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Process Yield Reconciliation

Category: Production/Manufacturing

Standard Operating Procedure (SOP)

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1.0 PURPOSE

This procedure defines the steps for reconciliation of process yield during pharmaceutical manufacturing at NovaThera Pharmaceuticals. It ensures accurate tracking of material usage, identifies discrepancies, and promotes adherence to Good Manufacturing Practices (GMP) to maintain product quality and compliance. This SOP details the reconciliation process at various stages of manufacturing to meet regulatory requirements and internal quality standards.

2.0 SCOPE

This SOP applies to all materials, intermediates, and finished products manufactured at NovaThera Pharmaceuticals Pvt. Ltd. It covers the entire manufacturing process from raw material dispensing to finished product packaging. It encompasses all batch sizes and product types processed within the production facility. This procedure excludes reconciliation of materials in the warehouse, which are covered under a separate SOP.

3.0 RESPONSIBILITY

QC Inspector:

• Verifies material weights and measures at dispensing and during in-process checks.

• Collects and analyzes samples for in-process testing according to established procedures.

• Reviews batch records for completeness and accuracy of yield data.

• Notifies the Production Supervisor of any discrepancies observed during inspection.

Production Supervisor:

• Oversees the manufacturing process and ensures adherence to approved batch records and SOPs.

• Ensures accurate recording of material usage, process parameters, and yield data in the batch record.

• Investigates any yield discrepancies identified during the reconciliation process.

• Implements corrective actions to prevent recurrence of yield deviations.

• Provides training to production personnel on proper material handling and documentation practices.

QA Manager:

• Reviews and approves batch records, including yield reconciliation documentation.

• Provides guidance and support to the production team on quality-related issues.

• Conducts audits of the manufacturing process to ensure compliance with GMP requirements.

• Approves investigations of yield deviations and ensures the effectiveness of corrective actions.

• Monitors trends in yield data to identify potential areas for process improvement.

Head of QA:

• Has overall responsibility for the quality assurance program at NovaThera Pharmaceuticals.

• Provides final approval for batch release after reviewing all relevant documentation, including yield reconciliation.

• Ensures that all SOPs are current and compliant with regulatory requirements.

• Oversees the investigation and resolution of significant quality issues related to yield discrepancies.

4.0 MATERIALS & EQUIPMENT

PPE:

• Safety glasses

• Laboratory coat

• Gloves (nitrile or appropriate for the material being handled)

• Dust mask or respirator (as required by the material SDS)

Equipment:

• Calibrated weighing balances (e.g., BLN-01, BLN-02, BLN-03, BLN-04)

- Calibrated measuring devices (e.g., graduated cylinders, volumetric flasks)
- Sifters (SFT-01, SFT-02, SFT-03)
- Blenders (e.g., BDR-01, BDR-02)
- Tablet press (TCP-01, TCP-02, TCP-03)
- Encapsulation machine (ECM-01, ECM-02)
- Coating pan (CPN-01)
- Data entry computer with appropriate software
- Calibrated pH meter (PHM-01)
- Calibrated conductivity meter (CDM-01)

Documentation:

- Approved Batch Manufacturing Record (BMR)
- Material Dispensing Record
- In-Process Control (IPC) checklist
- Yield Reconciliation Form (NT-YRF-001)
- Deviation Report Form (NT-DRF-001)
- Equipment Calibration Log
- Material Safety Data Sheets (SDS)

5.0 PROCEDURE

5.1 Material Dispensing and Weighing

5.1.1 The Production Supervisor reviews the BMR to determine the required quantities of each raw material.

5.1.2 The Production Supervisor retrieves the raw materials from the designated storage area, ensuring the material is within its expiration date.

5.1.3 The Production Supervisor verifies the identity and integrity of the raw material containers against the BMR.

5.1.4 The Production Supervisor records the lot number and quantity of each raw material dispensed in the Material Dispensing Record.

5.1.5 The QC Inspector verifies the dispensed quantities against the BMR and initials the Material Dispensing Record.

5.1.6 The Production Supervisor weighs each raw material using a calibrated weighing balance (BLN-01, BLN-02, BLN-03, BLN-04) ensuring the balance is tared before weighing.

5.1.7 The Production Supervisor records the actual weight of each raw material in the Material Dispensing Record and BMR.

5.1.8 The QC Inspector verifies the accuracy of the weights recorded and signs the Material Dispensing Record.

5.1.9 Any discrepancies between the target and actual weights must be investigated immediately. The Production Supervisor initiates a Deviation Report (NT-DRF-001) if the discrepancy exceeds the allowable limits defined in the BMR.

5.1.10 The weighed materials are transferred to the next stage of the manufacturing process, ensuring proper labeling and traceability.

5.2 In-Process Yield Monitoring

5.2.1 During each stage of the manufacturing process (e.g., blending, granulation, tableting, encapsulation), the Production Supervisor monitors the yield of the intermediate product.

5.2.2 The Production Supervisor records the quantity of material transferred between each stage in the BMR.

5.2.3 The QC Inspector performs in-process checks (IPC) at specified intervals, including weight variation, hardness, friability, and disintegration

testing, as outlined in the BMR.

5.2.4 The QC Inspector documents the IPC results in the IPC checklist.

5.2.5 If the IPC results are outside the specified limits, the Production Supervisor must stop the process and initiate an investigation.

5.2.6 Any material losses during the process (e.g., spillage, equipment malfunctions) must be documented in the BMR and Yield Reconciliation Form (NT-YRF-001).

5.3 Blending Process

5.3.1 The Production Supervisor transfers the weighed raw materials to the blender (BDR-01, BDR-02), following the sequence specified in the BMR.

5.3.2 The Production Supervisor sets the blending parameters (time, speed) according to the BMR.

5.3.3 After blending, the Production Supervisor samples the blend and submits it to the QC Inspector for content uniformity testing.

5.3.4 The QC Inspector performs the content uniformity testing and documents the results in the IPC checklist.

5.3.5 If the content uniformity results are within the specified limits, the Production Supervisor proceeds to the next stage.

5.3.6 If the content uniformity results are outside the specified limits, the Production Supervisor adjusts the blending parameters and repeats the sampling and testing process.

5.3.7 The Production Supervisor records the weight of the blended material after the blending process.

5.4 Tableting/Encapsulation Process

5.4.1 The Production Supervisor transfers the blended material to the tablet press (TCP-01, TCP-02, TCP-03) or encapsulation machine (ECM-01, ECM-02).

5.4.2 The Production Supervisor sets the machine parameters (tablet weight, hardness, capsule fill weight) according to the BMR.

5.4.3 The Production Supervisor monitors the tablet/capsule production rate and records the number of tablets/capsules produced.

5.4.4 The QC Inspector performs in-process checks on the tablets/capsules, including weight variation, hardness, friability, disintegration, and content uniformity testing.

5.4.5 The QC Inspector documents the IPC results in the IPC checklist.

5.4.6 The Production Supervisor removes any rejected tablets/capsules from the production line and records the quantity of rejected units.

5.4.7 The Production Supervisor records the weight of the accepted tablets/capsules after the tableting/encapsulation process.

5.5 Coating Process (if applicable)

5.5.1 If the tablets require coating, the Production Supervisor transfers the tablets to the coating pan (CPN-01).

5.5.2 The Production Supervisor prepares the coating solution according to the BMR.

5.5.3 The Production Supervisor sets the coating parameters (spray rate, air temperature, pan speed) according to the BMR.

5.5.4 The Production Supervisor monitors the coating process and records the weight of the coated tablets.

5.5.5 The QC Inspector performs in-process checks on the coated tablets, including weight gain, coating thickness, and appearance.

5.5.6 The QC Inspector documents the IPC results in the IPC checklist.

5.6 Final Product Packaging

5.6.1 The Production Supervisor transfers the finished product (tablets, capsules) to the packaging line.

5.6.2 The Production Supervisor verifies that the correct packaging materials (bottles, blisters, labels, cartons) are used.

5.6.3 The Production Supervisor monitors the packaging process and records the number of units packaged.

5.6.4 The QC Inspector performs final inspection of the packaged product to ensure proper labeling, sealing, and appearance.

5.6.5 The QC Inspector documents the inspection results in the BMR.

5.6.6 The Production Supervisor records the final yield of the packaged product in the BMR and Yield Reconciliation Form (NT-YRF-001).

5.7 Yield Reconciliation Calculation

5.7.1 The Production Supervisor calculates the theoretical yield for each stage of the manufacturing process based on the BMR.

5.7.2 The Production Supervisor calculates the actual yield for each stage based on the recorded data.

5.7.3 The Production Supervisor calculates the percentage yield for each stage using the following formula:

Percent Yield = (Actual Yield / Theoretical Yield) x 100

5.7.4 The Production Supervisor documents the theoretical yield, actual yield, and percentage yield for each stage in the Yield Reconciliation Form (NT-YRF-001).

5.7.5 The Production Supervisor identifies any yield deviations by comparing the percentage yield to the acceptable limits defined in the BMR.

5.7.6 If a yield deviation occurs, the Production Supervisor initiates an investigation to determine the root cause.

6.0 POST-RECONCILIATION ACTIVITIES

6.1 The Production Supervisor reviews the Yield Reconciliation Form (NT-YRF-001) for completeness and accuracy.

6.2 The Production Supervisor signs and dates the Yield Reconciliation Form (NT-YRF-001).

6.3 The QC Inspector reviews the Yield Reconciliation Form (NT-YRF-001) and verifies the accuracy of the calculations and data.

6.4 The QC Inspector signs and dates the Yield Reconciliation Form (NT-YRF-001).

6.5 If a yield deviation occurred, the Production Supervisor and QC Inspector collaborate to complete a Deviation Report (NT-DRF-001), documenting the investigation findings, root cause, and corrective actions.

6.6 The QA Manager reviews the Yield Reconciliation Form (NT-YRF-001) and Deviation Report (NT-DRF-001) (if applicable).

6.7 The QA Manager approves the Yield Reconciliation Form (NT-YRF-001) and Deviation Report (NT-DRF-001) after ensuring that all discrepancies have been adequately addressed.

6.8 The completed BMR, Yield Reconciliation Form (NT-YRF-001), and Deviation Report (NT-DRF-001) are submitted to the QA department for final review and batch release.

6.9 The Head of QA reviews all documentation prior to final batch release.

7.0 SAFETY PRECAUTIONS

7.1 Always wear appropriate PPE (safety glasses, laboratory coat, gloves, dust mask or respirator) when handling raw materials and during the manufacturing process.

7.2 Refer to the Material Safety Data Sheets (SDS) for specific safety information on each raw material.

7.3 Handle chemicals with caution and avoid contact with skin and eyes.

7.4 Ensure adequate ventilation in the manufacturing area to prevent the buildup of dust or fumes.

7.5 Use calibrated weighing balances and measuring devices to ensure accurate measurements.

7.6 Follow proper equipment operating procedures to prevent equipment malfunctions or accidents.

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

7.8 Dispose of waste materials according to established waste disposal procedures.

7.9 Keep the work area clean and organized to prevent accidents.

7.10 In case of eye contact, flush immediately with copious amounts of water and seek medical attention.

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:	_____	_____	_____
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