SOP Number	SOP-MFG-WG-004	**Version**	4.2
Title	Wet Granulation Manufacturing Process for Tablet Dosage Forms	**Effective Date**	01-Apr-2024
Department	Manufacturing — Solid Dosage Forms	**Review Date**	31-Mar-2025
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Applicable Products	Paracetamol 500mg Tablets (AURO-PARA-500), all wet granulation products	**Pages**	4

1. PURPOSE

This Standard Operating Procedure defines the controlled process parameters, equipment specifications, and quality control checkpoints for the manufacture of oral solid dosage forms using the wet granulation process. Compliance with this SOP is mandatory for all manufacturing personnel at Aurobindo Pharma Unit III. Deviations from any critical process parameter (CPP) must be immediately reported and documented per SOP-QA-DEV-001.

2. SCOPE

This SOP applies to all wet granulation manufacturing operations at Unit III, including but not limited to: Paracetamol 500mg Tablets, Metformin 500mg Tablets, and Ibuprofen 400mg Tablets. The procedure covers dispensing through to compression.

3. CRITICAL PROCESS PARAMETERS (CPPs) AND ACCEPTABLE RANGES

The following parameters are classified as Critical Process Parameters. Exceedance of any CPP limit constitutes a process deviation and must be recorded immediately in the batch manufacturing record and reported to QA.

Process Step	Equipment	Parameter	Lower Limit	Upper Limit	Unit	Criticality	Action if Exceeded
Dispensing	EQP_DISP_01	API Weight	498.0	502.0	kg	Critical	Stop — re-weigh, investigate
Dispensing	EQP_DISP_01	Excipient Weight	Per BMR	Per BMR	kg	Critical	Stop — re-weigh, investigate
Granulation	EQP_GRAN_01	Inlet Air Temp	60.0	70.0	°C	**Critical**	Stop immediately — raise deviation
Granulation	EQP_GRAN_01	Product Bed Temp	60.0	70.0	°C	**Critical**	Stop immediately — raise deviation
Granulation	EQP_GRAN_01	Outlet Air Temp	40.0	50.0	°C	**Major**	Notify QA — continue with monitoring
Granulation	EQP_GRAN_01	Impeller Speed	220	280	rpm	Major	Adjust and document
Granulation	EQP_GRAN_01	Binder Addition Rate	2.8	3.5	kg/min	Major	Adjust and document
Drying	EQP_DRYR_01	Inlet Air Temp	60.0	70.0	°C	Critical	Stop — raise deviation
Drying	EQP_DRYR_01	Product Temperature	45.0	60.0	°C	Critical	Stop — raise deviation
Drying	EQP_DRYR_01	LOD (Post-Drying)	1.0	2.5	%	Critical	Reject granules — investigate
Compression	EQP_COMP_01	Main Compression Force	10.0	15.0	kN	Critical	Stop — adjust tooling
Compression	EQP_COMP_01	Tablet Hardness	5.0	8.0	kP	Critical	Stop — adjust compression
Compression	EQP_COMP_01	Average Tablet Weight	495.0	505.0	mg	Critical	Stop — check die/punch
Compression	EQP_COMP_01	Friability	0.0	1.0	%	Critical	Reject — investigate granule quality

4. GRANULATION PROCESS — DETAILED PROCEDURE

4.1 Equipment Preparation and Pre-Use Checks

- Verify EQP_GRAN_01 (Fluid Bed Granulator / High Shear Granulator) cleaning status. Confirm online cleaning certificate is within validity period.
- Check equipment calibration certificate for temperature sensors (inlet, outlet, product bed). Calibration must be current (≤6 months). Record calibration certificate numbers in BMR.
- Perform pre-use equipment function test: run equipment at low speed for 2 minutes, verify temperature readings are within ±1°C of reference thermometer.
- Verify that all filter bags are in place and undamaged. Record in equipment pre-use log.
- Set temperature controller setpoint to 65°C (centre of 60–70°C range). Allow 15 minutes for thermal equilibration before charging materials.

4.2 Granulation Execution

CRITICAL: Monitor temperature throughout the granulation process. If inlet air temperature or product bed temperature exceeds 70°C at any point, STOP the process immediately, remove materials, and raise a process deviation per SOP-QA-DEV-001. Do NOT continue granulation above the upper temperature limit.

Step	Action	Time	Check	Record In
1	Load pre-weighed API and excipients into granulator bowl	T=0 min	Weight verified by two operators	BMR Page 3
2	Dry mix at impeller speed 150 rpm for 5 minutes	T+5 min	Visual — uniform mixing	BMR Page 3
3	Start air flow. Allow bed temperature to reach 60–65°C	T+10 min	Temperature reading — confirm ≥60°C	BMR Page 3
4	Begin binder (PVP K30 solution) addition at 30 g/min	T+15 min	Flow meter reading, binder temp 20-25°C	BMR Page 3
5	Continue granulation — monitor temperature every 15 min	T+30 min	Temperature must remain 60–70°C	BMR Page 3
6	Check endpoint — granule visual assessment	T+45 min	Granule size uniformity, no overwetting	BMR Page 4
7	Stop binder addition. Continue drying phase in granulator	T+50 min	Temperature maintained 60–70°C	BMR Page 4
8	Collect in-process LOD sample	T+60 min	Target LOD: 1.5–3.0%	BMR Page 4 / LIMS
9	Discharge granules to fluid bed dryer (EQP_DRY_01)	T+65 min	Weight of wet granules recorded	BMR Page 4

4.3 Temperature Deviation Response Protocol

If temperature exceeds the upper limit (>70°C inlet or product bed):

- STOP granulation process immediately — do not continue adding binder
- Record exact time, parameter reading, and equipment status in BMR
- Notify production supervisor and QA Analyst within 15 minutes
- Quarantine all granules in process
- Raise deviation report per SOP-QA-DEV-001 within 2 hours
- Do NOT proceed to drying without QA authorisation
- Evaluate impact on product quality — assay and dissolution testing mandatory
- Equipment must be taken out of service for investigation: inspect temperature sensor, thermocouple, and heating element

5. KNOWN EQUIPMENT RISKS — EQP_GRAN_01

Risk	Root Cause	Frequency	Detection Method	Control
Temperature overshoot	Thermocouple drift or heating element failure	Low (current process)	Process alarm (>70°C)	Calibrate thermocouple every 6 months. PM every 12 months. Manual check every 15 min
Temperature sensor failure	Sensor wire corrosion, connector loosening	Low	SST at start of each batch	Replace sensor every 12 months. Check connecto
Inadequate binder distribution	Spray nozzle blockage	Medium	Visual granule inspection	Clean nozzle before each batch. Check flow rate d
Overwetting	Excessive binder or prolonged addition	Low	LOD IPC check	Monitor binder volume vs. standard. Stop addition

6. IN-PROCESS CONTROLS AND SAMPLING

The following in-process tests are mandatory for each batch. Results must be entered in the LIMS system within 30 minutes of testing. Any result outside specification triggers an immediate QA notification.

IPC Test	Specification	Frequency	Entered In	Action if OOS
Granulation LOD (in-process)	1.5 – 3.0%	Once at endpoint	LIMS + BMR	Extend drying. Re-test. Notify QA if repeat fa
Post-Drying LOD	1.0 – 2.5%	Once per batch	LIMS + BMR	Reject granules. Raise deviation. Investigate
Tablet Hardness	5.0 – 8.0 kP	Every 30 min during compression	LIMS + BMR	Adjust compression force. Notify QA if >2 co
Tablet Weight	495.0 – 505.0 mg	Every 30 min during compression	LIMS + BMR	Adjust feed frame. Stop if >505 mg or <495
Friability	≤ 1.0%	Once per batch	LIMS + BMR	Reject if >1.0%. Review granule quality and
Assay (Finished Product)	98.0 – 102.0% LC	Once per batch (QC release)	LIMS	OOS investigation per SOP-QA-OOS-001. E
Dissolution (Finished Product)	≥ 80% in 30 min (Q)	Once per batch (QC release)	LIMS	OOS investigation. Evaluate granulation pro

7. REGULATORY REFERENCES

- ICH Q8(R2): Pharmaceutical Development — design space and CPP definition
- ICH Q10: Pharmaceutical Quality System — deviation and CAPA management
- Schedule M (India GMP): Hot Air Oven / FBD process controls
- WHO TRS 986 Annex 2: OOS investigation applicable to granulation deviations
- Aurobindo Internal SOP-QA-DEV-001: Deviation Reporting and Management
- Aurobindo Internal SOP-QA-OOS-001: OOS Investigation Procedure

8. APPROVAL SIGNATURES

Role	Name	Signature	Date
Author	V. Srinivas, Sr. Production Manager	_____	01-Apr-2024
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