Transfer 8.0 mL of this solution to a 50-mL volumetric flask, dilute with Mobile phase to volume, and mix. Pass a portion of this solution through a filter having a 0.5-µm or finer porosity, discarding the first 10 mL of the filtrate. Use the clear filtrate as the Assay preparation.

Procedure—Proceed as directed for Procedure in the Assay under Acetaminophen Capsules. Calculate the quantity, in g, of acetaminophen (C₈H₉NO₂) in the portion of Acetaminophen for Effervescent Oral Solution taken by the formula:

\[ 62.5(C / r_S) \]

in which \( C \) is the concentration, in mg per mL, of USP Acetaminophen RS in the Standard preparation; and \( r_U \) and \( r_S \) are the acetaminophen peak responses obtained from the Assay preparation and the Standard preparation, respectively.

**Acetaminophen Capsules**

» Acetaminophen Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of acetaminophen (C₈H₉NO₂).

**Packaging and storage**—Preserve in tight containers, and store at controlled room temperature or in a cool place.

**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: Transfer a portion of Capsules, equivalent to about 20 mg of acetaminophen, to a beaker, add 20 mL of methanol, and heat on a steam bath until melted. Remove the beaker from the steam bath, allow to cool with occasional stirring, and filter: the clear filtrate (test solution) responds to the Aminophen peak responses obtained from the Thin-layer Chromatographic Identification Test (201), a solvent system consisting of a mixture of methylene chloride and methanol (4:1) being used.

**Assay**—

**Mobile phase, Standard preparation, and Chromatographic system**—Proceed as directed in the Assay under Acetaminophen Capsules.

**Assay preparation**—Tare a small dish and a glass rod, place in the dish not fewer than 5 Suppositories, heat gently on a steam bath until melted, then stir, cool while stirring, and weigh. Transfer an accurately weighed portion of the mass, equivalent to about 100 mg of acetaminophen, to a separator, add 30 mL of solvent hexane, and mix to dissolve. Add 30 mL of water, shake gently, and allow the phases to separate. [NOTE—If an emulsion forms, allow sufficient time for it to separate.] Transfer the aqueous layer to a 200-mL volumetric flask, wash with 10 mL of water, then add the washings to the volumetric flask, dilute with Mobile phase to volume, and mix. T Add 5.0 mL of this solution to a 250-mL volumetric flask, dilute with Mobile phase to volume, and mix. Pass a portion of this solution through a filter having a 0.5-µm or finer porosity, discarding the first 10 mL of the filtrate. Use the clear filtrate as the Assay preparation.

**Procedure**—Proceed as directed for Procedure in the Assay under Acetaminophen Capsules. Calculate the quantity, in mg, of acetaminophen (C₈H₉NO₂) in each Suppository taken by the formula:

\[ 10,000C(A/W)(r_U / r_S) \]

in which \( C \) is the concentration, in mg per mL, of USP Acetaminophen RS in the Standard preparation; \( A \) is the average weight, in mg, of each Suppository taken; \( W \) is the weight, in mg, of the Suppository mass taken; and \( r_U \) and \( r_S \) are the acetaminophen peak responses obtained from the Assay preparation and the Standard preparation, respectively.

**Acetaminophen Oral Suspension**

» Acetaminophen Oral Suspension is a suspension of Acetaminophen in a suitable aqueous vehicle. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of acetaminophen (C₈H₉NO₂).

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

**USP Reference standards** (11)—

USP Acetaminophen RS

**Identification**—Transfer a volume of Oral Suspension, equivalent to about 240 mg of acetaminophen, to a separator, add 50 mL of ethyl acetate, and shake. Filter the ethyl acetate extract through a funnel containing glass wool and about 10 g of anhydrous sodium sulfate. Collect the filtrate in a beaker, and evaporate on a steam bath until dryness. Dry the residue in vacuum over silica gel: the crystalline so obtained respond to the Identification Test A under Acetaminophen.

**Uniformity of dosage units** (905)—

FOR ORAL SUSPENSION PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

**Deliverable volume** (698)—

FOR ORAL SUSPENSION PACKAGED IN MULTIPLE-UNIT CONTAINERS: meets the requirements.

**Limit of 4-aminophenol**—

**Diluent**—Prepare a mixture of water, methanol, and formic acid (425:75:2).

**Mobile phase**—Prepare a filtered and degassed mixture of 0.01 M sodium butanesulfonate in Diluent. Make adjustments if necessary (see System Suitability under Chromatography (621)).

**Standard solution**—Dissolve an accurately weighed quantity of USP 4-Aminophenol RS, and dilute quantitatively, and step-wise if necessary, with Mobile phase to obtain a solution having a known concentration of about 24 µg per mL.

**Test solution**—Transfer an accurately measured portion of Oral Suspension, equivalent to about 120 mg of acetaminophen, to a 25-mL volumetric flask, dissolve in and dilute with Mobile phase to volume, and mix.

**Chromatographic system** (see Chromatography (621))—The liquid chromatograph is equipped with a 272-nm detector and a 4.6-mm × 20-cm column that contains 10-µm packing L1. The flow rate is about 2.0 mL per minute. Chromatograph the Standard solution and the Test solution, and record the peak areas as directed for Procedure.

**Procedure**—Separately inject equal volumes (about 20 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the areas for the major peaks: the peak area of 4-aminophenol obtained from the Test solution is not greater than the corresponding peak area obtained from the Standard solution.

**pH** (791): between 4.0 and 6.9.

**Assay**—

**Mobile phase, Standard preparation, and Chromatographic system**—Proceed as directed in the Assay under Acetaminophen Capsules.

**Assay preparation**—Transfer an accurately measured volume of Oral Suspension, previously well-shaken, equivalent to about 100 mg of acetaminophen, to a 200-mL volumetric flask, add
about 100 mL of Mobile phase, and shake by mechanical means for 10 minutes. Dilute with Mobile phase to volume, and mix. Transfer 5.0 mL of this solution to a 250-mL volumetric flask, dilute with Mobile phase to volume, and mix. Pass a portion of this solution through a filter having a 0.5-μm or finer porosity, discarding the first 10 mL of the filtrate. Use the clear filtrate as the Assay preparation.

Procedure—Proceed as directed for Procedure in the Assay under Acetaminophen Capsules. Calculate the quantity, in mg, of acetaminophen \( (C_8H_9NO_2) \) in each mL of the Oral Suspension taken by the formula:

\[
10,000(C/V)(r_0 / r_i)
\]

in which \( C \) is the concentration, in mg per mL, of USP Acetaminophen RS in the Standard preparation; \( V \) is the volume, in mL, of Oral Suspension taken; and \( r_0 \) and \( r_i \) are the acetaminophen peak responses obtained from the Assay preparation and the Standard preparation, respectively.

**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.

For Tablets Labeled as Chewable—

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

Apparatus 2: 75 rpm.

Time: 45 minutes.

Procedure—Proceed as directed for Procedure for Acetaminophen Tablets.

Tolerances—Not less than 75% \((Q)\) of the labeled amount of \( C_8H_9NO_2 \) is dissolved in 45 minutes.

**Uniformity of dosage units** (905): meet the requirements.

**Assay**—

Mobile phase, Standard preparation, and Chromatographic system—Proceed as directed in the Assay under Acetaminophen Capsules.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of acetaminophen, to a 200-mL volumetric flask, add about 100 mL of Mobile phase, shake by mechanical means for 10 minutes, sonicate for about 5 minutes, dilute with Mobile phase to volume, and mix. Transfer 5.0 mL of this solution to a 250-mL volumetric flask, dilute with Mobile phase to volume, and mix. Pass a portion of this solution through a filter having a 0.5-μm or finer porosity, discarding the first 10 mL of the filtrate. Use the clear filtrate as the Assay preparation.

Procedure—Proceed as directed for Procedure in the Assay under Acetaminophen Capsules. Calculate the quantity, in mg, of acetaminophen \( (C_8H_9NO_2) \) in the portion of Tablets taken by the formula:

\[
10,000C(r_0 / r_i)
\]

in which \( C \) is the concentration, in mg per mL, of USP Acetaminophen RS in the Standard preparation; and \( r_0 \) and \( r_i \) are the acetaminophen peak responses obtained from the Assay preparation and the Standard preparation, respectively.

**Acetaminophen Extended-Release Tablets**

> Acetaminophen Extended-Release 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.

**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

**Identification**—

A: Infrared Absorption (197K)—Use a portion of powdered Tablets.

B: 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.

**Dissolution** (711)—

**TEST 1**—

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

Apparatus 2: 50 rpm.

Times: 15 minutes, 1 hour, and 3 hours.

Procedure—Determine the amount of \( C_8H_9NO_2 \) dissolved from UV absorbances at 280 nm, using a filtered portion of the solution under test in comparison with a Standard solution having a known concentration of USP Acetaminophen RS in the same Medium.

Tolerances—The percentages of the labeled amount of \( C_8H_9NO_2 \) dissolved at the times specified conform to Acceptance Table 2.