PERFORMANCE TESTS

• **DISSOLUTION** ⟨711⟩, *Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms, Procedure for a pooled sample for immediate-release dosage forms*

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Sample solution: Mix 9.0 mL of a filtered portion of the solution with 1.0 mL of 1% phosphoric acid solution.

Analysis: Determine the percentage of the labeled amount of acetaminophen, chlorpheniramine maleate, and dextromethorphan hydrobromide dissolved, using the *Analysis* set forth in the *Assay* for *Acetaminophen*, the *Assay* for *Chlorpheniramine Maleate*, and the *Assay* for *Dextromethorphan Hydrobromide*, respectively, making any necessary volumetric adjustments.

Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$), chlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$), and dextromethorphan hydrobromide monohydrate ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$) is dissolved.

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

Medium: 0.1 M hydrochloric acid; 900 mL

Apparatus 2, Time, Sample solution, Analysis, and Tolerances: Proceed as directed in *Test 1*.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2, Time, Sample solution, Analysis, and Tolerances: Proceed as directed in *Test 1*.

• **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:** The label states the name and quantity of each active ingredient and indicates its function (or purpose) in the article. 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

USP Chlorpheniramine Maleate RS

USP Dextromethorphan Hydrobromide RS

Acetaminophen and Codeine Phosphate Capsules

DEFINITION

Acetaminophen and Codeine Phosphate Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$).

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*.

• **B. THIN-LAYER CHROMATOGRAPHY**

Standard solution: 12 mg/mL each of USP Acetaminophen RS and USP Codeine Phosphate RS in methanol

Sample solution: Transfer a portion of Capsule contents, equivalent to 12 mg of codeine phosphate, to a separator. Add 5 mL of water, 1 mL of ammonium hydroxide, and 5 mL of methylene chloride. Shake for 1 min, and allow the layers to separate. Use the clear lower layer.

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Methanol and ammonium hydroxide (49:1)

Analysis

Samples: *Standard solution* and *Sample solution*

Allow the spots to dry after applying each sample to the adsorbent. Develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by examination under short-wavelength UV light.

Acceptance criteria: The R_F values of the two principal spots of the *Sample solution* correspond to those of the *Standard solution*.

ASSAY

• **PROCEDURE**

Solution A: Dissolve 2.04 g of monobasic potassium phosphate in 950 mL of water. Add 2 mL of triethylamine, adjust with phosphoric acid to a pH of 2.35, and dilute with water to 1000 mL.

Mobile phase: Methanol and *Solution A* (8:92)

Codeine phosphate standard stock solution: 0.3 mg/mL of USP Codeine Phosphate RS in *Mobile phase*

Standard solution: 0.3 mg/mL of USP Acetaminophen RS and 0.3*J* mg/mL of codeine phosphate in *Mobile phase*, prepared as follows. Transfer an appropriate amount of USP Acetaminophen RS and a suitable volume (multiplied by *J*) of *Codeine phosphate standard stock solution* (*J* being the ratio of the labeled amount, in mg, of codeine phosphate to that of acetaminophen) to a suitable volumetric flask. Dilute with *Mobile phase* to volume.

Sample stock solution: Nominally 3.0 mg/mL of acetaminophen and 3.0*J* mg/mL of codeine phosphate (equivalent to 2.93*J* mg/mL of anhydrous codeine phosphate) in *Mobile phase*, prepared as follows. Transfer a portion of the combined contents, equivalent to 300 mg of acetaminophen, from NLT 20 Capsules, to a 100-mL volumetric flask. Add 75 mL of *Mobile phase*, and sonicate for 10 min. Dilute with *Mobile phase* to volume.

Sample solution: Dilute 5.0 mL of the *Sample stock solution* with *Mobile phase* to 50 mL, and pass a portion through a filter of 1-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 30 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between acetaminophen and codeine

Relative standard deviation: NMT 2.0% for acetaminophen; NMT 3.0% for codeine