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Preparation and Review of Batch Manufacturing Records

Category: Production

Standard Operating Procedure (SOP)

Company: NovaThera Pharmaceuticals Pvt. Ltd., Pune, India

Department: Production

Title: Preparation and Review of Batch Manufacturing Records

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1.0 PURPOSE

This Standard Operating Procedure (SOP) outlines the procedure for the preparation, review, and approval of Batch Manufacturing Records (BMRs) at NovaThera Pharmaceuticals Pvt. Ltd. It ensures consistent and accurate documentation of all steps involved in pharmaceutical manufacturing, adhering to Good Manufacturing Practices (GMP) as outlined by regulatory bodies, including FDA, ICH, and WHO. This procedure aims to maintain data integrity, product quality, and traceability throughout the entire manufacturing process, fostering a culture of quality and continuous improvement. The BMR serves as a critical record for regulatory inspections and product release, ensuring compliance with all applicable regulations and internal quality standards. This SOP facilitates the generation of accurate and reliable data, contributing to robust product lifecycle management and patient safety. It also supports the principles of Quality by Design (QbD) and continuous process verification.

2.0 SCOPE

This SOP applies to all personnel involved in the preparation, execution, and review of Batch Manufacturing Records (BMRs) for all pharmaceutical products manufactured at NovaThera Pharmaceuticals Pvt. Ltd., Pune, India. It encompasses all stages of the manufacturing process, from raw material dispensing to final product packaging. This includes, but is not limited to, solid oral dosage

forms (tablets, capsules), liquids, semi-solids, and sterile products. This SOP covers both manual and electronic BMR systems. It also applies to all batch sizes, pilot, registration, and commercial batches. Excluded from this SOP are activities related to clinical trial material manufacturing (Phase I & II) and analytical testing performed outside of the manufacturing process. This SOP is applicable to all manufacturing areas including dispensing, granulation, compression, coating, filling, and packaging. This SOP is compliant with current GMP guidelines, ICH Q7, Q9, Q10, and relevant regulatory requirements.

3.0 RESPONSIBILITY

QC Inspector: Responsible for performing in-process quality checks, verifying compliance with established standards, documenting observations accurately in the BMR, and immediately reporting any deviations to the Production Supervisor. The QC Inspector will verify equipment cleanliness and calibration status before each batch. The inspector will also ensure proper sampling of in-process materials and record results accurately in the BMR. Performance will be measured by the number of deviations detected and reported, as well as the accuracy and completeness of BMR entries.

Production Supervisor: Responsible for overseeing the manufacturing process, ensuring adherence to approved procedures, and directing production personnel. The Production Supervisor is responsible for reviewing and approving completed BMR sections during the manufacturing process, addressing deviations promptly, and ensuring that all entries are accurate and complete. They are also responsible for ensuring the proper training of production personnel on this SOP. The supervisor has the authority to stop the production process if deviations occur that impact product quality. Performance will be measured by the on-time completion of batches and the number of deviations requiring investigation.

QA Manager: Responsible for the overall review and approval of completed BMRs. The QA Manager will ensure that all deviations are adequately investigated and resolved, that all required documentation is present and accurate, and that the BMR demonstrates compliance with GMP regulations and internal quality standards. The QA Manager also oversees the implementation of corrective and preventative actions (CAPA) arising from BMR reviews. The QA manager is responsible for ensuring the ongoing training of production and quality personnel on BMR requirements.

Head of QA: Responsible for providing strategic oversight of the BMR process, ensuring alignment with regulatory requirements and industry best practices. The Head of QA serves as the primary liaison with regulatory agencies regarding BMR-related matters. The Head of QA approves changes to this SOP and ensures that it is regularly reviewed and updated. The Head of QA is responsible for the final release of product based on a complete and satisfactory BMR review.

4.0 MATERIALS & EQUIPMENT

PPE:

- Safety Glasses (ANSI Z87.1 compliant)
- Nitrile Gloves (Powder-free, appropriate size)

- Hairnet
- Shoe Covers
- Dust Mask (NIOSH approved N95 respirator may be required for certain processes)
- Cleanroom Garments (Appropriate for the manufacturing area classification)

Equipment:

- Weighing Balance (ACC-01, calibrated daily with NIST traceable weights)
- Blender (BLN-04, calibrated annually)
- Tablet Press (TCP-01, calibrated quarterly)
- Coating Pan (CPN-02, calibrated annually)
- Sifter (SFT-02, inspected before each use)
- Granulator (GRN-03, calibrated annually)
- Automated Inspection System (INS-01, calibrated monthly)
- Temperature and Humidity Monitoring System (TMP-01, calibrated annually)

Documentation:

- Batch Manufacturing Record (BMR) Template (Version Controlled, latest version on file server)
- Standard Operating Procedure (SOP-PROD-001, latest approved version)
- Equipment Logbooks (Maintenance and Calibration Records)
- Deviation Reports (Form DEV-001)
- Corrective Action/Preventive Action (CAPA) Forms (Form CAPA-001)
- Cleaning Logs (CLN-LOG)

Reagents/Chemicals:

- Raw Materials (Pharma Grade, meeting compendial requirements - USP/EP/BP) - Specifications available on the intranet.
- Cleaning Agents (GMP Grade, validated for residue removal) - MSDS available on the intranet.

5.0 PROCEDURE

5.1 Pre-Activity Preparation

5.1.1 Review the BMR template for the specific product and batch size to ensure it is the correct version. Verify the revision date against the document control system.

5.1.2 Ensure all necessary materials, equipment, and documentation are available and readily accessible.

5.1.3 Verify the cleanliness of the manufacturing area and equipment according to the cleaning SOPs. Check the cleaning log (CLN-LOG) to confirm the last cleaning date and time.

5.1.4 Verify that all equipment is calibrated and in good working order. Check the equipment logbooks for the calibration status. Calibration stickers should be present and valid on each piece of equipment.

5.1.5 Ensure that all personnel involved in the manufacturing process are properly trained on this SOP and the specific BMR requirements.

5.1.6 Verify that all raw materials have been released by Quality Control and are within their expiry dates. Check the material release certificates and the material quarantine status in the ERP system.

5.1.7 Confirm the environmental monitoring data for the manufacturing area is within acceptable limits. Review the temperature and humidity records (TMP-01) for the area.

5.1.8 Before starting, the Production Supervisor and QC Inspector will sign and date the "Pre-Activity Checklist" section of the BMR to confirm all preparations are complete. This serves as a checkpoint to verify that all pre-activity steps have been performed.

5.2 Raw Material Dispensing

5.2.1 Dispense raw materials according to the quantities specified in the BMR. Use the calibrated weighing balance (ACC-01).

5.2.2 Verify the identity and quantity of each raw material against the BMR. Perform a double check by a second trained operator.

5.2.3 Record the batch number, supplier, and quantity of each raw material dispensed in the BMR.

5.2.4 Affix a label to each dispensed raw material container with the material name, batch number, quantity, and date.

5.2.5 Store dispensed raw materials in a designated area until ready for use.

5.2.6 If any discrepancies are observed during dispensing, immediately notify the Production Supervisor and initiate a deviation report (Form DEV-001). Do not proceed until the deviation is resolved.

5.2.7 After dispensing, the Production Supervisor and the operator performing the dispensing must sign and date the dispensing section of the BMR to confirm the accuracy and completeness of the dispensing process. This serves as a critical quality control checkpoint.

5.3 Granulation (Example Process Step)

5.3.1 Transfer the dispensed raw materials to the granulator (GRN-03).

5.3.2 Set the granulator parameters (mixing speed, granulation time) according to the BMR instructions.

5.3.3 Add the binder solution (if applicable) at the specified rate and duration.

5.3.4 Monitor the granulation process closely to ensure proper granule formation.

5.3.5 Take samples of the granules at specified intervals for in-process testing (moisture content, particle size distribution). Refer to section 5.4 for In-Process Controls.

5.3.6 Record all process parameters (mixing speed, granulation time, binder addition rate, temperature) in the BMR.

5.3.7 If any deviations occur during the granulation process (e.g., improper granule formation, equipment malfunction), immediately notify the Production Supervisor and initiate a deviation report (Form DEV-001).

5.3.8 After completion of the granulation process, the Production Supervisor will inspect the granules and sign and date the granulation section of the BMR to confirm that the process was completed according to the instructions.

5.4 In-Process Controls

5.4.1 Moisture Content: Sample granules every 30 minutes (or as specified in the BMR) and test using a calibrated moisture analyzer. Acceptance Criteria: 1-3% moisture content. Record results in the BMR. If results are outside the acceptance criteria, adjust the drying parameters accordingly (if applicable) and repeat the test. Document all corrective actions taken.

5.4.2 Particle Size Distribution: Sample granules every hour (or as specified in the BMR) and analyze using a calibrated sieve shaker. Acceptance Criteria: 90% of granules between 250 μm and 850 μm. Record results in the BMR. If results are outside the acceptance criteria, adjust the granulation parameters accordingly and repeat the test. Document all corrective actions taken.

5.4.3 Blend Uniformity: After blending, sample the blend from multiple locations within the blender (BLN-04) and analyze for assay uniformity.

Acceptance Criteria: RSD ≤ 5%. Record results in the BMR. If results are outside the acceptance criteria, continue blending for an additional period and repeat the test. Document all corrective actions taken.

5.4.4 Tablet Hardness (if applicable): Sample tablets every 15 minutes from the tablet press (TCP-01) and measure the hardness using a calibrated tablet hardness tester. Acceptance Criteria: 8-12 kp. Record results in the BMR. If results are outside the acceptance criteria, adjust the tablet press parameters accordingly and repeat the test. Document all corrective actions taken.

5.4.5 Tablet Weight (if applicable): Sample tablets every 15 minutes from the tablet press (TCP-01) and measure the weight using a calibrated balance (ACC-01). Acceptance Criteria: ±5% of target weight. Record results in the BMR. If results are outside the acceptance criteria, adjust the tablet press parameters accordingly and repeat the test. Document all corrective actions taken.

5.4.6 Visual Inspection: Conduct visual inspection of in-process materials and final product to detect any defects. Acceptance Criteria: Absence of foreign matter, cracks, chips, or other visible defects. Record observations in the BMR. Reject any defective materials.

5.4.7 Environmental Monitoring: Regularly monitor the temperature and humidity of the manufacturing area. Acceptance Criteria: Temperature 20-25°C, Humidity 40-60% RH. Record results in the BMR. If results are outside the acceptance criteria, investigate the cause and take corrective actions.

5.5 Compression (Example Process Step, assuming solid dosage form)

5.5.1 Transfer the dried granules to the tablet press (TCP-01).

5.5.2 Set the tablet press parameters (tablet weight, hardness, thickness) according to the BMR instructions.

5.5.3 Monitor the tablet compression process closely to ensure proper tablet formation.

5.5.4 Take samples of the tablets at specified intervals for in-process testing (tablet weight, hardness, thickness, disintegration). Refer to section 5.4 for In-Process Controls.

5.5.5 Record all process parameters (tablet weight, hardness, thickness, press speed) in the BMR.

5.5.6 If any deviations occur during the compression process (e.g., tablet capping, lamination, sticking), immediately notify the Production Supervisor and initiate a deviation report (Form DEV-001).

5.5.7 After completion of the compression process, the Production Supervisor will inspect the tablets and sign and date the compression section of the BMR to confirm that the process was completed according to the instructions.

[Continue adding process steps as needed, including coating, filling, packaging, and other relevant steps for the specific product being manufactured. Ensure each step includes detailed instructions, process parameters, in-process controls, and documentation requirements. All deviations should be recorded and addressed promptly.]

6.0 POST-ACTIVITY PROCEDURES

6.1 Verify that all sections of the BMR have been completed accurately and completely.

6.2 Reconcile all materials used during the manufacturing process. Account for any discrepancies and document them in the BMR.

6.3 Ensure that all equipment used during the manufacturing process has been cleaned according to the cleaning SOPs. Record the cleaning date and time in the equipment logbooks.

6.4 Store the completed BMR in a designated area for review by the QA Manager.

6.5 Upload the electronic BMR to the electronic document management system (EDMS), if applicable. Ensure the electronic BMR is a true and accurate representation of the original record.

6.6 Dispose of any unused raw materials and packaging materials according to the waste disposal SOPs.

6.7 Perform a final visual inspection of the manufacturing area to ensure it is clean and free of debris.

6.8 The Production Supervisor will sign and date the "Post-Activity Checklist" section of the BMR to confirm that all post-activity procedures have been completed.

7.0 SAFETY PRECAUTIONS

7.1 Wear appropriate PPE at all times while in the manufacturing area.

7.2 Handle raw materials and chemicals according to the Material Safety Data Sheets (MSDS).

7.3 Follow all safety procedures for operating equipment.

7.4 Report any accidents or injuries immediately to the Production Supervisor.

7.5 In case of a chemical spill, follow the spill control procedures outlined in the safety manual.

7.6 Ensure adequate ventilation in the manufacturing area.

7.7 Know the location of emergency exits, fire extinguishers, and first aid kits.

7.8 Perform a risk assessment before starting any new manufacturing process.

7.9 Emergency contact numbers are posted in the manufacturing area.

8.0 QUALITY CONTROL MEASURES

8.1 In-process testing shall be conducted as per the approved BMR and relevant SOPs.

8.2 Sampling plans shall be statistically sound and representative of the batch.

8.3 Acceptance criteria shall be clearly defined and based on product specifications and regulatory requirements.

8.4 All testing shall be performed using validated analytical methods.

8.5 All results shall be recorded accurately and completely in the BMR.

8.6 Any out-of-specification (OOS) results shall be investigated according to the OOS SOP.

8.7 Retention samples shall be taken from each batch and stored according to the retention sample SOP.

8.8 Perform regular audits of the BMR process to ensure compliance with GMP regulations and internal quality standards.

8.9 Implement a change control system to manage any changes to the BMR or manufacturing process.

8.10 Adhere to ALCOA+ principles (Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, Available) in all documentation practices.

9.0 DOCUMENTATION AND RECORDS

9.1 All entries in the BMR shall be legible, accurate, and complete.

9.2 All entries shall be made in indelible ink.

9.3 Any corrections shall be made by drawing a single line through the incorrect entry, initialing and dating the correction, and writing the correct entry next to it.

9.4 The BMR shall be reviewed and approved by the QA Manager before product release.

9.5 The BMR shall be retained for a minimum of one year after the expiry date of the batch, or as required by local regulations.

9.6 Electronic records shall be backed up regularly and stored securely.

9.7 Access to electronic records shall be controlled through user accounts and passwords.

9.8 Audit trails shall be enabled for all electronic records to track any changes made to the data.

9.9 Ensure data integrity of all records, both paper and electronic, to prevent unauthorized access, alteration, or deletion.

10.0 DEVIATIONS AND CORRECTIVE ACTIONS

10.1 Any deviation from the approved BMR or manufacturing process shall be documented in a deviation report (Form DEV-001).

10.2 The deviation report shall include a description of the deviation, the root cause of the deviation, and the corrective and preventive actions (CAPA) taken to prevent recurrence.

10.3 The deviation report shall be reviewed and approved by the QA Manager.

10.4 CAPA shall be implemented and tracked to ensure effectiveness.

10.5 Deviations shall be classified as major, minor, or critical based on their potential impact on product quality.

10.6 Critical deviations shall be reported to regulatory agencies as required.

10.7 The effectiveness of CAPA shall be evaluated periodically to ensure continuous improvement.

10.8 A deviation management system shall be in place to track all deviations and CAPA.

11.0 TRAINING REQUIREMENTS

11.1 All personnel involved in the preparation, execution, and review of BMRs shall be trained on this SOP.

11.2 Training shall include classroom instruction, on-the-job training, and periodic refresher training.

11.3 Training records shall be maintained for all personnel.

11.4 Training shall cover the principles of GMP, data integrity, and deviation management.

11.5 Personnel shall be trained on the specific equipment and processes they are responsible for.

11.6 Training effectiveness shall be evaluated through written exams and practical assessments.

11.7 Specific training on data integrity and ALCOA+ principles must be completed by all personnel handling BMR documentation.

12.0 REVIEW AND REVISION

12.1 This SOP shall be reviewed at least annually, or more frequently if necessary, to ensure it remains current and accurate.

12.2 The review shall be conducted by the QA Manager in consultation with the Production Supervisor and other relevant personnel.

12.3 Any revisions to this SOP shall be approved by the Head of QA.

12.4 The revision history shall be maintained in the document control system.

12.5 All changes to this SOP shall be communicated to all affected personnel.

12.6 Change control procedures shall be followed for any changes to the BMR or manufacturing process.

13.0 APPROVALS

Prepared By: Production Supervisor

Reviewed By: QA Manager

Approved By: Head of QA

Date:

Controlled Document Notice

Document Approval

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

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