[NOTE—The correction factor is used due to baseline shift.]

Acceptance criteria

Benzyl alcohol: The response of the benzyl alcohol peak from the *Sample solution* is NMT that of the benzyl alcohol peak from *Standard solution A*, corresponding to NMT 0.5%.

Benzaldehyde: The response of the benzaldehyde peak from the *Sample solution* is NMT that of the benzaldehyde peak from *Standard solution B*, corresponding to NMT 0.15%.

(Chloromethyl)benzene: The response of the (chloromethyl)benzene peak from the *Sample solution* is NMT 0.1 times that of the principal peak in the chromatogram from *Standard solution A*, corresponding to NMT 0.05%.

SPECIFIC TESTS

- **MICROBIAL ENUMERATION TESTS** ⟨**61**⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨**62**⟩**:** Solution containing less than 5.0% of benzalkonium chloride meets the requirements of the test for absence of *Pseudomonas aeruginosa*.
- **ACIDITY OR ALKALINITY**

Sample solution: An appropriate quantity of the Solution, equivalent to 500 mg of benzalkonium chloride solid, prepared from Benzalkonium Chloride Solution and carbon dioxide-free water

Analysis: To the *Sample solution* add 0.1 mL of bromocresol purple TS.

Acceptance criteria: NMT 0.1 mL of 0.1 N hydrochloric acid or 0.1 N sodium hydroxide is required to change the color of the indicator.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and prevent contact with metals.
- **LABELING:** Label it to indicate the concentration of benzalkonium chloride, and to indicate the name and quantity of coloring agent added. The labeling also indicates the concentration of alcohol added.
- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Alcohol RS
USP Benzyl Alcohol RS
USP Benzaldehyde RS
USP Benzalkonium Chloride RS

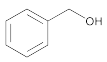
Benzethonium Chloride—*see Benzethonium Chloride General Monographs*

Benzoic Acid—*see Benzoic Acid General Monographs*

Benzyl Alcohol

Attributes	EP	JP	USP
Definition	+	+	+
Refractive Index	+	+	+
Acidity	+	+	+
Benzaldehyde and Other Related Substances	+	+	+
Peroxide Value	+	+	+
Residue on Evaporation	+	+	+
Assay	+	+	+

Legend: + will adopt and implement; – will not stipulate.
Nonharmonized attributes: Characters, Clarity of Solution, Color of Solution, Labeling, and Packaging and Storage
Local attributes: Identification (IR) (USP), Reference Standards (USP)
Reagents and Reference materials: Each pharmacopeia will adapt the text to take account of local reference materials and reagent specifications.



C_7H_8O 108.1
Phenylmethanol [100-51-6].

DEFINITION

Benzyl Alcohol contains NLT 98.0% and NMT the equivalent of 100.5% of phenylmethanol (C_7H_8O).

IDENTIFICATION

- **•INFRARED ABSORPTION** ⟨**197F**⟩**:** On undried specimen•

ASSAY

- **PROCEDURE**

Phenolphthalein solution: Dissolve 0.1 g of phenolphthalein in 80 mL of ethanol (96%), and dilute with water to 100.0 mL. To test for sensitivity, add 100 mL of carbon dioxide-free water to 0.1 mL of the *Phenolphthalein solution*. The solution is colorless. NMT 0.2 mL of 0.02 M sodium hydroxide is required to change the color to pink.

Sample: 0.900 g

Analysis: To the *Sample* add 15 mL of a freshly prepared mixture of pyridine and acetic anhydride (7:1), and boil under a reflux condenser on a water bath for 30 min. Cool, and add 25 mL of water. Using 0.25 mL of *Phenolphthalein solution* as the indicator, titrate with 1 M sodium hydroxide VS. Carry out a blank titration. Calculate the percentage content of C_7H_8O:

$$\text{Result} = 10.81 \times (n_1 - n_2)/m$$

n_2 = amount of 1 M sodium hydroxide used for the sample (mL)
n_1 = amount of 1 M sodium hydroxide used for the blank (mL)
m = amount of sample taken (g)

Acceptance criteria: 98.0%–100.5%

IMPURITIES

Inorganic Impurities

- **FATS AND FIXED OILS,** *Peroxide Value* ⟨**401**⟩**:** NMT 5
- **RESIDUE ON EVAPORATION**

Analysis: After ensuring that the Benzyl Alcohol complies with the test for *Fats and Fixed Oils, Peroxide Value*, evaporate 10.0 g to dryness in a tared quartz or porcelain crucible or platinum dish on a hot plate at a temperature not exceeding 200°. Ensure that the Benzyl Alcohol does not boil during evaporation. Dry the residue on the hot plate for 1 h, and allow to cool in a desiccator.

Acceptance criteria: The residue weighs NMT 5 mg, corresponding to NMT 0.05%.

Organic Impurities

- **PROCEDURE: BENZALDEHYDE AND OTHER RELATED SUBSTANCES**

Sample solution: Use the Benzyl Alcohol sample under examination.

Standard solution A: Dissolve 0.100 g of ethylbenzene in 10.0 mL of the *Sample solution*. Dilute 2.0 mL of this solution with the *Sample solution* to 20.0 mL.

Standard solution B: Dissolve 2.000 g of dicyclohexyl in 10.0 mL of the *Sample solution*. Dilute 2.0 mL of this solution with the *Sample solution* to 20.0 mL.

Reference solution A (for use in nonparenteral applications)**:** Dissolve 0.750 g of benzaldehyde and 0.500 g of cyclohexylmethanol in the *Sample solution*, and dilute with the *Sample solution* to 25.0 mL. Add 1.0 mL of this solution to a mixture of 2.0 mL of *Standard solution A* and 3.0 mL of *Standard solution B*, and dilute with the *Sample solution* to 20.0 mL.

Reference solution B (for use in parenteral applications)**:** Dissolve 0.250 g of benzaldehyde and 0.500 g of cyclohexylmethanol in the *Sample solution*, and dilute with the *Sample solution* to 25.0 mL. Add 1.0 mL of this solution to a mixture of 2.0 mL of *Standard solution A* and 2.0 mL of *Standard solution B*, and dilute with the *Sample solution* to 20.0 mL.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Carrier: Helium, chromatography grade

Carrier linear velocity: 25 cm/s, at 50°

Detector temperature: 310°

Column: 30-m × 0.32-mm, 0.5-µm film thickness, G16

Temperature

Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	5	220	35

Injector: 200°

System suitability

Sample: For nonparenteral applications, use *Reference solution A*. For parenteral applications, use *Reference solution B*.

[NOTE—The retention time of benzyl alcohol is about 26 min. The relative retention times for ethylbenzene, dicyclohexyl, benzaldehyde, cyclohexylmethanol, and benzyl alcohol are about 0.28, 0.59, 0.68, 0.71, and 1.0, respectively.]

Injection volume: 0.1 µL without air plug

Suitability requirements

Sensitivity: Adjust the sensitivity of the detector so that the height of the peak due to ethylbenzene is NLT 30% of the full scale of the recorder.

Resolution: NLT 3.0 between the peaks corresponding to benzaldehyde and cyclohexylmethanol

Analysis

Samples: *Sample solution* and *Reference solution A* for non-parenteral applications and *Reference solution B* for parenteral applications

Acceptance criteria (non-parenteral applications)**:** If any peaks are present in the chromatogram obtained with the *Sample solution* that have the same retention times as the peaks due to ethyl benzene and dicyclohexyl, subtract the areas of any such peaks from the peak areas at these retention times in the chromatograms of *Reference solution A* or *Reference solution B* (corrected peak areas of ethylbenzene and dicyclohexyl). Any such peaks in the *Sample solution* should be included in the assessments for the total of other peaks.

In the chromatogram obtained with the *Sample solution*, the area of any peak corresponding to benzaldehyde is NMT the difference between the area of the peak due to benzaldehyde in the chromatogram obtained with *Reference solution A* (0.15%) and the area of the peak due to benzaldehyde in the chromatogram obtained with the *Sample solution*.

In the chromatogram obtained with the *Sample solution*, the area of any peak corresponding to cyclohexylmethanol is NMT the difference between the area of the peak due to cyclohexylmethanol in the chromatogram obtained with *Reference solution A* (0.10%) and the area of the peak due to cyclohexylmethanol in the chromatogram obtained with the *Sample solution*.

In the chromatogram obtained with the *Sample solution*, the sum of the areas of any peak with a relative retention time less than that of benzyl alcohol and apart from the peaks due to benzaldehyde and cyclohexylmethanol is NMT four times the area of ethylbenzene in *Reference solution A*, corrected if necessary as described above (0.04%).

In the chromatogram obtained with the *Sample solution*, the sum of the areas of any peak with a relative retention time greater than that of benzyl alcohol is NMT the area of dicyclohexyl in *Reference solution A*, corrected if necessary as described above (0.3%).

Disregard any peak with an area less than 0.01 times that of the peak due to ethylbenzene in the chromatogram of *Reference solution A*, corrected if necessary as described above.

Acceptance criteria (parenteral applications)**:** If any peaks are present in the chromatogram obtained with the *Sample solution* that have the same retention times as the peaks due to ethyl benzene and dicyclohexyl, subtract the areas of any such peaks from the peak areas at these retention times in the chromatograms of *Reference solution A* or *Reference solution B* (corrected peak areas of ethylbenzene and dicyclohexyl). Any such peaks in the *Sample solution* should be included in the assessments for the total of other peaks.

In the chromatogram obtained with the *Sample solution*, the area of any peak corresponding to benzaldehyde is NMT the difference between the area of the peak due to benzaldehyde in the chromatogram obtained with *Reference solution B* (0.05%) and the area of the peak due to benzaldehyde in the chromatogram obtained with the *Sample solution*.

In the chromatogram obtained with the *Sample solution*, the area of any peak corresponding to cyclohexylmethanol is NMT the difference between the area of the peak due to cyclohexylmethanol in the chromatogram obtained with *Reference solution B* (0.10%) and the area of the peak due to cyclohexylmethanol in the chromatogram obtained with the *Sample solution*.

In the chromatogram obtained with the *Sample solution*, the sum of the areas of any peak with a relative retention time less than that of benzyl alcohol and apart from the peaks due to benzaldehyde and cyclohexylmethanol is NMT two times the area of ethylbenzene in *Reference solution B*, corrected if necessary as described above (0.02%).

In the chromatogram obtained with the *Sample solution*, the sum of the areas of any peak with a relative retention time greater than that of benzyl alcohol is NMT the area of dicyclohexyl in *Reference solution B*, corrected if necessary as described above (0.2%).

Disregard any peak with an area less than 0.01 times that of the peak due to ethylbenzene in the chromatogram of *Reference solution B*, corrected if necessary as described above.

SPECIFIC TESTS

- **ACIDITY**

Phenolphthalein solution: Prepare as directed in the *Assay*.

Analysis: To 10 mL of Benzyl Alcohol add 10 mL of ethanol (96%) and 1 mL of *Phenolphthalein solution*.

Acceptance criteria: NMT 1 mL of 0.1 M sodium hydroxide is required to change the color of the indicator to pink.

- **+CLARITY OF SOLUTION**

[NOTE—The *Sample solution* is to be compared to *Reference suspension 1* in diffused daylight 5 min after preparation of *Reference suspension 1*.]

Hydrazine solution: Transfer 1.0 g of hydrazine sulfate to a 100-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Allow to stand 4–6 h before use.

Methenamine solution: Transfer 2.5 g of methenamine to a 100-mL glass-stoppered flask, add 25.0 mL of water, insert the glass stopper, and mix to dissolve.

Primary opalescent suspension: [NOTE—This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.] Transfer 25.0 mL of *Hydrazine solution* to the *Methenamine solution* in the 100-mL glass-stoppered flask. Mix, and allow to stand for 24 h.

Opalescence standard: [NOTE—This suspension should not be used beyond 24 h after preparation.] Transfer 15.0 mL of the *Primary opalescent suspension* to a 1000-mL volumetric flask, dilute with water to volume, and mix.

Reference suspension 1: Transfer 5.0 mL of the *Opalescence standard* to a 100-mL volumetric flask, and dilute with water to volume.

Reference suspension 2: Transfer 10.0 mL of the *Opalescence standard* to a second 100-mL volumetric flask, and dilute with water to volume.

Sample solution: Dissolve 2.0 g of Benzyl Alcohol in 60 mL of water.

Analysis: Transfer a sufficient portion of the *Sample solution* to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm, to obtain a depth of 40 mm. Similarly transfer portions of *Reference suspension 1*, *Reference suspension 2*, and water to separate matching test tubes. Compare the *Sample solution*, *Reference suspension 1*, *Reference suspension 2*, and water in diffused daylight, viewing vertically against a black background (see *Spectrophotometry and Light-Scattering* ⟨851⟩*, Visual Comparison*). [NOTE—The diffusion of light must be such that *Reference suspension 1* can readily be distinguished from water, and that *Reference suspension 2* can readily be distinguished from *Reference suspension 1*.]

Acceptance criteria: The *Sample solution* shows the same clarity as that of water, or its opalescence is not more pronounced than that of *Reference suspension 1*.✦

- ✦**COLOR OF SOLUTION**

Sample solution: Use the *Sample solution* prepared in the test for *Clarity of Solution*.

Analysis: Transfer a sufficient portion of the *Sample solution* to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm, to obtain a depth of 40 mm. Similarly transfer a portion of water to a separate matching test tube. Compare the color of the *Sample solution* with that of water in diffused daylight, viewing vertically against a white background (see *Spectrophotometry and Light-Scattering* ⟨851⟩*, Visual Comparison*).

Acceptance criteria: The *Sample solution* has the color of water.✦

- **REFRACTIVE INDEX** ⟨**831**⟩**:** 1.538–1.541 at 20°

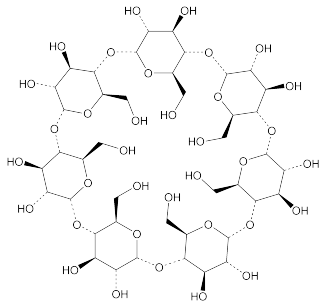
ADDITIONAL REQUIREMENTS

- ✦**LABELING:** Where Benzyl Alcohol is intended for use in the manufacture of parenteral applications, it is so labeled.✦
- ✦**PACKAGING AND STORAGE:** Preserve in tight containers, protected from light.✦
- ✦**USP REFERENCE STANDARDS**

USP Benzyl Alcohol RS✦

Benzyl Benzoate—*see Benzyl Benzoate General Monographs*

Betadex



$(C_6H_{10}O_5)_7$ 1134.98
Beta Cyclodextrin [7585-39-9].

» Betadex is a nonreducing cyclic compound composed of seven alpha-(1-4) linked D-glucopyranosyl units. It contains not less than 98.0 percent and not more than 102.0 percent of $(C_6H_{10}O_5)_7$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers. No storage requirements specified.

USP Reference standards ⟨11⟩**—**
USP Alpha Cyclodextrin RS
USP Beta Cyclodextrin RS
USP Gamma Cyclodextrin RS
USP Dextrose RS

Color and clarity of solution—Dissolve 0.2 g in 20.0 mL of freshly boiled and cooled water: the resulting solution is clear and colorless.

Identification—

A: *Infrared Absorption* ⟨197K⟩: on undried specimen.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

C: It meets the requirements of the test for *Specific rotation*.

D: Mix 0.2 g with 2 mL of iodine TS, warm in a water bath to dissolve the test specimen, and allow to stand at room temperature: a yellow-brown precipitate is formed.

Specific rotation ⟨781S⟩**:** between +160° and +164° (*t* = 20°).

Test solution: 10 mg per mL, in water.

Microbial enumeration tests ⟨61⟩ and **Tests for specified microorganisms** ⟨62⟩**—**The total aerobic microbial count does not exceed 1000 cfu per g, and the total combined molds and yeasts count does not exceed 100 cfu per g. It meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli*.

pH ⟨791⟩**—**Add 0.1 mL of a saturated solution of potassium chloride to 10 mL of Betadex aqueous solution (1 in 100). The pH of the solution is between 5.0 and 8.0.

Water, *Method I* ⟨921⟩**:** not more than 14.0%.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Heavy metals, *Method II* ⟨231⟩**:** not more than 5 ppm.

Reducing sugars—

Cupric solution—Dissolve 15 g of cupric sulfate in water to make 100 mL.

Tartrate solution—Dissolve 2.5 g of anhydrous sodium carbonate, 2.5 g of potassium sodium tartrate, 2.0 g of sodium bicarbonate, and 20 g of anhydrous sodium sulfate in water to make 100 mL.

Cupric-tartaric solution—Immediately before use, mix 1 part of *Cupric solution* with 25 parts of *Tartrate solution*.

Ammonium molybdate reagent—Mix 10 mL of a solution of disodium arsenate (6 in 100), 50 mL of a solution of ammo-