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Analytical Method for Assay and Impurities of Aspirin Tablets

Category: Quality Control Laboratory

Standard Operating Procedure (SOP)

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1.0 PURPOSE

This procedure outlines the standardized analytical method for determining the assay and impurities of aspirin tablets in pharmaceutical manufacturing at NovaThera Pharmaceuticals, ensuring product quality and compliance with regulatory standards. This SOP ensures accurate and reliable analytical results are obtained consistently.

2.0 SCOPE

This SOP applies to the Quality Control Laboratory at NovaThera Pharmaceuticals and covers the analysis of all aspirin tablets received for testing, regardless of batch size or manufacturing location, including both in-process and finished product samples. It encompasses the preparation of standards, samples, and mobile phases, as well as the operation, maintenance, and data analysis of the High-Performance Liquid Chromatography (HPLC) system.

3.0 RESPONSIBILITY

QC Inspector: Performs sample preparation, standard preparation, HPLC system operation, data acquisition, and initial data analysis. Responsible for adhering to the SOP and accurately documenting all activities in the designated laboratory notebook and electronic systems.

Production Supervisor: Ensures that representative samples of aspirin tablets are collected and submitted to the Quality Control Laboratory with appropriate documentation. Responsible for maintaining proper documentation of the manufacturing process and notifying the QC Inspector of any deviations that may affect product quality.

QA Manager: Reviews analytical data, approves test results, and ensures compliance with GMP regulations and internal quality standards. Responsible for investigating any out-of-specification (OOS) results and implementing corrective and preventive actions (CAPA) as necessary.

Head of QA: Provides overall oversight of the quality control function and ensures that all activities are conducted in accordance with GMP regulations and company policies. Approves the SOP and any revisions.

4.0 MATERIALS & EQUIPMENT

PPE: Safety glasses, laboratory coat, nitrile gloves

Equipment:

- High-Performance Liquid Chromatography (HPLC) system with UV-Vis detector (HPLC-001)
- Analytical balance (BAL-002), calibrated
- Ultrasonic bath (USB-001)
- Volumetric flasks (various sizes)
- Pipettes (various sizes)
- HPLC vials
- HPLC column (C18, 4.6 mm x 150 mm, 5 µm particle size or equivalent)
- Mobile phase reservoir bottles
- Syringe filters (0.45 µm)

Documentation:

- Laboratory notebook
- HPLC system software
- Analytical test request form (QC-FRM-001)
- HPLC instrument logbook (QC-LOG-001)
- Deviation report form (QA-FRM-001)
- Out-of-Specification (OOS) investigation form (QA-FRM-002)

5.0 PROCEDURE

5.1 Standard Preparation

5.1.1 The QC Inspector obtains the aspirin reference standard from the designated controlled storage area, verifying the lot number, expiry date, and certificate of analysis (COA).

5.1.2 The QC Inspector accurately weighs approximately 25 mg of aspirin reference standard using the analytical balance (BAL-002) and records the exact weight in the laboratory notebook.

5.1.3 The QC Inspector quantitatively transfers the weighed aspirin reference standard to a 25 mL volumetric flask.

5.1.4 The QC Inspector adds approximately 20 mL of mobile phase (as described in section 5.3) to the volumetric flask and sonicates in the ultrasonic bath (USB-001) until the aspirin is completely dissolved.

5.1.5 The QC Inspector dilutes to volume with mobile phase and mixes thoroughly to obtain a standard solution with a concentration of approximately 1.0 mg/mL.

5.1.6 The QC Inspector filters a portion of the standard solution through a 0.45 µm syringe filter into an HPLC vial.

5.1.7 The QC Inspector labels the HPLC vial with the standard name, concentration, date, and initials.

5.1.8 The QC Inspector stores the standard solution in the refrigerator (2-8°C) and records the preparation details in the laboratory notebook. The standard solution is stable for [Specify stability duration based on validation data].

5.2 Sample Preparation

5.2.1 The QC Inspector obtains a representative sample of aspirin tablets from the Production Supervisor, ensuring that the sample is accompanied by the analytical test request form (QC-FRM-001).

5.2.2 The QC Inspector randomly selects 20 tablets from the sample and accurately determines the average tablet weight.

5.2.3 The QC Inspector grinds the 20 tablets to a fine powder using a mortar and pestle or a suitable mechanical grinder.

5.2.4 The QC Inspector accurately weighs an amount of powdered tablet equivalent to approximately 25 mg of aspirin based on the label claim and average tablet weight. The exact weight is recorded in the laboratory notebook.

5.2.5 The QC Inspector quantitatively transfers the weighed tablet powder to a 25 mL volumetric flask.

5.2.6 The QC Inspector adds approximately 20 mL of mobile phase (as described in section 5.3) to the volumetric flask and sonicates in the ultrasonic bath (USB-001) for 15 minutes to ensure complete dissolution of the aspirin.

5.2.7 The QC Inspector allows the solution to cool to room temperature and then dilutes to volume with mobile phase and mixes thoroughly.

5.2.8 The QC Inspector filters a portion of the sample solution through a 0.45 µm syringe filter into an HPLC vial.

5.2.9 The QC Inspector labels the HPLC vial with the sample name, batch number, date, and initials.

5.2.10 The QC Inspector stores the sample solution at room temperature and records the preparation details in the laboratory notebook. The sample solution should be analyzed within [Specify stability duration based on validation data].

5.3 Mobile Phase Preparation

5.3.1 The QC Inspector prepares the mobile phase by mixing [Specify percentage] of [Specify solvent A, e.g., acetonitrile] and [Specify percentage] of [Specify solvent B, e.g., water containing 0.1% phosphoric acid].

5.3.2 The QC Inspector uses HPLC grade solvents and deionized water for mobile phase preparation.

5.3.3 The QC Inspector filters the mobile phase through a 0.45 µm filter under vacuum to remove particulate matter.

5.3.4 The QC Inspector degasses the mobile phase using vacuum or sonication before use.

5.3.5 The QC Inspector records the mobile phase composition, date of preparation, and initials in the laboratory notebook.

5.4 HPLC System Operation

5.4.1 The QC Inspector ensures that the HPLC system (HPLC-001) is properly maintained and calibrated, and that the instrument logbook (QC-LOG-001) is up-to-date.

5.4.2 The QC Inspector turns on the HPLC system and allows it to warm up for at least 30 minutes.

5.4.3 The QC Inspector sets the HPLC system parameters according to the validated method:

- Column: C18, 4.6 mm x 150 mm, 5 µm particle size or equivalent
- Mobile phase: [Specify percentage] of [Specify solvent A] and [Specify percentage] of [Specify solvent B]
- Flow rate: 1.0 mL/min
- Injection volume: 10 µL
- Column temperature: 30°C
- Detection wavelength: 280 nm

5.4.4 The QC Inspector injects the standard solution at least five times to ensure system suitability.

5.4.5 The QC Inspector evaluates the system suitability parameters, including peak symmetry (tailing factor), resolution between aspirin and any known impurities, and %RSD of peak area of replicate standard injections. System suitability criteria should meet the following specifications:

- Tailing factor: NMT 2.0
- Resolution: NLT 2.0
- %RSD: NMT 2.0%

5.4.6 If the system suitability criteria are not met, the QC Inspector investigates the cause and takes corrective action, such as replacing the column, adjusting the mobile phase composition, or cleaning the system. All corrective actions are documented in the laboratory notebook.

5.4.7 Once system suitability is achieved, the QC Inspector injects the sample solutions in duplicate.

5.4.8 The QC Inspector records the chromatograms and peak areas for aspirin and any identified impurities in the laboratory notebook and electronic data system.

5.5 Data Analysis

5.5.1 The QC Inspector uses the HPLC system software to integrate the peaks corresponding to aspirin and any identified impurities in the standard and sample chromatograms.

5.5.2 The QC Inspector calculates the assay of aspirin in the tablets using the following formula:

$$\text{Assay (\%)} = (\text{Sample Peak Area} / \text{Standard Peak Area}) \times (\text{Standard Weight} / \text{Sample Weight}) \times (\text{Standard Purity} / 100) \times (\text{Average Tablet Weight} / \text{Label Claim}) \times 100$$

5.5.3 The QC Inspector calculates the percentage of each identified impurity using the following formula:

$$\text{Impurity (\%)} = (\text{Impurity Peak Area} / \text{Aspirin Peak Area}) \times (\text{Aspirin Standard Concentration} / \text{Sample Concentration}) \times 100$$

5.5.4 The QC Inspector compares the levels of each identified impurity to the established acceptance criteria. Impurity limits should comply with ICH guidelines and internal specifications.

5.5.5 The QC Inspector documents all calculations in the laboratory notebook and electronic data system.

5.5.6 The QC Inspector verifies that all data is accurate and complete before reporting the results.

6.0 POST-ANALYSIS ACTIVITIES

6.1 The QC Inspector reviews the analytical data and ensures that all results are within the acceptance criteria.

6.2 The QC Inspector reports the results on the analytical test report form (QC-FRM-001) and submits it to the QA Manager for review and approval.

6.3 The QA Manager reviews the analytical data and approves the test results if all criteria are met. If any results are out-of-specification (OOS), the QA Manager initiates an OOS investigation according to SOP QA-SOP-001.

6.4 The QC Inspector cleans the HPLC system according to the instrument manufacturer's instructions and records the cleaning in the HPLC instrument logbook (QC-LOG-001).

6.5 The QC Inspector disposes of the used solvents and solutions in accordance with the company's environmental health and safety guidelines.

6.6 The QC Inspector stores the remaining sample and standard solutions in the designated refrigerator for the specified retention period.

6.7 The QC Inspector archives the analytical data in the designated electronic data storage system.

7.0 SAFETY PRECAUTIONS

7.1 Always wear safety glasses, laboratory coat, and nitrile gloves when handling chemicals and samples.

7.2 Work in a well-ventilated area to avoid inhalation of solvent vapors.

7.3 Avoid contact of chemicals with skin and eyes. In case of contact, flush immediately with copious amounts of water and seek medical attention.

7.4 Dispose of waste solvents and solutions in designated containers according to the company's environmental health and safety guidelines.

7.5 Use caution when handling glassware to avoid breakage and potential injuries.

7.6 Handle HPLC solvents with care as some are flammable or toxic. Consult the Material Safety Data Sheets (MSDS) for specific hazards and precautions.

7.7 Do not operate the HPLC system without proper training and authorization.

7.8 If any spills occur, clean them up immediately using appropriate absorbent materials.

8.0 APPROVALS

Prepared By: QC Inspector

Reviewed By: QA Manager

Approved By: Head of QA

Date:

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