Ibuprofen Oral Suspension

Ibuprofen Oral Suspension contains 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, and store at controlled room temperature.

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

**Identification**

A: Transfer a volume of Oral Suspension, equivalent to about 200 mg of ibuprofen, to a separator containing about 10 mL of chloroform, and shake for about 1 minute. Allow the layers to separate, and pass the lower chloroform layer through a filter containing about 2 g of anhydrous sodium sulfate. Use the filtrate as the test solution. [NOTE—Retain a portion of this test solution for use in Identification test B.] Separately apply 10-μL portions of the test solution and of a Standard solution containing 20 mg per mL of USP Ibuprofen RS in chloroform to a thin-layer chromatographic plate (see Chromatography (621)) coated with a 0.25-mm layer of chromatographic silica gel and previously activated by heating at 105 °C for 30 minutes. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of n-hexane, butyl acetate, and glacial acetic acid (17:3:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and dry in a current of cool air. Examine the chromatograms under short-wavelength UV light: the Rf values of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

B: Infrared Absorption (197K)—Prepare the test specimen and the standard as follows. Evaporate about 20 drops of the test solution and the Standard solution retained from Identification test A to dryness in a current of air without heating.

**Dissolution** (711)—

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

Apparatus 2: 50 rpm.

Time: 60 minutes.

Determine the percentage of the labeled amount of C$_{13}$H$_{18}$O$_2$ dissolved by the following procedure:

Mobile phase and Chromatographic system—Proceed as directed in the Assay.

Internal standard solution—Prepare a solution of benzophenone in acetonitrile containing about 0.3 mg per mL.

Standard solution—Dissolve an accurately weighed quantity of USP Ibuprofen RS in Dissolution Medium to obtain a solution having a known concentration of about 0.011 mg per mL, J being the labeled quantity, in mg, of ibuprofen in each mL of the Oral Suspension. Mix 10.0 mL of this solution and 10.0 mL of the Internal standard solution, pass the mixture through a filter having a 0.5-μm or finer porosity, and use the filtrate as the Standard solution.

Test solution—Filter a portion of the solution under test. Mix 10.0 mL of the filtrate and 10.0 mL of the Internal standard solution, pass the mixture through a filter having a 0.5-μm or finer porosity, and use the filtrate as the Test solution.

Procedure—Using an accurately tared syringe, draw about 10 mL of well-mixed Oral Suspension into the syringe, which is connected to tubing, and accurately weigh. [NOTE—The tubing of the syringe is placed into a zone that is between the surface of the Dissolution Medium and the top of the rotating blade.] Express the Oral Suspension into the Dissolution Medium. Promptly reconnect the syringe, and determine the weight, W$_0$, in g, of the Oral Suspension added to the Dissolution Medium. Separately inject equal volumes (about 10 μL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the percentage of the labeled amount of C$_{13}$H$_{18}$O$_2$ dissolved by the formula:

$$\text{Percentage} = \left( \frac{90,000 \times C \times (D/W) \times (R_s / R_t)}{\text{weight of Oral Suspension}} \right) \times 100$$

in which C is the concentration, in mg per mL, of USP Ibuprofen RS in the Standard solution; L is the labeled quantity, in mg per mL, of ibuprofen in the Oral Suspension; D is the density, in g per mL, of the Oral Suspension, determined as directed for Density in the Assay; W$_0$ is the weight, in g, of the Oral Suspension added to the Dissolution Medium; and R$_S$ and R$_T$ are the ratios of the ibuprofen peak areas obtained from the Test solution and the Standard solution, respectively.

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)—

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.

**pH** (791): between 3.6 and 4.6.

**Deliverable volume** (698): meets the requirements.

**Limit of ibuprofen related compound C**

**Mobile phase and Diluent**—Proceed as directed in the Assay.

**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 0.5 mg per mL. Transfer 3.0 mL of this stock solution to a 50-mL volumetric flask, dilute with Diluent to volume, and mix. Transfer 2.0 mL of this solution to a second 50-mL volumetric flask, add 18 mL of Diluent, dilute with acetonitrile to volume, mix, and pass through a filter having a porosity of 0.22-μm. This Standard solution contains about 0.0012 mg of ibuprofen related compound C per mL.

**Test solution**—Transfer 20.0 mL of the portion of the stock solution retained from the Assay preparation in the Assay into a 50-mL volumetric flask, dilute with acetonitrile to volume, mix, and pass through a filter having a porosity of 0.22-μm.

**System suitability solution**—Transfer 1.5 mL of the stock solution of USP Ibuprofen Related Compound C RS prepared as directed for Standard solution and 9.0 mL of the stock solution of USP Ibuprofen RS prepared as directed for Standard preparation in the Assay to a 25-mL volumetric flask, dilute with acetonitrile to volume, mix, and pass through a filter having a porosity of 0.22-μm. This solution contains about 0.03 mg of ibuprofen related compound C and about 0.4 mg of ibuprofen per mL.

**Chromatographic system** (see Chromatography (621))—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains 5-μm packing L7. The flow rate is about 2 mL per minute. Chromatograph the System suitability solution, and record the peak responses as directed for Procedure: the relative retention times are about 1.3 for ibuprofen related compound C and 1.0 for ibuprofen; the resolution, R, between ibuprofen and ibuprofen related compound C is not less than 1.5; and the tailing factor is not more than 2.0. Chromatograph the Standard solution, and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 0.2%.

**Procedure**—Separately inject equal volumes (about 35 μL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the per centage of ibuprofen related
compound C in the Oral Suspension, based on the labeled content of ibuprofen, taken by the formula:

\[(12,500C/D)(f_0 / f_R)\]

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 0.48 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-mm × 15-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:

\[125C(W/W_0)(f_0 / f_R)\]

in which \( C \) is the concentration, in mg per mL, of USP Ibuprofen RS in the Standard solution; \( D \) is the density, in g per mL, of Oral Suspension; \( W_0 \) is the weight, in g, of the portion of Oral Suspension taken to prepare the Assay preparation; and \( f_0 \) and \( f_R \) 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 per cent 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 wavelengths 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:

\[10,000C(A / W_0)(R_0 / R_1)\]

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; \( I \) is the quantity, in mg, of ibuprofen per Tablet as obtained in the Assay; and \( R_0 \) and \( R_1 \) are the ratios of the ibuprofen related compound C peak response to the benzophenone 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.