Test solution—Pipet into a 125-mL separator a volume of a filtered portion of the solution under test that is estimated to contain about 0.4 mg of hydrocodone bitartrate. Add 2 drops of 6 N ammonium hydroxide, and extract with three 25-mL portions of chloroform. Filter the extracts through about 3 g of anhydrous sodium sulfate supported on filter paper, and combine the filtered extracts in a 100-mL volumetric flask. Add chloroform through the filter to volume, and mix.

Procedure—Pipet 10 mL of the *Standard solution* into a 125-mL separator, and add 25.0 mL of chloroform. Pipet 25 mL of the *Test solution* into a second 125-mL separator, and add 10.0 mL of water. Pipet 25 mL of chloroform and 10 mL of water into a third 125-mL separator to provide a blank. Treat each mixture as follows. Add 30 mL of *Phosphate buffer–bromothymol blue solution*, and shake vigorously for not less than 15 minutes. Allow the layers to separate, and pass the chloroform layer through filter paper, discarding the first 10 mL of the filtrate. Determine the absorbances of the clear filtrates in 3-cm cells at the wavelength of maximum absorbance at about 415 nm, using the solution from the blank to set the spectrometer. Calculate the amount of $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$ dissolved by the formula:

$$(494.49 / 449.46)100(C_S / V_U)(A_U / A_S)$$

in which 494.49 and 449.46 are the molecular weights of the hydrated and anhydrous forms of hydrocodone bitartrate, respectively; C_S is the concentration, in µg per mL, of USP Hydrocodone Bitartrate RS in the *Standard solution*; V_U is the volume of the filtered solution under test that is estimated to contain 0.4 mg of hydrocodone bitartrate; and A_U and A_S are the absorbances of the solutions from the *Test solution* and the *Standard solution*, respectively.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—Transfer 1 finely powdered Tablet to a 50-mL volumetric flask, add 0.1 N sulfuric acid to volume, and mix. Filter if necessary, discarding the first 20 mL of the filtrate. Concomitantly determine the absorbances of this solution and a solution of USP Hydrocodone Bitartrate RS in the same medium, having a known concentration of about 100 µg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 280 nm, with a suitable spectrophotometer, using 0.1 N sulfuric acid as the blank. Calculate the quantity, in mg, of $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2\ ^1/_2H_2O$ in the Tablet taken by the formula:

$$(494.49 / 449.46)(TC / D)(A_U / A_S)$$

in which 494.49 and 449.46 are the molecular weights of the hydrated and anhydrous forms of hydrocodone bitartrate, respectively; T is the labeled quantity, in mg, of hydrocodone bitartrate in the Tablet; C is the concentration, in µg per mL, of USP Hydrocodone Bitartrate RS in the Standard solution; D is the concentration, in µg per mL, of the solution from the Tablet, based upon the labeled quantity per Tablet and the extent of dilution; and A_U and A_S are the absorbances of the solution from the Tablet and the Standard solution, respectively.

Assay—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of hydrocodone bitartrate, to a 250-mL separator with the aid of 10 mL of water. Add a small piece of red litmus paper, then add, dropwise, 6 N ammonium hydroxide until the litmus paper turns blue (about 3 drops). Extract with 25-, 25-, 20-, 20-, 15-, and 15-mL portions of chloroform, and filter the chloroform extracts through a small pledget of cotton into a 250-mL conical flask. Evaporate the combined chloroform extracts almost to dryness, remove the flask from the steam bath, and evaporate the remainder of the chloroform with the aid of a current of air. Dissolve the residue in 80 mL of glacial acetic acid, warming, if necessary. Cool, and titrate with 0.02 N perchloric acid VS, determining the endpoint potentiometrically (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.02 N perchloric acid is equivalent to 9.890 mg of $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$.

Hydrocodone Bitartrate and Acetaminophen Tablets

» Hydrocodone Bitartrate and Acetaminophen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of hydrocodone bitartrate disesquihydrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$) and acetaminophen ($C_8H_9NO_2$).

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—The labeling indicates the *Dissolution* test with which the product complies.

USP Reference standards ⟨11⟩—
USP Acetaminophen RS
USP Hydrocodone Bitartrate RS

Identification—

A: Finely powder 1 Tablet, and transfer about half of the powder to a test tube. Add 1 mL of 1 N sodium hydroxide and 10 mL of water, and centrifuge. Add 5 or 6 drops of ferric chloride TS: a deep blue color develops, and almost immediately a gray-black precipitate forms *(presence of acetaminophen)*.

B: The retention times of the hydrocodone bitartrate peak and the acetaminophen peak in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Dissolution, *Procedure for a Pooled Sample* ⟨711⟩—

TEST 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*.

Medium: pH 5.8 ± 0.05 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Proceed as directed in the *Assay*, making any necessary modifications.

Tolerances—Not less than 80% *(Q)* each of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and hydrocodone bitartrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$) are dissolved in 30 minutes.

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

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus, Time, and *Procedure*—Proceed as directed under *Test 1*.

Tolerances—Not less than 80% *(Q)* each of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and hydrocodone bitartrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$) is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Buffer solution—Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water.