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Title:	Operation, Cleaning, and Maintenance of the Granulator (e.g., RMG)	**Version:**	1.0
Company:	NovaThera Pharmaceuticals Pvt. Ltd.	**Effective Date:**	2025-01-01
Location:	Pune, India	**Review Date:**	2026-01-01

Operation, Cleaning, and Maintenance of the Granulator (e.g., RMG)

Category: Production/Manufacturing

Standard Operating Procedure (SOP)

Company: NovaThera Pharmaceuticals Pvt. Ltd.

Department: Production

Title: Operation, Cleaning, and Maintenance of the Rapid Mixer Granulator (RMG)

SOP No.: SOP-PROD-004

Version No.: 1.0

Effective Date: 2025-01-01

1.0 PURPOSE

This Standard Operating Procedure (SOP) outlines the procedure for the proper operation, cleaning, and preventive maintenance of the Rapid Mixer Granulator (RMG), Model RMG-01, used in pharmaceutical manufacturing at NovaThera Pharmaceuticals Pvt. Ltd. This procedure ensures consistent granulation, prevents cross-contamination, and prolongs the lifespan of the equipment, adhering to Good Manufacturing Practices (GMP).

2.0 SCOPE

This SOP applies to all personnel involved in the operation, cleaning, and maintenance of the Rapid Mixer Granulator (RMG), Model RMG-01, used in the production of solid oral dosage forms at NovaThera Pharmaceuticals Pvt. Ltd., Pune, India. It covers all products and batches granulated using this equipment. This SOP does not cover major repairs requiring specialized engineering services.

3.0 RESPONSIBILITY

QC Inspector:

• Verifies the cleanliness of the RMG prior to use and after cleaning according to the cleaning validation protocol.

• Performs in-process checks during granulation as specified in the batch manufacturing record (BMR).

• Collects samples for quality control testing.

• Reviews and approves the RMG usage and cleaning logs.

Production Supervisor:

• Ensures that all personnel operating the RMG are adequately trained and qualified.

• Oversees the granulation process and ensures adherence to this SOP and the BMR.

• Notifies maintenance personnel of any equipment malfunctions or deviations.

• Ensures proper documentation of all activities in the RMG usage logbook.

• Ensures that all cleaning activities are performed as per this SOP.

QA Manager:

• Reviews and approves this SOP and any revisions.

• Oversees the implementation of this SOP and ensures compliance with GMP regulations.

• Investigates any deviations from this SOP and implements corrective and preventative actions (CAPA).

• Reviews cleaning validation reports and approves the RMG for use.

Head of QA:

• Approves this SOP.

• Has overall responsibility for ensuring GMP compliance.

• Makes the final decision on any issues related to the operation, cleaning, and maintenance of the RMG.

4.0 MATERIALS & EQUIPMENT

PPE:

• Safety glasses

• Dust mask/Respirator (N95 or equivalent)

• Gloves (Nitrile or equivalent)

• Dedicated cleanroom gown

• Dedicated cleanroom head cover

• Dedicated cleanroom shoes

Equipment:

• Rapid Mixer Granulator (RMG), Model RMG-01

- Weighing balance, calibrated (BAL-02)
- Measuring cylinders of various sizes
- Spatulas (stainless steel)
- Cleaning solutions: Purified Water, 70% Isopropyl Alcohol (IPA), Detergent solution (e.g., LabKlenz)
- Lint-free cloths
- Cleaning brushes (various sizes, nylon bristles)
- Vacuum cleaner with HEPA filter
- Portable blower
- pH meter (PHM-01)

Documentation:

- Rapid Mixer Granulator Usage Logbook (LOG-PROD-004)
- Cleaning Logbook (LOG-QA-002)
- Equipment Maintenance Logbook (LOG-ENG-001)
- Batch Manufacturing Record (BMR)
- Deviation Report Form (FRM-QA-001)
- Cleaning Validation Protocol and Report
- Material Safety Data Sheets (MSDS) for all cleaning agents

5.0 PROCEDURE

5.1 Pre-Operation Checks

5.1.1 The Production Supervisor reviews the BMR to verify the material requirements, batch size, and granulation parameters.

5.1.2 The Production Supervisor checks the RMG Usage Logbook (LOG-PROD-004) to ensure the equipment is within its calibration and maintenance schedule.

5.1.3 The QC Inspector verifies the cleanliness of the RMG, including the bowl, impeller, chopper, and discharge port, based on the cleaning validation protocol. The QC Inspector documents the cleanliness

verification in the RMG Usage Logbook (LOG-PROD-004).

5.1.4 The Production Supervisor verifies that all required materials are available and have been released by Quality Control.

5.1.5 The Production Supervisor ensures that the RMG is properly assembled, and all connections are secure.

5.1.6 The Production Supervisor verifies that the RMG is level and stable.

5.1.7 The Production Supervisor inspects the RMG for any signs of damage or malfunction. If any issues are found, the Production Supervisor notifies the maintenance department and documents the issue in the Equipment Maintenance Logbook (LOG-ENG-001). The RMG must not be operated until the issue is resolved and documented.

5.1.8 The Production Supervisor confirms that the exhaust system connected to the RMG is functional.

5.2 Granulation Process

5.2.1 The Production Supervisor charges the required amount of each ingredient into the RMG bowl, according to the BMR.

5.2.2 The Production Supervisor sets the RMG parameters (impeller speed, chopper speed, granulation time) as specified in the BMR.

5.2.3 The Production Supervisor starts the RMG and adds the binder solution (if applicable) at the rate specified in the BMR.

5.2.4 During the granulation process, the Production Supervisor monitors the consistency and appearance of the granules.

5.2.5 The QC Inspector performs in-process checks as specified in the BMR, including granule size, moisture content, and bulk density. Results are recorded in the BMR.

5.2.6 If the granules do not meet the specified requirements, the Production Supervisor adjusts the RMG parameters (impeller speed, chopper speed, granulation time) as necessary, with proper documentation and QA approval.

5.2.7 Once the granulation is complete, the Production Supervisor stops the RMG.

5.2.8 The Production Supervisor discharges the granules from the RMG into a pre-weighed container, ensuring minimal loss of material.

5.2.9 The Production Supervisor records the actual yield of granules in the BMR.

5.3 Post-Granulation

5.3.1 The Production Supervisor transfers the granules to the fluid bed dryer (FBD-01) for drying, following the SOP for FBD operation.

5.3.2 The Production Supervisor cleans the RMG immediately after use, following the cleaning procedure outlined in Section 5.4 of this SOP.

5.3.3 The Production Supervisor documents all activities in the RMG Usage Logbook (LOG-PROD-004) and the BMR.

5.4 Cleaning Procedure

5.4.1 The Production Supervisor dons the appropriate PPE (safety glasses, dust mask, gloves, cleanroom gown, head cover, and shoes).

5.4.2 The Production Supervisor removes any loose powder and granules from the RMG bowl using a vacuum cleaner with a HEPA filter.

5.4.3 The Production Supervisor disassembles the RMG components that come into contact with the product (impeller, chopper, bowl) according to the manufacturer's instructions.

5.4.4 The Production Supervisor washes all disassembled parts with a detergent solution (e.g., LabKlenz) and hot purified water. The pH of the cleaning solution should be checked to ensure it is within the acceptable range (typically pH 6-8).

5.4.5 The Production Supervisor rinses all parts thoroughly with purified water until all traces of detergent are removed.

5.4.6 The Production Supervisor wipes all parts with lint-free cloths and inspects them for any remaining residue.

5.4.7 The Production Supervisor sanitizes all parts with 70% Isopropyl Alcohol (IPA).

5.4.8 The Production Supervisor allows the parts to air dry completely.

5.4.9 The Production Supervisor reassembles the RMG.

5.4.10 The Production Supervisor wipes down the exterior of the RMG with 70% IPA.

5.4.11 The QC Inspector verifies the cleanliness of the RMG according to the cleaning validation protocol. This may involve visual inspection, swab testing, or rinse testing.

5.4.12 The QC Inspector documents the cleaning verification in the Cleaning Logbook (LOG-QA-002).

5.4.13 If the RMG does not meet the cleanliness criteria, the cleaning procedure must be repeated until the criteria are met.

5.4.14 The Production Supervisor documents all cleaning activities in the Cleaning Logbook (LOG-QA-002), including the date, time, cleaning agent used, and the signature of the person performing the cleaning.

5.5 Preventive Maintenance

5.5.1 The Production Supervisor schedules preventive maintenance for the RMG according to the manufacturer's recommendations and the preventive maintenance schedule.

5.5.2 Preventive maintenance includes:

- Lubricating moving parts.
- Checking and tightening bolts and screws.
- Inspecting and replacing worn parts (e.g., seals, bearings).
- Calibrating the RMG parameters (impeller speed, chopper speed).
- Inspecting electrical connections.

5.5.3 Preventive maintenance should be performed by qualified maintenance personnel.

5.5.4 All preventive maintenance activities must be documented in the Equipment Maintenance Logbook (LOG-ENG-001).

6.0 POST-MAINTENANCE ACTIVITIES

6.1 Following any maintenance activity (routine or repair), the Production Supervisor and QC Inspector must verify the equipment's cleanliness and proper function before returning it to service.

6.2 The Production Supervisor performs a test run of the RMG using a placebo batch to ensure it is operating correctly.

6.3 The QC Inspector takes samples from the placebo batch and analyzes them to ensure that the RMG is not introducing any contaminants.

6.4 The Production Supervisor updates the Equipment Maintenance Logbook (LOG-ENG-001) with details of the maintenance performed, the date, and the name of the person who performed the maintenance.

6.5 The QA Manager reviews the maintenance records and approves the RMG for use.

7.0 SAFETY PRECAUTIONS

7.1 Always wear appropriate PPE (safety glasses, dust mask, gloves, cleanroom gown, head cover, and shoes) when operating or cleaning the RMG.

7.2 Ensure that the RMG is properly grounded to prevent electrical shock.

7.3 Do not operate the RMG if it is damaged or malfunctioning.

7.4 Follow lockout/tagout procedures before performing any maintenance on the RMG.

7.5 Use caution when handling cleaning agents. Refer to the MSDS for specific safety information.

7.6 Avoid contact with moving parts when the RMG is in operation.

7.7 Report any accidents or incidents immediately to the Production Supervisor.

7.8 Ensure adequate ventilation when using volatile cleaning agents such as Isopropyl Alcohol.

7.9 Do not exceed the maximum capacity of the RMG.

8.0 APPROVALS

Prepared By: Production Supervisor

Reviewed By: QA Manager

Approved By: Head of QA

Date:

Document Approval

Role	Name	Signature	Date
Prepared by:	_____	_____	_____
Reviewed by (QA):	_____	_____	_____
Approved by (Head QA):	_____	_____	_____

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