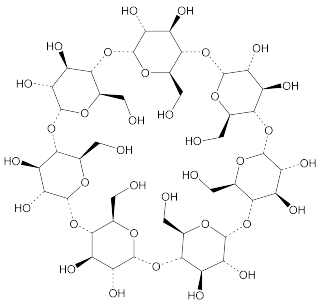
- **Refractive Index** ⟨831⟩: 1.538–1.541 at 20°

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 ammonium molybdate (1 in 10), and 90 mL of diluted sulfuric acid, and dilute with water to 200 mL.

Test solution—Transfer an accurate quantity of Betadex, equivalent to 1.0 g to a 100-mL volumetric flask; dissolve in and dilute with water that has been previously boiled and cooled to room temperature, to volume; and mix. To 1 mL of this solution add 1 mL of *Cupric-tartaric solution*. Heat on a water bath for 10 minutes, then cool to room temperature. Add 10 mL of *Ammonium molybdate reagent*, and allow to stand for 15 minutes.

Standard stock solution—Prepare a solution having a known concentration of 20 mg per L for USP Dextrose RS, calculated on the anhydrous basis.

Standard solution—Prepare as directed for the *Test solution*, at the same time, except to use 1 mL of *Standard stock solution* in place of 1 mL of 10 mg/mL Betadex solution.

Procedure—Measure the absorbance of the *Test solution* and the *Standard solution* at the wavelength of maximum absorbance at 740 nm relative to that of water, with a suitable spectrophotometer. The absorbance of the *Test solution* is not greater than that of the *Standard solution* (0.2%).

Light-absorbing impurities—

Test solution—Transfer an accurate quantity of Betadex, equivalent to 1.0 g on the anhydrous basis, to a 100-mL volumetric flask; dissolve in and dilute with water that has been previously boiled and cooled to room temperature, to volume; mix; and pass through a 0.2-µm filter.

Procedure—Determine the absorbance of the *Test solution* in a 1-cm cell with a suitable spectrophotometer, after correcting for the blank: between 230 nm and 350 nm, the absorbance is not greater than 0.10; and between 350 nm and 750 nm, the absorbance is not greater than 0.05.

Related compounds—

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

System suitability solution—Prepare as directed for *System suitability preparation* in the *Assay*.

Standard solution—Transfer 5.0 mL of the *System suitability solution* into a 50-mL volumetric flask, and dilute with water to volume.

Test solution—Use the *Assay stock preparation,* prepared as directed in the *Assay*.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. For the *Test solution,* the areas of any peaks corresponding to alfadex (alpha cyclodextrin) or to gamma cyclodextrin are not greater than half of the area of the corresponding peaks in the chromatogram of the *Standard solution* (0.25%); and the sum of the areas of all the peaks, excluding the principal peak, the peaks corresponding to alfadex or to

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gamma cyclodextrin, and artifact peaks, is not greater than the area of the peak corresponding to betadex (beta cyclodextrin) in the chromatogram of the *Standard solution* (0.5%).

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water and methanol (93 : 7). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability preparation—Dissolve accurately weighed quantities of USP Alpha Cyclodextrin RS, USP Beta Cyclodextrin RS, and USP Gamma Cyclodextrin RS in water, and dilute if necessary, to obtain a solution having known concentrations of 0.5 mg of each per mL for USP Alpha Cyclodextrin RS and USP Beta Cyclodextrin RS, each calculated on the anhydrous basis, and 0.5 mg per mL for USP Gamma Cyclodextrin RS, calculated on the dried basis.

Standard preparation—Dissolve an accurately weighed quantity of USP Beta Cyclodextrin RS in water to obtain a solution having a known concentration of about 1.0 mg per mL, calculated on the anhydrous basis.

Assay stock preparation—Transfer 250 mg of Betadex, accurately weighed, to a 25-mL volumetric flask, and dissolve in water, with the aid of heat, if necessary. Cool, and dilute with water to volume.

Assay preparation—Transfer 5.0 mL of the *Assay stock preparation* to a 50-mL volumetric flask, and dilute with water to volume.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a refractive index detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The temperature for the refractive index detector is maintained at 40°, and the temperature for the analytical column is maintained at 30°. The flow rate is about 1.5 mL per minute. Chromatograph the *System suitability preparation,* and identify the components based on their relative retention times, which are 0.4, 0.5, and 1.0 for gamma cyclodextrin, alfadex, and betadex, respectively. Record the peak responses as directed for *Procedure:* the resolution, *R,* between the gamma cyclodextrin and alfadex peaks is not less than 1.5; the tailing factors for the three cyclodextrins are between 0.8 and 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $(C_6H_{10}O_5)_7$ in the portion of Betadex taken by the formula:

$$100(10) \times (25)\{C / [W(1 - 0.01A)]\}(r_U / r_S)$$

in which 10 is a dilution factor for preparing the *Assay preparation* from the *Assay stock preparation;* 25 is the volume, in mL, of the *Assay stock preparation; C* is the concentration, in mg per mL, of USP Beta Cyclodextrin RS in the *Standard preparation; W* is the weight, in mg, of Betadex taken to prepare the *Assay stock preparation; A* is the percentage of *Water* in the Betadex taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Boric Acid

H_3BO_3 61.83
Boric acid (H_3BO_3).
Boric acid (H_3BO_3) [*10043-35-3*].

» Boric Acid contains not less than 99.5 percent and not more than 100.5 percent of H_3BO_3, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label the container with a warning that it is not for internal use.

Solubility in alcohol—One g dissolves completely in 10 mL of boiling alcohol.

Completeness of solution—One g dissolves in 25 mL of water, producing a clear solution.

Identification—It responds to the tests for *Borate* ⟨191⟩.

Loss on drying ⟨731⟩**—**Dry it over silica gel for 5 hours: it loses not more than 0.5% of its weight.

Heavy metals, *Method I* ⟨231⟩**—**Dissolve 1 g in 23 mL of water, and add 2 mL of 1 N acetic acid: the limit is 0.002%.

Assay—Dissolve about 2 g of Boric Acid, accurately weighed, in 100 mL of a mixture of equal volumes of glycerin and water, previously neutralized to phenolphthalein TS, and titrate with 1 N sodium hydroxide VS. Discharge the pink color by the addition of 50 mL of glycerin, neutralized to phenolphthalein TS, and continue the titration until the pink color reappears. Each mL of 1 N sodium hydroxide is equivalent to 61.83 mg of H_3BO_3.

Butane

C_4H_{10} 58.12
n-Butane [*106-97-8*].

» Butane contains not less than 97.0 percent of *n*-butane (C_4H_{10}).
Caution—Butane is highly flammable and explosive.

Packaging and storage—Preserve in tight cylinders, and prevent exposure to excessive heat.

Identification—

A: The IR absorption spectrum of it exhibits maxima, among others, at about the following wavelengths, in µm: 3.4 (*vs*), 6.8 (*s*), 7.2 (*m*), and 10.4 (*m*).

B: The vapor pressure of a test specimen, obtained as directed in the *General Sampling Procedure* under *Propellants* (see *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩), determined at 21° by means of a suitable pressure gauge, is between 205 and 235 kPa absolute (30 and 34 psia).

Water: not more than 0.001%, determined as directed for *Water Content* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

High-boiling residues: not more than 5 µg per mL, determined as directed for *High-Boiling Residues, Method II,* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

Acidity of residue—Add 10 mL of water to the residue obtained in the test for *High-boiling residues*, mix by swirling for about 30 seconds, add 2 drops of methyl orange TS, insert the stopper in the tube, and shake vigorously: no pink or red color appears in the aqueous layer.

Limit of sulfur compounds—Carefully open the container valve to produce a moderate flow of gas. Do not direct the gas stream toward the face, but deflect a portion of the stream toward the nose: the odor is free from the characteristic odor of sulfur compounds.

Assay—

Chromatographic system—Under typical conditions, the gas chromatograph is equipped with a thermal-conductivity detector and contains a 3-mm × 6-m aluminum column packed with 10 weight percent of liquid phase G30 on nonacid-washed support S1C, helium is used as the carrier gas at a flow rate of 50 mL per minute, and the temperature of the column is maintained at 33°.

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