STANDARD OPERATING PROCEDURE

Analysis and Release of Paracetamol 500mg Tablets

Parameter	Details
Department	Quality Control
Applicable To	QC Analysts, QC Supervisors, QA Personnel
Supersedes	New Document
Review Frequency	Annual or as required

1.0 OBJECTIVE

To establish a standardized procedure for the quality control testing and release of Paracetamol 500mg tablets, ensuring compliance with current regulatory requirements, pharmacopoeial monographs (BP/USP), and internal quality standards. This procedure aims to guarantee that all released products meet predetermined specifications for safety, efficacy, and quality.

2.0 SCOPE

This Standard Operating Procedure applies to all personnel involved in the quality control testing and release of Paracetamol 500mg tablets at PharmGen Quality Systems International. The procedure encompasses:

• All laboratory analysts performing release testing

• Quality Control Supervisors responsible for data review

• Quality Assurance personnel involved in batch disposition

• Documentation and data integrity requirements

• All equipment and instrumentation used in testing

3.0 RESPONSIBILITIES

Role	Responsibilities
QC Analyst	Execute tests per SOP; document results in LIMS; report anomalies immediately; maintain sample integrity and chain of custody.
QC Supervisor	Review raw data and calculations; verify system suitability; approve/reject test results; initiate investigations for OOS results.
QC Manager	Ensure resource availability; approve SOPs; oversee laboratory compliance; review trend data.
QA Manager	Final batch disposition; CAPA approval; regulatory interface; audit coordination.

4.0 DEFINITIONS AND ABBREVIATIONS

Term	Definition
API	Active Pharmaceutical Ingredient
BP	British Pharmacopoeia
CAPA	Corrective and Preventive Action
CGMP	Current Good Manufacturing Practice
HPLC	High-Performance Liquid Chromatography
LIMS	Laboratory Information Management System
NLT	Not Less Than
NMT	Not More Than
OOS	Out-of-Specification
RH	Relative Humidity
SOP	Standard Operating Procedure
USP	United States Pharmacopeia

5.0 ENVIRONMENTAL CONTROLS

All testing shall be performed in a controlled laboratory environment. The following conditions must be maintained and documented throughout the testing process:

Parameter	Specification	Monitoring Frequency
Temperature	22°C - 25°C	Continuous (data logger)
Relative Humidity	40% - 60% RH	Continuous (data logger)
Particulate Matter	ISO Class 8 (at rest)	Weekly

6.0 PRODUCT SPECIFICATIONS

The following specifications apply to Paracetamol 500mg Tablets and shall be used as acceptance criteria for batch release:

Parameter	Acceptance Criteria	Reference	Test Method
Appearance	White to off-white, round, biconvex tablets with break line on one side. Free from visible defects.	BP/USP	Visual
Identification	Positive for Paracetamol by HPLC retention time and UV spectrum	BP/USP	HPLC
Assay (Paracetamol)	95.0% - 105.0% of labeled amount	BP	HPLC
Dissolution	NLT 80% (Q) in 30 minutes in phosphate buffer pH 5.8	USP	USP Apparatus II
Hardness	4.0 - 8.0 kg/cm^2	Internal	Hardness Tester
Friability	NMT 1.0% w/w	USP	Friabilator
Weight Variation	Average weight ± 5.0%	BP	Analytical Balance
Disintegration	NMT 15 minutes in water at 37°C ± 2°C	USP	Disintegration Apparatus
Related Substance J	NMT 10 ppm	BP	HPLC
Microbial Limits	TAMC: NMT 10^3 CFU/g; TYMC: NMT 10^2 CFU/g	USP	Microbiology

7.0 MATERIALS AND EQUIPMENT

7.1 Reagents and Solvents

Item	Grade	Storage
Methanol	HPLC Grade	Flammable cabinet, RT
Acetonitrile	HPLC Grade	Flammable cabinet, RT
Potassium Dihydrogen Phosphate	AR Grade	Chemical storage, RT
Sodium Hydroxide	AR Grade	Chemical storage, RT
Paracetamol Reference Standard	USP/BP RS	2-8°C, desiccator
Water	HPLC Grade / Milli-Q	Fresh preparation

7.2 Equipment

Equipment	Specification	Calibration Frequency
HPLC System	Quaternary pump, autosampler, UV-VIS detector, column oven	Annual (IQ/OQ/PQ)
Analytical Balance	Readability: 0.01 mg	Daily verification, Annual calibration
Dissolution Apparatus	USP Apparatus II (Paddle), 6-station	Semi-annual
UV-VIS Spectrophotometer	190-1100 nm range	Annual
Hardness Tester	Digital, 0-500 N range	Annual
Friabilator	25 rpm, compliant to USP	Annual

8.0 ANALYTICAL PROCEDURE - ASSAY BY HPLC

8.1 Chromatographic Conditions

Parameter	Specification
Column	Octadecylsilyl silica gel (C18), 250 mm x 4.6 mm, 5 µm particle size
Mobile Phase	Methanol : Water (15:85 V/V)
Flow Rate	1.5 mL/min
Injection Volume	20 µL
Detection Wavelength	245 nm (UV)
Column Temperature	25°C ± 2°C
Run Time	10 minutes
Retention Time (Expected)	Approximately 5.0 minutes

8.2 System Suitability Requirements

Parameter	Acceptance Criteria

Tailing Factor	NMT 2.0
Theoretical Plates	NLT 2000
%RSD of Peak Area (n=5)	NMT 2.0%
Resolution (from nearest peak)	NLT 2.0

8.3 Sample Preparation

Step 1: Collect a composite sample of 20 tablets from the batch.

Step 2: Accurately weigh the composite sample and record the weight.

Step 3: Crush the tablets to a fine powder using a mortar and pestle.

Step 4: Pass the powder through a #40 mesh sieve to ensure homogeneity.

Step 5: Transfer an accurately weighed portion of powder (equivalent to 100 mg Paracetamol) into a 100 mL volumetric flask.

Step 6: Add approximately 50 mL of mobile phase and sonicate for 15 minutes with intermittent shaking.

Step 7: Allow to cool to room temperature and dilute to volume with mobile phase.

Step 8: Filter through a 0.45 µm PVDF membrane filter, discarding the first 3 mL of filtrate.

Step 9: Further dilute as required to achieve a final concentration of approximately 100 µg/mL.

8.4 Standard Preparation

Step 1: Accurately weigh approximately 50 mg of Paracetamol Reference Standard (USP/BP RS).

Step 2: Transfer to a 50 mL volumetric flask.

Step 3: Dissolve in mobile phase with sonication for 5 minutes.

Step 4: Dilute to volume with mobile phase (Stock Solution: 1000 µg/mL).

Step 5: Further dilute 10 mL of stock to 100 mL with mobile phase (Working Standard: 100 µg/mL).

8.5 Calculation

The percentage of labeled amount of Paracetamol is calculated using the following formula:

$$\% \text{ Label Claim} = \left(A_{sample} / A_{standard}\right) \times \left(C_{standard} / C_{sample}\right) \times \left(P / 100\right) \times 100$$

Where:
A_{sample} = Peak area of sample solution
$A_{standard}$ = Peak area of standard solution
$C_{standard}$ = Concentration of standard solution (µg/mL)
C_{sample} = Concentration of sample solution (µg/mL)
P = Purity of reference standard (%)

9.0 DATA INTEGRITY AND DOCUMENTATION

All analytical data must be generated and maintained in compliance with 21 CFR Part 11 and ALCOA+ principles (Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, Available).

- All raw data, including chromatograms, must be electronically archived with audit trails enabled.
- Manual entries must be in permanent ink with single-line strikethroughs for corrections, initialed and dated.
- Backup of electronic data must be performed daily.
- Re-integration or reprocessing of chromatographic data requires documented justification.
- All calculations must be verified by a second analyst or supervisor.

10.0 OUT-OF-SPECIFICATION (OOS) RESULTS

Any result falling outside the acceptance criteria shall be handled in accordance with QA-SOP-OOS-001 'Investigation of Out-of-Specification Results'. The following immediate actions must be taken:

1. STOP testing immediately upon identification of OOS result.

2. Retain all sample solutions, standards, and reagents used in the analysis.

3. Secure all equipment and vials for supervisor review.

4. Notify the QC Supervisor within 30 minutes of result identification.

5. Complete OOS Notification Form (QC-FORM-OOS-01) and submit to QA.

6. Do not discard any materials until Phase I investigation is complete.

11.0 REFERENCES

- British Pharmacopoeia (Current Edition) - Paracetamol Tablets Monograph
- United States Pharmacopeia (Current Edition) - Acetaminophen Tablets Monograph
- 21 CFR Part 211 - Current Good Manufacturing Practice for Finished Pharmaceuticals
- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- FDA Guidance for Industry: Investigating Out-of-Specification (OOS) Test Results
- ICH Q7 - Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
- QA-SOP-OOS-001 - Investigation of Out-of-Specification Results
- QC-SOP-HPLC-001 - Operation and Maintenance of HPLC Systems

12.0 REVISION HISTORY

Rev.	Date	Description of Change	Author
01	25-Feb-2026	Initial Release	Dr. S. Patel

DOCUMENT APPROVAL

Role	Name	Signature	Date
Prepared By	Dr. Sunita Patel (QC Analyst)		25-Feb-2026
Reviewed By	Mr. Rajesh Kumar (QC Supervisor)		25-Feb-2026
Approved By	Dr. Ananya Sharma (QC Manager)		25-Feb-2026
Quality Assurance	Mr. Vikram Singh (QA Manager)		25-Feb-2026