Process Validation Report

QC Department

Students: Jackeline Garrido, Mst Farjana Akter Chowdhury and Gloria Alberto
PHS : 512
CUNY York College
Fall 2023

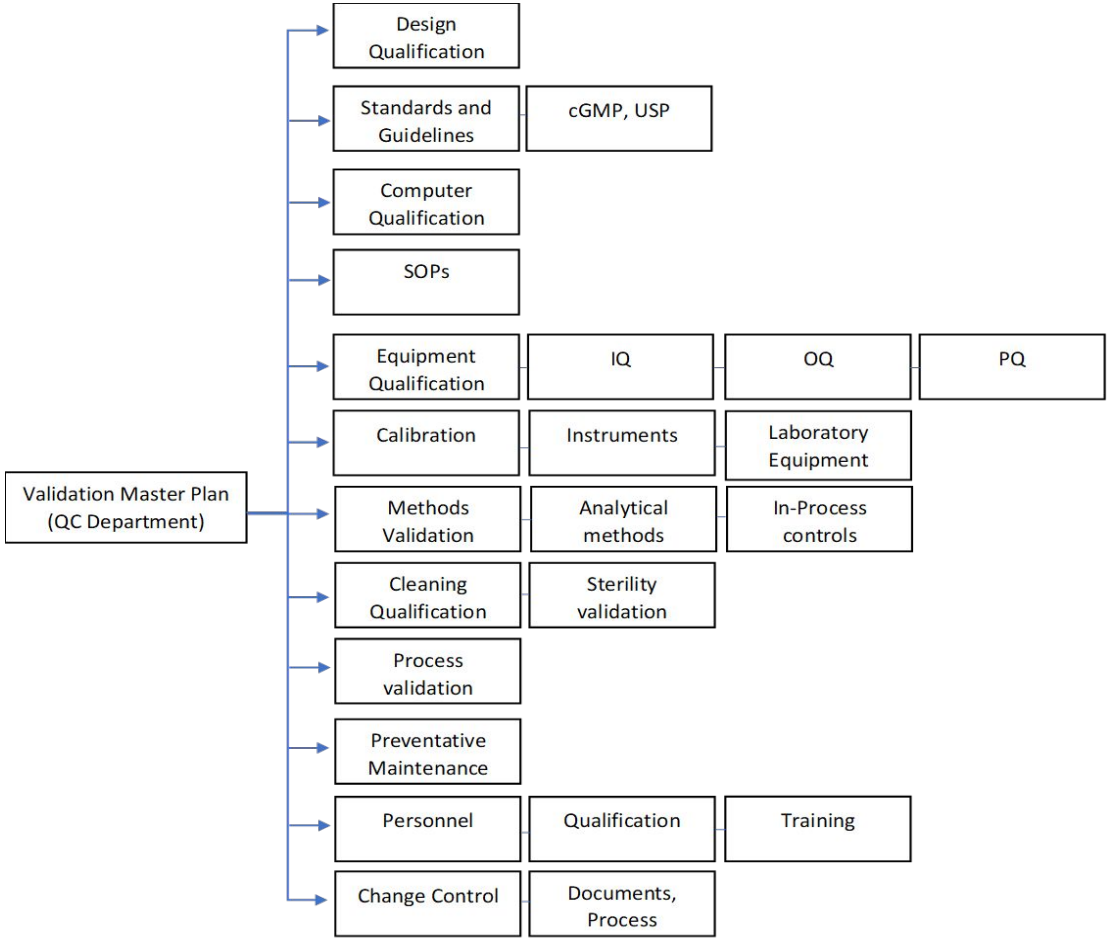
Introduction

Quality Control- A set of processes, procedures, and activities designed to maintain and enhance the quality of products or services.

Different QC stages

- Incoming Quality Control (IQC)
- In Process Quality Control (IPQC)
- Final Quality Control (FQC)
- Outgoing Quality Control (OQC)

For the drug N-(4-Hydroxyphenyl) Acetamide, QC department role is to ensure that raw materials, in-process products, and finished products are developed and manufactured with the highest quality, following cGMP guideline and USP Pharmacopoeia standards


Validation Master Plan (QC Department)
Design Qualification
Standards and Guidelines
cGMP, USP
Computer Qualification
SOPs
Equipment Qualification
IQ
OQ
PQ
Calibration
Instruments
Laboratory Equipment
Methods Validation
Analytical methods
In-Process controls
Cleaning Qualification
Sterility validation
Process validation
Preventative Maintenance
Personnel
Qualification
Training
Change Control
Documents, Process

Incoming Quality Control (IQC)

- Equipment/ Instruments
  - -HPLC
  - -FTIR
  - -Physical Testing
- Systems
- Personnel
- Procedures/ Documents

Background for HPLC

- HPLC- column chromatography
- Types of HPLC:

-**Normal Phase HPLC**: Uses a polar stationary phase (like silica gel) and a non-polar mobile phase.

-**Reverse Phase HPLC**: Employs a non-polar stationary phase and a polar mobile phase, which is the most commonly used technique.

-**Size Exclusion Chromatography (SEC)**: Separates molecules based on their size.

-**Ion-Exchange Chromatography (IEC)**: Separates ions based on their charge.

Applications of HPLC

- **Pharmaceuticals:** Analysis of drugs, impurities, and quality control.
- **Biochemistry:** Separation and analysis of proteins, peptides, amino acids, etc.
- **Environmental Analysis:** Detection of pollutants and contaminants in water, soil, and air.
- **Food and Beverage Industry:** Analysis of food additives, contaminants, and nutritional components.
- **Forensics:** Identification of drugs, toxins, and compounds in forensic samples.

Advantages of HPLC

- **High Sensitivity and Resolution:** Detects and separates components in minute concentrations.
- **Versatility:** Can analyze a wide range of compounds with different properties.
- **Quantitative Analysis:** Accurately measures concentrations of components.
- **Automation:** Allows for high-throughput analysis with minimal manual intervention.

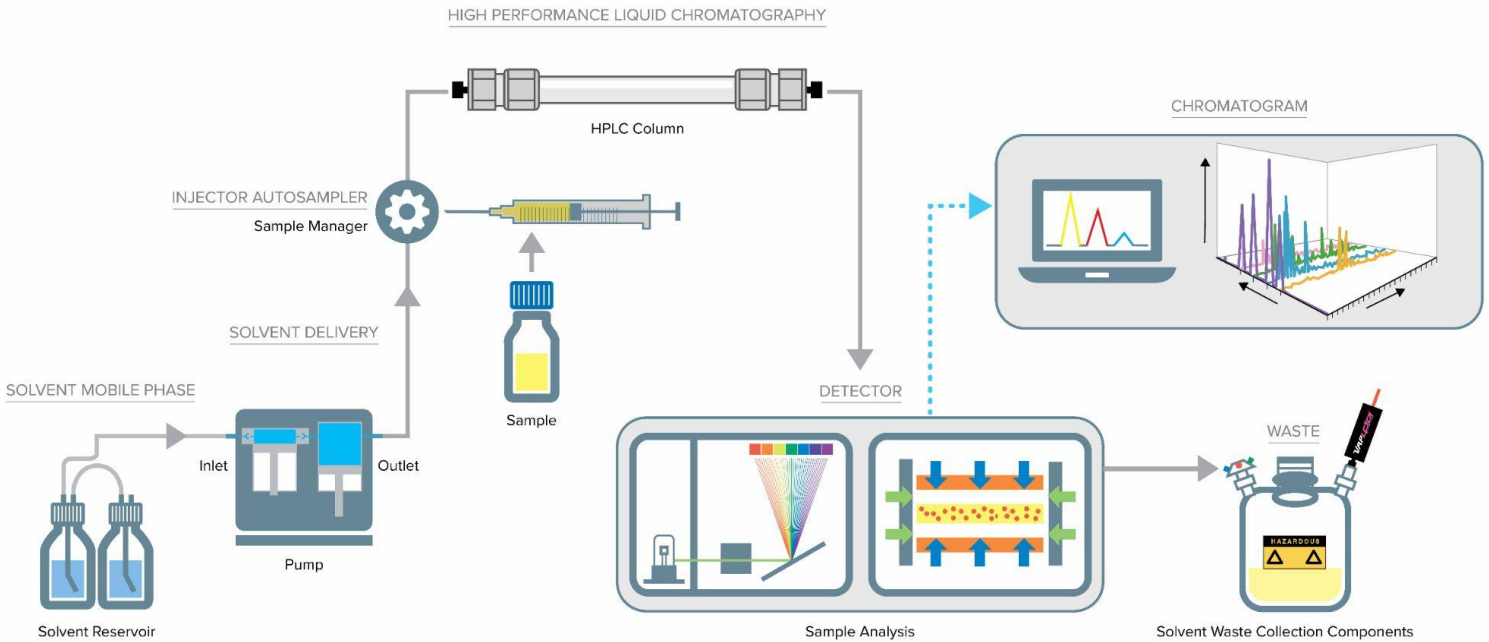
HPLC test for N-(4-Hydroxyphenyl)Acetamide SOP

1. Purpose
2. Scope
3. Responsibilities
4. Equipment and materials
5. Test procedure
6. Documentation
7. Data analysis
8. Calibration
9. Precautions
10. References
11. SOP Distribution
12. Revision history

Equipment and Materials

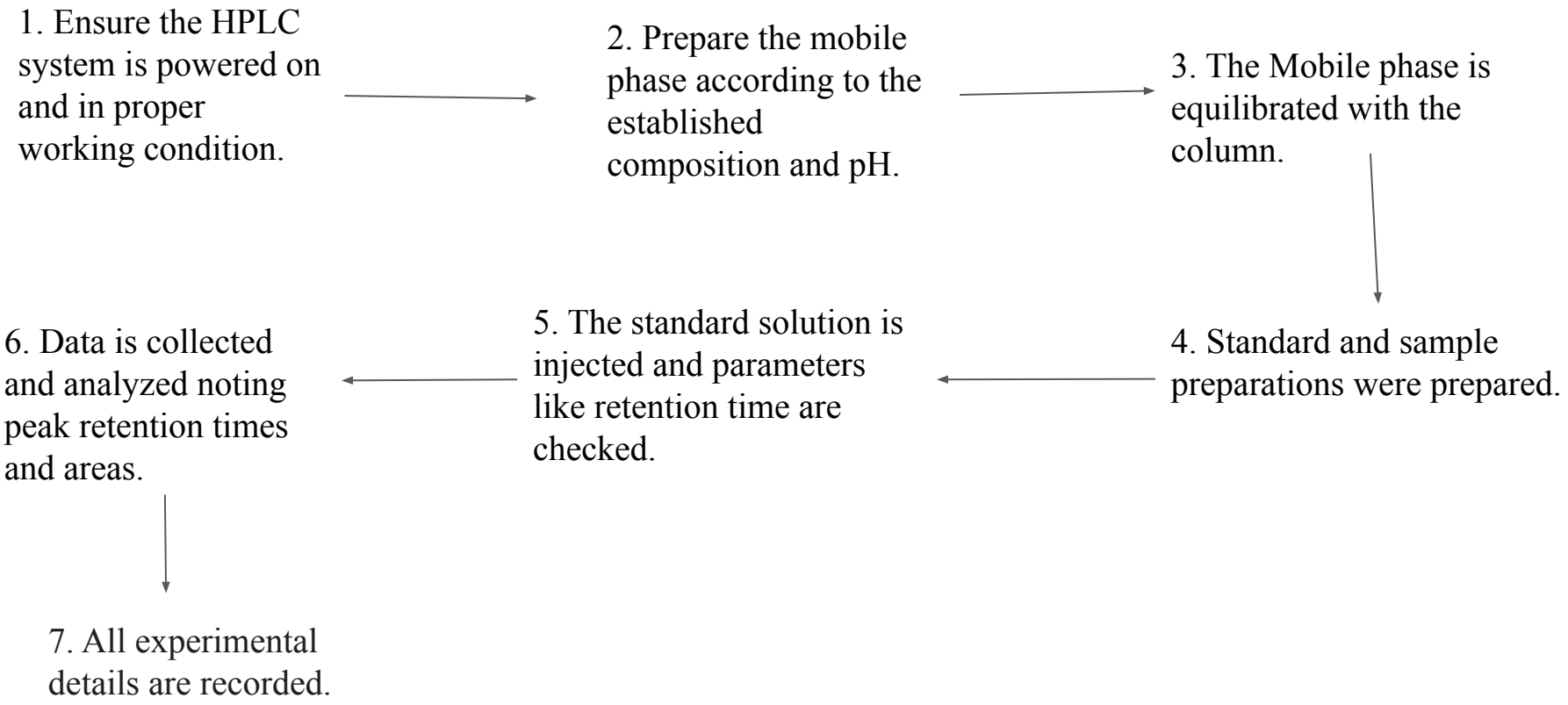
- Agilent 1260 Infinity II LC System
- Column
- Autosampler
- Pump
- Detector
- Mobile Phase
- Standard and samples
- Consumables and accessories
- Solvents and reagents

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY WORKFLOW



Cole-Parmer®

HPLC test for N-(4-Hydroxyphenyl)Acetamide SOP



Challenges of HPLC

- **Column Maintenance:** Columns need regular cleaning and conditioning to maintain efficiency.
- **Mobile Phase Selection:** Choosing the appropriate solvent system is crucial for optimal separation.
- **Detector Sensitivity:** Some compounds may require specific detectors for detection.
- **Method Development:** Requires expertise to optimize separation conditions for different samples.

Calibration HPLC

Calibration is a critical aspect of ensuring the accuracy, reliability, and precision of High-Performance Liquid Chromatography (HPLC) systems.

Components to be calibrated:

1. Pump Calibration
2. Injector Calibration
3. Detector Calibration
4. Column Efficiency and Performance

HPLC Calibration Procedure

1. Preparation of standards
2. System preparation
3. Pump calibration
4. Injector calibration
5. Detector calibration
6. Column performance evaluation
7. Data analysis and documentations
8. System suitability test

In Process Quality Control (IPQC)

Equipment/ Instrument

- Identity tests
- Quality test
- Purity test (DSC)
- Potency test
- Disintegration apparatus

- Systems
- Personnel
- Document/ procedures

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

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Differential scanning calorimetry

References:
1. Thermal Methods. In: Chatwal GR, Anand SK. Instrumental Methods of Chemical Analysis. Fifth Edition: Himalaya Publication House, 2002. P.2.701 2.749-2.751 2.
2.Thermal Analysis. In:Willard HH, Merritt LL, Dean JA, Settle FA. Instrumental Methods of Analysis. Seventh edition: CBS publishers,2012.p. 761.

(Holly Chan, February 2014)

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

Background:

-Technique was developed in 1960

- DSC is a thermal analysis technique that measures how materials respond to a wide range of temperatures.

- The test quantifies how heat affects chemical composition, melting point, crystallization behavior, oxidation, and more.

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

1. **Purpose**

- Identification of components
- Purity assessment
- Phase transition
- Polymorphism detection
- Quality and consistency
- Stability studies

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

2. DSC Types

Types of DSC Instuments

RIPER
AUTONOMOUS
NAAC &
NBA (UG)
SIRO- DSIR

- Two basic types of DSC instruments: Heat flux DSC, Power compensated DSC

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

3.Responsibilities

1.DSC team :

- Scientists and engineers
- Technicians

2.Management:

- Lab manager or department head
- Safety officer
- QA/ QC manager

3.Individual users

- Authorized users
- Data analyst

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

4. Equipment and materials

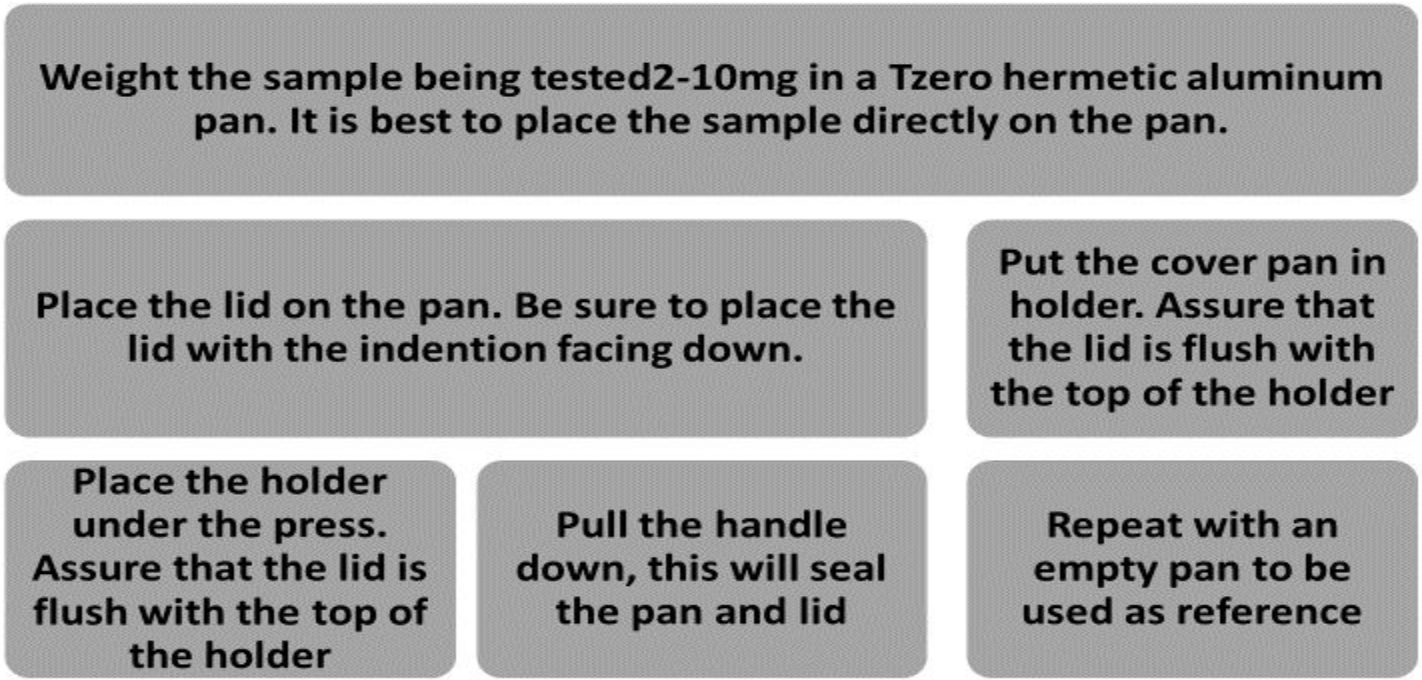
- DSC Instrument (Model TA Q-20)
- Balance
- Data Analysis Software
- Vacuum pump
- Gas flow controller
- Autosampler
- Sample pans
- Reference pans
- Standard reference materials
- Crucibles
- Purge gas
- Sealing materials

DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

5. Preparing DSC for operation

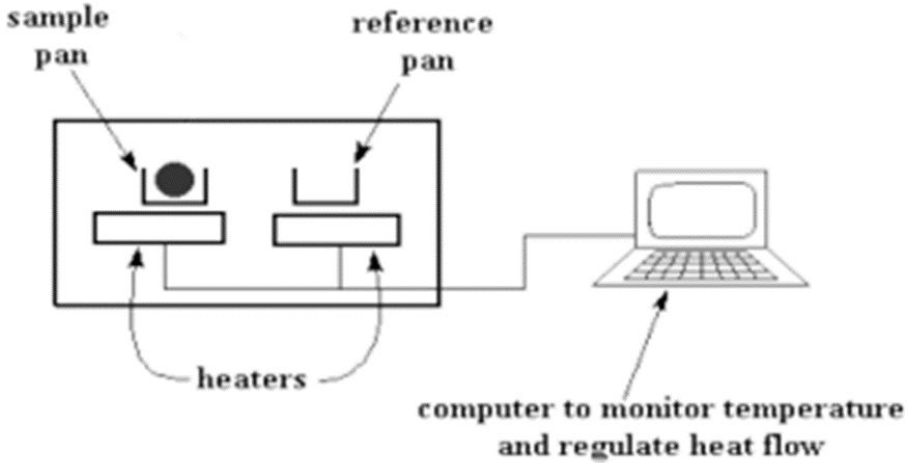
DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

Sample preparation procedure



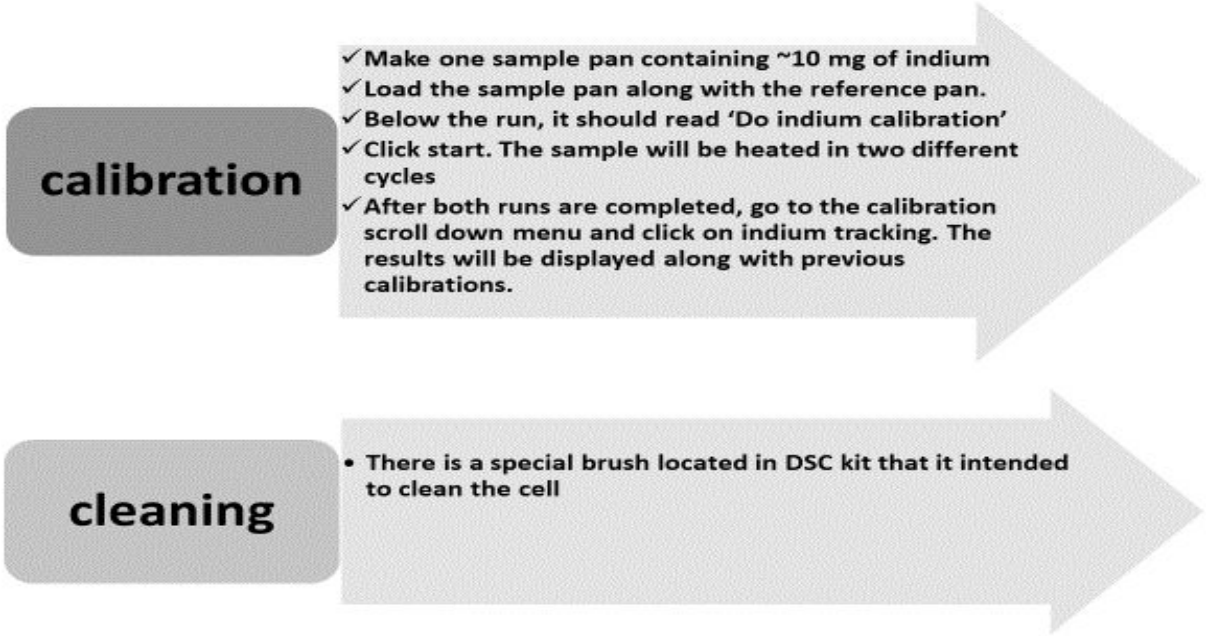
DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

How DSC work



DSC test for N-(4-Hydroxyphenyl) Acetamide SOP

Maintenance Procedure



Dissolution test for N-(4-Hydroxyphenyl) Acetamide SOP

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USP Apparatus 2

References:

- Operating Procedure for Dissolution Test (DT) Apparatus : Pharmaguideline. www.pharmaguideline.com. Accessed December 5, 2023. Link
- GMP QAA. Quality Assurance, GMP and Pharma Jobs: Operation and calibration of dissolution test apparatus. Accessed December 7, 2023. Link
- USP *Dissolution* <711>.

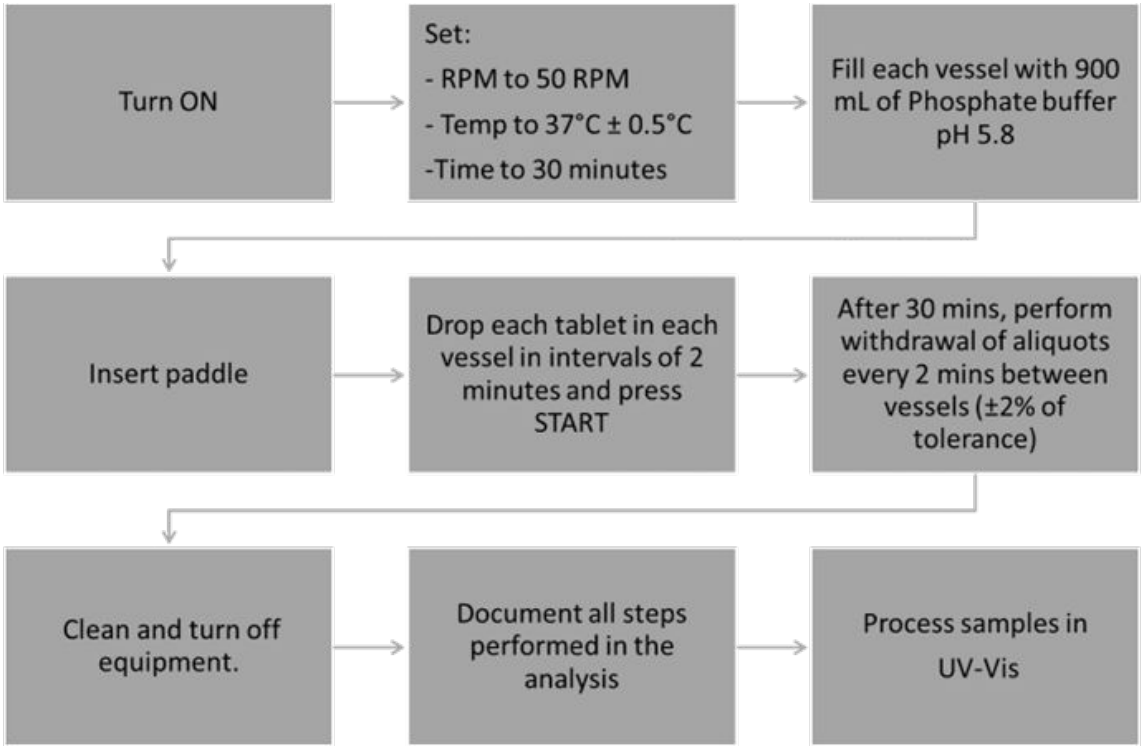
Dissolution test for N-(4-Hydroxyphenyl) Acetamide SOP

Equipments and materials

- Dissolution test apparatus II as per USP <711>.
- Disposable syringes.
- Disposable needles.
- Syringe filters.
- Medium (Phosphate buffer pH 5.8).
- Weighing balance.
- Calibrated thermometer.
- Stopwatch.
- UV-Vis.

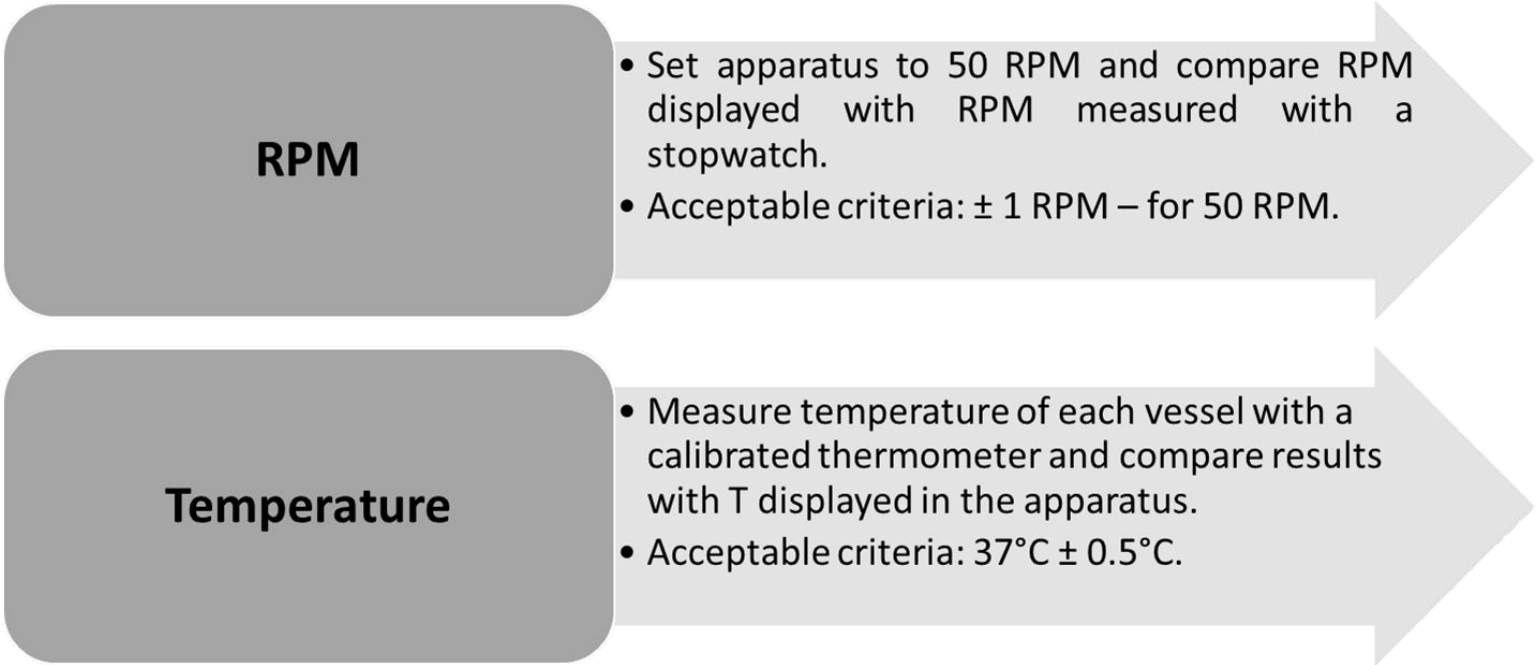
Dissolution test for N-(4-Hydroxyphenyl) Acetamide SOP

Test procedure



Dissolution test for N-(4-Hydroxyphenyl) Acetamide SOP

Calibration



USP Monograph reference for Dissolution QC test

Acetaminophen Tablets

» Acetaminophen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of acetaminophen ($C_8H_9NO_2$).

Packaging and storage—Preserve in tight containers, and store at controlled room temperature.

Labeling—Label Tablets that must be chewed to indicate that they are to be chewed before swallowing.

USP Reference standards ⟨11⟩—*USP Acetaminophen RS.*

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

B: Triturate an amount of powdered Tablets, equivalent to about 50 mg of acetaminophen, with 50 mL of methanol, and filter: the clear filtrate (test solution) responds to the *Thin-layer Chromatographic Identification Test* ⟨201⟩, a solvent system consisting of a mixture of methylene chloride and methanol (4 : 1) being used.

Dissolution ⟨711⟩—

Medium: pH 5.8 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_8H_9NO_2$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 243 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Acetaminophen RS in the same *Medium.*

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_8H_9NO_2$ is dissolved in 30 minutes.

Final/Outgoing Quality Control

1. **Procedures**
- Quality and quantity check.
- Appearance check.
- Dimensions check.
2. **Personnel**
3. **Materials**
4. **Documents/SOPs**

Conclusion

- Importance of Quality Control in pharmaceutical industry.
- QC requires compliance with multiple regulations (USP, FDA, CFR,...)
- QC involves commitment from all personnel.
- Importance of training personnel.

References

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