Acceptance criteria: Meet the requirements

ASSAY

- **PROCEDURE**

Mobile phase: Methanol and water (1:3)

Standard solution: 0.01 mg/mL of USP Acetaminophen RS in *Mobile phase*

Sample stock solution: Nominally 0.5 mg/mL of acetaminophen prepared as follows. Weigh, and finely powder NLT 20 Tablets. Transfer 100 mg of acetaminophen from a portion of powdered Tablets to a 200-mL volumetric flask, add 100 mL of *Mobile phase*, shake by mechanical means for 10 min, sonicate for 5 min, and dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.01 mg/mL of acetaminophen in *Mobile phase* from the *Sample stock solution*. Pass a portion of this solution through a filter of 0.5-µm or finer pore size, discarding the first 10 mL of the filtrate. Use the clear filtrate.

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 243 nm
Column: 3.9-mm × 30-cm; packing L1
Flow rate: 1.5 mL/min
Injection volume: 10 µL

System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 1000 theoretical plates
Tailing factor: NMT 2
Relative standard deviation: NMT 2.0%

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Acetaminophen RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of acetaminophen in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION** ⟨711⟩

Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL
Apparatus 2: 50 rpm
Time: 30 min
Standard solution: A known concentration of USP Acetaminophen RS in *Medium*
Sample solution: A filtered portion of the solution under test, suitability diluted with *Medium* to obtain a concentration similar to that of the *Standard solution*
Instrumental conditions
Mode: UV
Analytical wavelength: Maximum absorbance at about 243 nm
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved.
Tolerances: NLT 80% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) is dissolved.
For Tablets labeled as chewable
Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL
Apparatus 2: 75 rpm
Time: 45 min
Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed above.
Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩: Meet the requirements

IMPURITIES

- **4-AMINOPHENOL IN ACETAMINOPHEN-CONTAINING DRUG PRODUCTS** ⟨227⟩: Meet the requirements

ADDITIONAL REQUIREMENTS

- **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

Acetaminophen Extended-Release Tablets

DEFINITION

Acetaminophen Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$).

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨197K⟩

Sample: A portion of powdered Tablets
Acceptance criteria: Meet the requirements

- **B.** The retention time of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Solution A: Phosphoric acid and water (1:9)
Mobile phase: Methanol, *Solution A*, and water (300:1:700)
Standard solution: 0.65 mg/mL of USP Acetaminophen RS in *Mobile phase*. Prepare by first dissolving in methanol, and then diluting with *Mobile phase* to volume.
Sample stock solution: Transfer 10 Tablets to a 250-mL volumetric flask containing 50 mL of water and a magnetic stir bar. Stir for at least 30 min or until the coating has dissolved. Add 150 mL of methanol, and stir for 45 min. Tablet cores should be disintegrated at least 15 min before ending the stirring. Remove the magnetic stir bar, and rinse into the flask with methanol. Dilute with methanol to volume, and centrifuge. Use the clear supernatant.
Sample solution: Dilute 5 mL of the *Sample stock solution* with *Mobile phase* to 200 mL.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 295 nm
Column: 3.9-mm × 15-cm; packing L1
Flow rate: 2.0 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 3.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*