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⟩

Test 1

Medium: Simulated gastric fluid TS (without enzyme); 900 mL

Apparatus 2: 50 rpm

Times: 15 min, 1 h, and 3 h

Standard solution: A known concentration of USP Acetaminophen RS in *Medium*

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium* to obtain a concentration similar to that of the *Standard solution*

Instrumental conditions

Mode: UV

Analytical wavelength: 280 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved.

Tolerances: See *Table 1*.

Table 1

Time	Amount Dissolved
Time	45%–65%
Time	60%–85%
Time	NLT 85%

The percentages of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

For gelatin-coated Tablets

Medium, Apparatus, Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed in *Test 1*.

Times: 30 min, 90 min, and 4 h

Tolerances: See *Table 2*.

Table 2

Time	Amount Dissolved
30 min	45%–65%
30 min	45%–65%
Time	NLT 80%

The percentages of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus, Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed in *Test 1*.

Times: 15 min, 1 h, and 3 h

Tolerances: See *Table 3*.

Table 3

Time	Amount Dissolved
15 min	45%–65%
1 h	45%–65%
Time	NLT 80%

The percentages of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

• **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.

• **Labeling:** Where the Tablets are gelatin-coated, the label so states. When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

• **USP Reference Standards** ⟨11⟩

USP Acetaminophen RS

Acetaminophen and Aspirin Tablets

DEFINITION

Acetaminophen and Aspirin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$).

IDENTIFICATION

• **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

[Note—Use clean and dry glassware. Inject the *Standard solution* and the *Sample solution* promptly after preparation.]

Solution A: Chloroform, methanol, and glacial acetic acid (78:20:2)

Mobile phase: Transfer 225 mg of tetramethylammonium hydroxide pentahydrate to a 1000-mL flask. Add 750 mL of water, 125 mL of methanol, 125 mL of acetonitrile, and 1.0 mL of glacial acetic acid. Stir for 3 min, and pass through a membrane filter of 0.5-µm or finer pore size.

Internal standard solution: 20 mg/mL of benzoic acid in *Solution A*

Standard solution: 3.25 mg/mL each of USP Acetaminophen RS and USP Aspirin RS, and 2.0 mg/mL of benzoic acid, from *Internal standard solution*, in *Solution A*

Sample solution: Nominally 3.25 mg/mL of acetaminophen in *Solution A*, prepared as follows. Transfer an equivalent of 325 mg of acetaminophen, from NLT 20 finely powdered Tablets, to a 100-mL volumetric flask. Add 10.0 mL of *Internal standard solution* and 50 mL of *Solution A*, and sonicate for 3 min. Dilute with *Solution A* to volume. Pass a portion of this solution through a filter of 2.5-µm or finer pore size. Use the filtrate.

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: *UV 280 nm*

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

[Note—The retention times for acetaminophen, salicylic acid (if present), aspirin, and benzoic acid are about 2, 3, 5, and 8 min, respectively.]

Suitability requirements

Relative standard deviation: NMT 3.0% for acetaminophen or aspirin for four replicate injections