\_\_\_ End Time:\_\_\_\_\_\_\_\_\_\_\_\_ | |
| 14.3 | Sampling (Applicable  / Not Applicable ) | Sampling thief ID Number: \_\_\_\_\_\_\_\_\_\_\_\_ | |
| Sample Quantity : \_\_\_\_\_\_\_\_\_\_\_\_\_\_ | |
| Sampled By (QA) (Sign& Date): | |
| **Checked By (Sign & Date):** | | | |
| 14.4 | **Unloading into containers** | Done / Not Done  | |
| 14.5 | Sampling (Applicable  / Not Applicable )   * **For blend analysis approximately 25g & for Blend Uniformity (1X-3X) 645 mg-1935 mg (Recommended sampling die size: 3.0 CC)** * **For Validation batches, Sampling Shall be done as per the validation protocol** | Sampling thief ID Number: \_\_\_\_\_\_\_\_\_\_\_\_ | |
| Sample Quantity : \_\_\_\_\_\_\_\_\_\_\_\_ | |
| Sampled By (QA)(Sign& Date): | |
| 14.6 | Weighing Record updated | Done / Not Done  | |
| **Checked By (Sign & Date):** | | | |
| **Note: Put ‘√’ mark as applicable on** **Yes /**  **No ;**  **Done /** **Not Done and**  **Applicable /** **Not Applicable** | | | |

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| **Step No.** | **Process Instructions** | | | | | | | | | | | | |
| **14.6** | **Weigh the Lubricated blend and record the mass in following table.** | | | | | | | | | **Weighing Balance ID No.: PDE-** | | |
| **Container No./**  **Bin No.** | **Gross Weight (Kg)** | **Tare Weight(Kg)** | **Net Weight(Kg)** | |  | **Container No./Bin No.** | | **Gross Weight (Kg)** | | **Tare Weight(Kg)** | **Net Weight(Kg)** |
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| **Total Net mass: \_\_\_\_\_\_\_\_\_\_\_\_\_\_ Kg Weighed By (Sign & Date):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** | | | | | | | | | | | |
| **End of activity By** | | | | | **Time** | | |  | | | | |
| **Name** | | |  | | | | |
| **Sign & Date** | | |  | | | | |
| **Verified By** | | | | | **Sign & Date** | | |  | | | | |

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| 1. **15.0 Yield & Reconciliation**  |  |  |  |  | | --- | --- | --- | --- | | A | Theoretical Mass of blend | | **80.625 Kg** | | B | Actual yield | | \_\_\_\_\_\_\_\_\_\_Kg | | C | Sample quantity for analysis | | \_\_\_\_\_\_\_\_\_\_ Kg | | D | Percentage yield [(B + C)/A x 100] | | \_\_\_\_\_\_\_\_\_\_%\* | | E | Rejects | | \_\_\_\_\_\_\_\_\_\_Kg | | F | Others | Handling Loss | \_\_\_\_\_\_\_\_\_\_Kg | | Spillage | \_\_\_\_\_\_\_\_\_\_Kg | | Others$ | \_\_\_\_\_\_\_\_\_\_Kg | | G | Reconciliation [(B+C+E+F)/A X 100] | | \_\_\_\_\_\_\_\_\_%\*\* |   \* Blend yield Limit: 95% to 100%.  \*\* Reconciliation Limit: 98% to 100%.  $Others quantity can be defined as dust collected in ADU and not limited to  Note : Any outlier to the yield limit shall be handled as per SOP on Procedure for Yield and Reconciliation of Drug Product (PD079†)  **Calculated by (Production) (Sign & Date) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Checked by (QA) (Sign & Date) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**   1. **In process Analytical Results**  |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Stage** | **Specification No.** | **Results (Pass / Fail)** | **References** | **Reviewed By (QA)**  **(Sign & Date)** | |  |  |  |  |  |   **† Current effective version to be referred.** |

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| **CONCLUSION**: The final-mix **Meet/Does not meet** the test specifications and therefore is **Released/ Not released** for further processing.     |  |  |  | | --- | --- | --- | | **Strength** | **Theoretical quantity of Blend (Kg)** | **Actual quantity of blend transferred to Compression Batch No.** | |  |  |  |   **Total Approved Blend Qty Transferred to Compression.:\_\_\_\_\_\_\_\_\_\_\_\_\_ Kg**  **Verified By(QA) (Sign & Date): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| **Deviations / Incidents if any:**  **Production : Quality Assurance:**  **(Sign & Date) (Sign & Date)** |