Chloroform—Use chloroform that meets the following additional requirement. To each of three glass-stoppered, 500-mL conical flasks add 50.0 mL of *Periodic acid solution*, then add 50 mL of chloroform and 10 mL of water to two of the flasks and 50 mL of water to the third flask. To each flask add 20 mL of potassium iodide TS, mix gently, and proceed as directed for *Procedure*, beginning with "allow to stand for 1 to 5 minutes." The difference between the volumes of 0.1 N sodium thiosulfate required in the titrations with and without the chloroform does not exceed 100 µL.

Procedure—Melt the Propylene Glycol Monostearate at a temperature not above 55°, and mix. Transfer a 3-g portion, accurately weighed, to a 100-mL beaker, and dissolve in 25 mL of *Chloroform*. Transfer this solution, with the aid of another 25-mL portion of *Chloroform*, to a separator, wash the beaker with 25 mL of water, and add the washing to the separator. Insert the stopper, shake vigorously for 30 to 60 seconds, and allow the layers to separate, adding 1 mL to 2 mL of glacial acetic acid, if necessary, to break any emulsion. Transfer the aqueous layer to a glass-stoppered, 500-mL conical flask, wash the chloroform layer with two 25-mL portions of water, combining the washings with the aqueous layer, and discard the chloroform layer. Add, with swirling, 50.0 mL of *Periodic acid solution* to the solution and to another glass-stoppered, 500-mL conical flask containing 75 mL of water to provide the blank. Allow to stand for 30 to 90 minutes. To each flask add 20 mL of potassium iodide TS, mix gently, and allow to stand for 1 to 5 minutes before titrating. Add 100 mL of water, and titrate with 0.1 N sodium thiosulfate VS until the brown iodine color fades to pale yellow, add 3 mL of starch TS, and continue the titration to the disappearance of the blue color. Propylene Glycol Monostearate contains not more than 1.0% of free glycerin and propylene glycol, calculated as propylene glycol taken by the formula:

$$[3.805N(B - T)] / W$$

in which 3.805 is the molecular weight of propylene glycol divided by 20; N is the exact normality of the sodium thiosulfate solution; B and T are the volumes, in mL, of sodium thiosulfate consumed in the titrations of the blank solution and test solution, respectively; and W is the weight, in g, of Propylene Glycol Monostearate taken.

Propylene glycol monoesters—Transfer about 25 g to a 500-mL, round-bottom flask, add 250 mL of alcohol and 7.5 g of potassium hydroxide, and mix. Connect a suitable condenser to the flask, reflux the mixture for 2 hours, cool, and transfer to an 800-mL beaker, rinsing the flask with about 100 mL of water and combining the rinsing with the mixture in the beaker. Heat on a steam bath to evaporate the alcohol, adding water occasionally to replace the alcohol, and continue the evaporation until the odor of alcohol can no longer be detected. Adjust the volume, with hot water, to about 250 mL, neutralize with a mixture of equal volumes of sulfuric acid and water, noting the volume used, and add a 10% excess of the dilute acid. Heat with stirring until the fatty acid layer separates, and transfer the fatty acids to a 500-mL separator. Wash the fatty acids with four 200-mL portions of hot water, and discard the washings. Dry the fatty acids at 105° for 1 hour, cool, and determine the *Acid value*, *A*, on a 1-g portion, accurately weighed, as directed for *Acid (Free Fatty Acids)* under *Fats and Fixed Oils* ⟨401⟩. Calculate the percentage of propylene glycol monoesters taken by the formula:

$$[M(H - F)] / 561.1;$$

calculate M, the average molecular weight of the monoesters, taken by the formula:

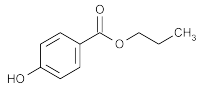
$$(56{,}110 / A) + 76.10 - 18.02;$$

and calculate F taken by the formula:

$$561.1G / 38.05$$

in which H is the *Hydroxyl value* of Propylene Glycol Monostearate, G is the content, in percentage, of glycerin and propylene glycol in Propylene Glycol Monostearate, 561.1 and 56,110 are 10 and 1000 times the molecular weight of potassium hydroxide, respectively, 38.05 is one-half of the molecular weight of propylene glycol (76.10), and 18.02 is the molecular weight of water.

Propylparaben



$C_{10}H_{12}O_3$ 180.20
Benzoic acid, 4-hydroxy-, propyl ester;
Propyl *p*-hydroxybenzoate [94-13-3].

DEFINITION
Propylparaben contains NLT 98.0% and NMT 102.0% of $C_{10}H_{12}O_3$.

IDENTIFICATION
- **A. Infrared Absorption** ⟨197M⟩
- **B. Melting Range or Temperature** ⟨741⟩**:** 96°–99°

ASSAY
- **Procedure**

Mobile phase, Sample solution, Standard solution B, and **Chromatographic system:** Proceed as described in the procedure for *Related Substances.*

System suitability

Sample: *Standard solution B*

Suitability requirements

Relative standard deviation: NMT 0.85% for 6 injections

Analysis

Samples: *Sample solution* and *Standard solution B*

Calculate the percentage of Propylparaben in the *Sample solution*:

$$\text{Result} = P \times (r_U \times C_S)/(r_S \times C_U)$$

P	= labeled purity of USP Propylparaben RS expressed as a percentage
r_U	= peak area of propylparaben from the *Sample solution*
C_S	= concentration of propylparaben in *Standard solution B*
r_S	= peak area of propylparaben from *Standard solution B*
C_U	= concentration of Propylparaben in the *Sample solution*

Acceptance criteria: 98.0%–102.0%

IMPURITIES

Inorganic Impurities

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%, determined on 1.0 g

Organic Impurities

• **PROCEDURE: RELATED SUBSTANCES**

Mobile phase: Methanol and a 6.8 g/L solution of potassium dihydrogen phosphate (65:35 v/v)

Sample solution: Dissolve 50.0 mg of Propylparaben in 2.5 mL of methanol, and dilute with *Mobile phase* to 50.0 mL. Dilute 10.0 mL of this solution with *Mobile phase* to 100.0 mL.

Standard solution A: 5.0 µg/mL each of *p*-hydroxybenzoic acid, USP Ethylparaben RS, and USP Propylparaben RS in *Mobile phase*

Standard solution B: Dissolve 50.0 mg of USP Propylparaben RS in 2.5 mL of methanol, and dilute with *Mobile phase* to 50.0 mL. Dilute 10.0 mL of this solution with *Mobile phase* to 100.0 mL.

Standard solution C: Dilute 1.0 mL of the *Sample solution* with *Mobile phase* to 20.0 mL. Dilute 1.0 mL of this solution with *Mobile phase* to 10.0 mL.

Chromatographic system

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

Mode: LC

Detector: UV 272 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.3 mL/min

Injection size: 10 µL

Run time: About 2.5 times the retention time of propylparaben

System suitability

Sample: *Standard solution A*

[NOTE—The retention time of propylparaben is about 4.5 min; the relative retention times for *p*-hydroxybenzoic acid and ethylparaben are about 0.3 and 0.7, respectively.]

Suitability requirements

Resolution: NLT 3.0 between the ethylparaben and propylparaben peaks

Analysis

Samples: *Sample solution* and *Standard solution C*

[NOTE—Disregard any limit that is 0.2 times the area of the principal peak in the chromatogram obtained with *Standard solution C* (0.1%).]

Acceptance criteria

***p*-Hydroxybenzoic acid:** The peak area in the *Sample solution*, multiplied by 1.4 to correct for the calculation of content, is NMT the area of the principal peak in *Standard solution C* (0.5%).

Unspecified impurities: The peak area of each impurity in the *Sample solution* is NMT the area of the principal peak in *Standard solution C* (0.5%).

Total impurities: The total peak area for all impurities in the *Sample solution* is NMT twice the area of the principal peak in *Standard solution C* (1.0%).

SPECIFIC TESTS

• **COLOR OF SOLUTION**

Sample solution: 100 mg/mL in alcohol

Comparison solution: Mix 2.4 mL of ferric chloride CS, 1.0 mL of cobaltous chloride CS, and 0.4 mL of cupric sulfate CS with 0.3 N hydrochloric acid to make 10 mL. Dilute 5 mL of this solution with 0.3 N hydrochloric acid to make 100 mL. [NOTE—Prepare and use this solution immediately.]

Analysis

Samples: Alcohol, *Sample solution*, and *Comparison solution*

Make the comparison by viewing the solutions downward in matched color-comparison tubes against a white surface (see *Color and Achromicity* ⟨631⟩).

Acceptance criteria: The *Sample solution* is clear and not more intensely colored than alcohol or the *Comparison solution*.

• **ACIDITY**

Sample solution: To 2 mL of *Sample solution* prepared in the test for *Color of Solution*, add 3 mL of alcohol, 5 mL of carbon dioxide-free water, and 0.1 mL of bromocresol green TS.

Analysis: Titrate with 0.10 N sodium hydroxide.

Acceptance criteria: NMT 0.1 mL is required to produce a blue color.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Ethylparaben RS

USP Propylparaben RS

Propylparaben Sodium

» Propylparaben Sodium contains not less than 98.5 percent and not more than 101.5 percent of $C_{10}H_{11}NaO_3$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩**—**

USP Propylparaben RS

Completeness of solution ⟨641⟩**—**One g of it, dissolved in water, meets the requirement.

Identification—

A: Dissolve 0.5 g in 5 mL of water, acidify with hydrochloric acid, and filter the resulting precipitate. Wash the precipitate with water, and dry it over silica gel for 5 hours: the IR absorption spectrum of a mineral oil dispersion of it exhibits maxima only at the same wavelengths as that of a similar preparation of USP Propylparaben RS.

B: Ignite about 0.3 g, cool, and dissolve the residue in about 3 mL of 3 N hydrochloric acid. A platinum wire dipped in this solution imparts an intense, persistent yellow color to a nonluminous flame.

pH ⟨791⟩: between 9.5 and 10.5, in a solution (1 in 1000).

Water, *Method I* ⟨921⟩: not more than 5.0%.

Chloride ⟨221⟩**—**A 0.2-g portion shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (0.035%).

Sulfate ⟨221⟩**—**A 0.25-g portion shows no more sulfate than corresponds to 0.30 mL of 0.020 N sulfuric acid (0.12%).

Assay—Gently reflux about 100 mg of Propylparaben Sodium, accurately weighed, with 30 mL of 1 N sodium hydroxide for 30 minutes. Cool, add 25.0 mL of potassium bromate solution (2.78 in 500), 5 mL of potassium bromide solution (1 in 8), and 10 mL of hydrochloric acid, and immediately insert the stopper into the flask. Cool, shake for 15 minutes, and allow to stand for 15 minutes. Quickly add 15 mL of potassium iodide TS, taking care to avoid the escape of bromine vapor, at once replace the stopper in the flask, and shake vigorously. Rinse the stopper and the neck of the flask with a small quantity of water, and titrate the liberated iodine with 0.1 N sodium thiosulfate VS, adding 3 mL of starch TS as the endpoint is approached. [NOTE—About 15 mL is needed.] Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩), and note the difference in volumes required. Each mL of the difference in volume of 0.1 N sodium thiosulfate is equivalent to 3.37 mg of $C_{10}H_{11}NaO_3$.

Protamine Sulfate—*see Protamine Sulfate General Monographs*