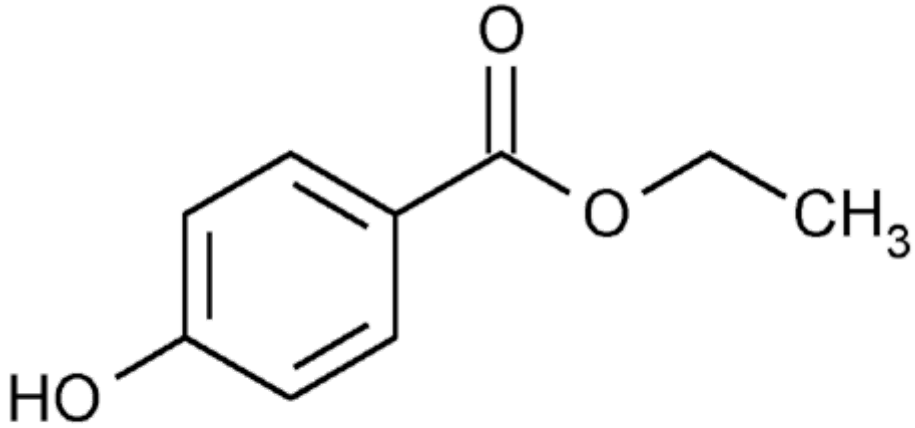
BRIEFING

Propylparaben. The European Pharmacopoeia is the coordinating pharmacopeia for the international harmonization of the compendial standards for the Propylparaben monograph, as part of the process of international harmonization of monographs and general analytical methods of the European, Japanese, and United States pharmacopeias. The following monograph, which represents the **ADOPTION STAGE 6** document, is based in part on comments from the Japanese Pharmacopoeia and the United States Pharmacopeia in response to the **OFFICIAL INQUIRY STAGE 4** draft prepared by the European Pharmacopoeia. Differences between the **ADOPTION STAGE 6** document and the current *NF* monograph include replacing the TLC method in the procedure for *Related Substances* and the titration method in the *Assay* with one HPLC method for both procedures.

(EXC: K. Moore.)
RTS—C58792

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

Change to read:

- **Procedure**

~~Sample:~~ ~~1.000 g of Propylparaben in a flask fitted with a ground-glass stopper~~

~~Analysis:~~ ~~Add 20.0 mL of 1 N sodium hydroxide VS, and heat at 70° for 1 h. Cool rapidly in an ice bath. Carry out the titration of the solutions at room temperature. Titrate the excess sodium hydroxide with 1 N sulfuric acid VS, continuing the titration until the second point of inflection (see *Titrimetry* ⟨541⟩). Perform a blank determination (see *Titrimetry* ⟨541⟩*, Residual Titrations*). Each mL of 1 N sodium hydroxide is equivalent to 166.2 mg of $C_{10}H_{12}O_3$~~

~~Acceptance criteria:~~ ~~98.0% 102.0%~~

■ **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% ■1S (*NF29*)

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨ 281 ⟩ **:** NMT 0.1%, determined on 1.0 g

Change to read:

Organic Impurities

- ~~**Procedure: Related Substances**~~

~~**Sample solution:** 10 mg/mL of Propylparaben in acetone~~

~~**Standard solution A:** 50 µg/mL of *Sample solution* in acetone~~

~~**Standard solution B:** Dissolve 10 mg of USP MPropylparaben RS in 1 mL of the *Sample solution*, and dilute with acetone to 10 mL.~~

~~**Chromatographic system**~~

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

~~**Mode:** TLC~~

~~**Adsorbent:** 0.25-mm layer of chromatographic octadecylsilanized silica gel mixture~~

~~**Application volume:** 2 µL~~

~~**Developing solvent system:** Methanol, glacial acetic acid, and water (70:1:30)~~

~~**Analysis**~~

~~**Samples:** *Sample solution*, *Standard solution A*, and *Standard solution B*~~

~~Examine the plate under short-wavelength UV light, and compare the intensities of any secondary spots observed in the chromatogram of the *Sample solution* with that of the principal spot in the chromatogram of *Standard solution A*.~~

~~**Acceptance criteria:** The intensity of any individual secondary spot in the chromatogram of the *Sample solution* is not greater than that of the principal spot in the chromatogram of *Standard solution A* (0.5%). The test is not valid unless the chromatogram of *Standard solution B* shows two clearly separated principal spots.~~

- **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

[NOTE—The run time is about 2.5 times the retention time of propylparaben.]

Injection size: 10 µL

System suitability

Sample: *Standard solution A*

[NOTE—The retention time of propylparaben is about 4.5 minutes; 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—To find the correction factor for the calculation of content, multiply the peak area of *p*-hydroxybenzoic acid by 1.4.]

[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* 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%).

■1S (*NF29*)

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 Propylparaben RS
  USP Ethylparaben RS

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Kevin T. Moore, Ph.D. Senior Scientific Liaison 1-301-816-8369	(EXC2010) Monographs - Excipients
Reference Standards	Lili Wang, Technical Services Scientist 1-301-816-8129 RSTech@usp.org	

USP32–NF27 Page 1329
Interim Revision Announcement: *USP23–NF18* No. 7 Page 3
Pharmacopeial Forum: Volume No. 36(5) Page 1405