compound C in the Oral Suspension, based on the labeled content of ibuprofen, taken by the formula:

\[ 12,500C(DL)(f_0 / f_r) \]

in which \( C \) is the concentration, in mg per mL, of USP Ibuprofen Related Compound C RS in the Standard solution; \( D \) is the quantity, in mL, of Oral Suspension taken to prepare the stock solution for the Assay preparation; \( L \) is the labeled quantity, in mg, of ibuprofen in each mL of Oral Suspension; and \( f_0 \) and \( f_r \) are the ibuprofen related compound C peak areas obtained from the Test solution and the Standard solution, respectively. Not more than 0.25% is found.

**Assay**—

**Mobile phase**—Dilute 0.7 mL of phosphoric acid with water to obtain 1000 mL of 0.01 M phosphoric acid. Prepare a mixture of this solution and acetonitrile (63:37). Make adjustments if necessary (see System Suitability under Chromatography (621)).

**Diluent**—Prepare a mixture of acetonitrile and water (1:1).

**Internal standard solution**—Prepare a solution of benzophenone in acetonitrile containing about 3.2 mg per mL.

**Standard preparation**—Quantitatively dissolve an accurately weighed quantity of USP Ibuprofen RS in Diluent to obtain a stock solution having a known concentration of about 1.2 mg per mL. Transfer 20.0 mL of this stock solution and 5.0 mL of Internal standard solution to a 50-mL volumetric flask, dilute with acetonitrile to volume, mix, and filter. This solution contains about 0.46 mg of ibuprofen per mL.

**Density**—Using a tared 50-mL volumetric flask, weigh 50 mL of Oral Suspension that has been previously well shaken to ensure homogeneity, allow to stand until the entrapped air has risen, and finally invert carefully just prior to transferring it to the volumetric flask. From the observed weight of 50 mL of the Oral Suspension, calculate the density, in g per mL, of the Oral Suspension.

**Assay preparation**—Transfer an accurately weighed portion of Oral Suspension, equivalent to about 60 mg of ibuprofen, to a 50-mL volumetric flask, dilute with Diluent to volume, and mix (stock solution). Transfer 20.0 mL of this stock solution and 5.0 mL of Internal standard solution to a second 50-mL volumetric flask, dilute with acetonitrile to volume, mix, and filter. [ NOTE—Retain a portion of the stock solution for use in the test for Limit of ibuprofen related compound C.]

**Chromatographic system** (see Chromatography (621))—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-μm × 13-cm column that contains 5-μm packing L7. The flow rate is about 2 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the relative retention times are about 0.9 for benzophenone and 1.0 for ibuprofen; the resolution, \( R_s \), between benzophenone and ibuprofen is not less than 1.5; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%

**Procedure**—Separately inject equal volumes (about 5 μL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of \( C_{13}H_{18}O_2 \) in each mL of the Oral Suspension taken by the formula:

\[ 125C(W/W)(R_0 / R_r) \]

in which \( C \) is the concentration, in mg per mL, of USP Ibuprofen RS in the Standard preparation; \( D \) is the density, in g per mL, of Oral Suspension; \( W \) is the weight, in g, of the portion of Oral Suspension taken to prepare the Assay preparation; and \( R_0 \) and \( R_r \) are the ratios of the ibuprofen peak areas to the benzophenone peak areas obtained from the Assay preparation and the Standard preparation, respectively.

### Ibuprofen Tablets

- **Ibuprofen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of \( C_{13}H_{18}O_2 \).**

**Packaging and storage**—Preserve in well-closed containers.

**Labeling**—Where the Tablets are gelatin-coated, the label so states.

**USP Reference standards** (11)—
- USP Ibuprofen RS
- USP Ibuprofen Related Compound C RS

**Identification**—

A: Grind 1 Tablet to a fine powder in a mortar, add about 5 mL of chloroform, and swirl. Filter the mixture, and evaporate the filtrate with the aid of a stream of nitrogen to dryness; the IR absorption spectrum of a mineral oil dispersion of the residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Ibuprofen RS.

B: Its retention time, relative to that of the internal standard, determined as directed in the Assay, corresponds to that of USP Ibuprofen RS.

**Dissolution** (711)—

Medium: pH 7.2 phosphate buffer (see under Buffers in the section Reagents, Indicators, and Solutions); 900 mL.

**Apparatus 2:** 50 rpm.

**Time:** 60 minutes.

**Procedure**—Determine the amount of \( C_{13}H_{18}O_2 \) dissolved from the absorbances at the wavelength of maximum absorbance at about 221 nm of 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 Ibuprofen RS in the same medium. [ NOTE—Where the Tablets are labeled as gelatin-coated, determine the amount of \( C_{13}H_{18}O_2 \) dissolved from the UV absorbance at the wavelength of maximum absorbance at about 266 nm from which is subtracted the absorbance at 280 nm, in comparison with the Standard solution similarly measured.]

**Tolerances**—Not less than 80% (Q) of the labeled amount of \( C_{13}H_{18}O_2 \) is dissolved in 60 minutes.

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

**Water, Method I** (921): not more than 5.0%, except that Tablets labeled as gelatin-coated are exempt from this requirement.

**Limit of ibuprofen related compound C**—Using the chromatograms of the Assay preparation and the Ibuprofen related compound C standard solution obtained as directed in the Assay, calculate the percentage of ibuprofen related compound C (\( C_{13}H_{18}O_2 \)) in the Tablets taken by the formula:

\[ 10,000C(A / W)(R_0 / R_r) \]

in which \( C \) is the concentration, in mg per mL, of USP Ibuprofen Related Compound C RS in the Ibuprofen related compound C standard solution; \( A \) is the average weight, in mg, of a Tablet; \( W \) is the weight of Tablet powder taken to prepare the Assay preparation; \( L \) is the quantity, in mg, of ibuprofen per Tablet as obtained in the Assay; and \( R_0 \) and \( R_r \) are the ratios of the ibuprofen related compound C peak response to the valerophenone peak response obtained from the Assay preparation and the Standard preparation, respectively: not more than 0.25% per Tablet is found.

**Assay**—

**Mobile phase, Internal standard solution, and Standard preparation**—Prepare as directed in the Assay under Ibuprofen.

**Ibuprofen related compound C standard solution**—Quantitatively dissolve an accurately weighed quantity of USP Ibuprofen Related Compound C RS in acetonitrile to obtain a stock solution having a known concentration of about 0.6 mg per mL.
Add 2.0 mL of this stock solution to 100 mL of Internal standard solution, and mix.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 1200 mg of ibuprofen, to a suitable container, add 100.0 mL of Internal standard solution, and shake for 10 minutes. [NOTE—Where the Tablets are coated, place an accurately counted number of Tablets, equivalent to not less than 1200 mg of ibuprofen, in a container, add an accurately measured volume of Internal standard solution, sufficient to obtain an Assay preparation containing about 12 mg of ibuprofen per mL, and about 15 glass beads, and shake until the Tablets are completely disintegrated.] Centrifuge a portion of the suspension so obtained and use the clear supernatant as the Assay preparation.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the relative retention times are about 0.75 for ibuprofen and 1.0 for valerophenone; the resolution, R, between ibuprofen and valerophenone is not less than 2.5; the tailing factors for the individual peaks are not more than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%. Chromatograph the Ibuprofen related compound C standard solution, and record the peak responses as directed for Procedure: the relative retention times are about 1.0 for valerophenone and 1.2 for ibuprofen related compound C; the resolution, R, between valerophenone and ibuprofen related compound C is not less than 2.5; the tailing factors for the individual peaks are not more than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 5 µL) of the Standard preparation, the Assay preparation, and the Ibuprofen related compound C standard solution into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of ibuprofen (C₁₃H₁₈O₂) and Pseudoephedrine Hydrochloride (C₁₀H₁₅NO·HCl) in each Tablet taken by the formula:

\[
100(C / A) (W / RS)(R / R) \mu L \text{ Tablets}
\]

in which C is the concentration, in mg per mL, of USP Ibuprofen RS in the Standard preparation; A is the average weight, in mg, of a Tablet; W is the weight, in mg, of a Tablet powder taken to prepare the Assay preparation; and RS and R are the ratios of the ibuprofen peak response to the valerophenone peak response obtained from the Assay preparation and the Standard preparation, respectively; or where intact Tablets were taken, calculate the quantity, in mg, of C₁₃H₁₈O₂ in each Tablet taken by the formula:

\[
CV/N(RS / R) \mu L \text{ Tablets}
\]

in which V is the volume, in mL, of Internal standard solution used to prepare the Assay preparation; N is the number of Tablets taken; and the other terms are as defined above.

Packaging and storage—Preserve in tight containers.

USP Reference standards (11)—
USP Ibuprofen RS
USP Pseudoephedrine Hydrochloride RS

Identification—
A: Place a Tablet in a small beaker, crack the Tablet coating, add 10 mL of methanol, and stir by mechanical means for about 10 minutes. Allow to settle, and use the clear supernatant as the Test solution. Prepare a Standard solution in methanol containing about 20 mg of USP Ibuprofen RS and 20 mg of USP Pseudoephedrine Hydrochloride RS per mL, β being the ratio of the labeled amount, in mg, of pseudoephedrine hydrochloride to the labeled amount, in mg, of ibuprofen per Tablet. Separate and apply 10 µL each of the Test solution and the Standard solution to a thin-layer chromatographic plate (see Chromatography (621)) covered with a 254-nm-layer of chromatographic silica gel mixture and activated by heating the plate at 105° for about 30 minutes. Place the plate in a chromatographic chamber equilibrated with a solvent system consisting of a mixture of chloroform, methanol, and glacial acetic acid (80:15:5). Develop the chromatograms until the solvent has moved about 10 cm from the origin. Remove the plate from the chromatographic chamber, place in a chamber containing iodine vapor for about 10 minutes, and examine the chromatograms: the principal spots obtained from the Test solution correspond in Rf value and appearance to those obtained from the Standard solution.

B: The retention times of the pseudoephedrine and ibuprofen peaks, relative to that of the butylparaben internal standard peak in the chromatogram of the Assay preparation correspond to those in the chromatogram of the Standard preparation, as obtained in the Assay.

Dissolution (711)—
Medium: pH 7.2 phosphate buffer (see under Buffers in the section Reagents, Indicators, and Solutions); 900 mL.
Apparatus 2: 50 rpm.
Times: 30 minutes (ibuprofen); 45 minutes (pseudoephedrine hydrochloride).

Procedure for ibuprofen—Determine the amount of ibuprofen (C₁₃H₁₈O₂) dissolved from UV absorbances at the wavelength of maximum absorbance at about 224 nm of filtered portions of the solution under test, suitably diluted with Medium, if necessary, in comparison with a Standard solution having a known concentration of USP Ibuprofen RS in the same medium.

Procedure for pseudoephedrine hydrochloride—MOBILE PHASE—Prepare a solution of monobasic potassium phosphate in water containing 500 mg per mL, and 1000 mL. Filter through a filter having a porosity of 0.5-µm or finer. Prepare a mixture of this solution and acetonitrile (500:500), and adjust with phosphoric acid to a pH of 3.3 ± 0.1. Make any necessary adjustments (see System Suitability under Chromatography (621)). Increasing the concentration of monobasic potassium phosphate or increasing the pH increases the retention time of pseudoephedrine.

STANDARD PREPARATION—Prepare a solution of USP Pseudoephedrine Hydrochloride RS in Dissolution Medium having a known concentration of about 900 mg per mL, P being the labeled quantity, in mg, of pseudoephedrine hydrochloride per Tablet.

CHROMATOGRAPHIC SYSTEM (see Chromatography (621))—The liquid chromatograph is equipped with a 215-nm detector, a guard column containing packing L10, and a 4.6-mm × 25-cm column that contains packing L10. The flow rate is about 1.5 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the tailing factor for the pseudoephedrine peak is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.

PROCEDURE—Pass a portion of the solution under test through a filter having a porosity of 0.5-µm or finer. Separately inject equal volumes (about 10 µL) of the filtrate and the Standard