Acceptance criteria: If the sieving residue fraction is more than 15%, the substance is classified as Type A; if the sieving residue fraction is NMT 15%, the substance is classified as Type B.

ASSAY

- **NITROGEN DETERMINATION,** *Method II* ⟨**461**⟩
  Sample: 0.1 g
  Analysis: Proceed as directed, using the *Sample*. In the *Procedure*, omit the use of hydrogen peroxide, and use 5 g of a powdered mixture of potassium sulfate, cupric sulfate, and titanium dioxide (33:1:1), instead of potassium sulfate and cupric sulfate (10:1). Heat until a clear, light green solution is obtained. Heat for an additional 45 min, and proceed as directed for *Procedure*, beginning with "Cautiously add to the digestion mixture 70 mL of water".
  Acceptance criteria: 11.0%–12.8% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%, determined on 1.0 g
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm
- **PEROXIDES**
  Sample suspension A: [NOTE—Use for Type A.] 40 mg/mL in water. To 25 mL of this suspension add 2 mL of titanium trichloride–sulfuric acid TS. Allow to stand for 30 min, and filter.
  Sample suspension B: [NOTE—Use for Type B.] 16 mg/mL in water. To 25 mL of this suspension add 2 mL of titanium trichloride–sulfuric acid TS. Allow to stand for 30 min, and filter.
  Compensation liquid A: [NOTE—Use for Type A.] 40 mg/mL in water. Filter, take 25 mL, and add 2 mL of a 13% solution of sulfuric acid.
  Compensation liquid B: [NOTE—Use for Type B.] 16 mg/mL in water. Filter, take 25 mL, and add 2 mL of a 13% solution of sulfuric acid.
  Analysis: Measure the absorbance of the filtrate at 405 nm against the appropriate compensation liquid.
  Acceptance criteria: NMT 0.35. For Type A, this corresponds to NMT 400 ppm expressed as H_2O_2; for Type B, this corresponds to NMT 1000 ppm expressed as H_2O_2.
- **VINYLPYRROLIDINONE**
  Mobile phase: Acetonitrile and water (1:9)
  Sample solution: 25 mg/mL of suspension in methanol. Shake for 60 min. Leave the bulk to settle, and pass through a filter of 0.2-µm pore size.
  Reference stock solution A: 5 µg/mL of vinylpyrrolidinone in methanol
  Reference stock solution B: 100 µg/mL of vinylpyrrolidinone and 5 mg/mL of vinyl acetate in methanol
  Reference solution A: A 1-in-20 solution of *Reference stock solution A* in *Mobile phase*
  Reference solution B: A 1-in-100 solution of *Reference stock solution B* in *Mobile phase*
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV
  Analytical wavelength: 235 nm
  Precolumn: 4-mm × 2.5-cm; 5-µm packing L1
  Column: 4-mm × 25-cm; 5-µm packing L1
  Column temperature: 40°
  Flow rate: 1 mL/min
  Injection size: 50 µL. [NOTE—After each injection of the *Sample solution*, wash the precolumn by passing the *Mobile phase* backwards, at the same flow rate as applied in the test, for 30 min.]
  System suitability
  Samples: *Reference solution A* and *Reference solution B*
  Suitability requirements
  Resolution: NLT 2.0 between vinylpyrrolidone and vinyl acetate, *Reference solution B*
  Relative standard deviation: NMT 2.0% for 6 injections, *Reference solution A*
  Analysis
  Samples: *Sample solution* and *Reference solution A*
  Record the chromatograms, and measure the responses for the vinylpyrrolidinone peak.
  Acceptance criteria: The area of the peak from the *Sample solution* is NMT the area of the principal peak from *Reference solution A* (NMT 10 ppm).

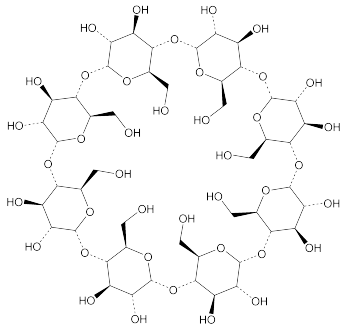
SPECIFIC TESTS

- **LOSS ON DRYING** ⟨**731**⟩**:** Dry 0.5 g at 105° to constant weight: it loses NMT 5.0% of its weight.
- **WATER-SOLUBLE SUBSTANCES**
  Sample: 25.0 g
  Analysis: Transfer the *Sample* to a 400-mL beaker, add 200 mL of water, and stir on a magnetic stirrer, using a 5-cm stirring bar, for 1 h. Transfer to a 250-mL volumetric flask with the aid of 25 mL of water. Add water to volume. Allow the bulk of the solids to settle. Pass 100 mL of the relatively clear supernatant through a membrane filter of 0.45-µm pore size, protected against clogging by superimposing a membrane filter of 3-µm pore size. While filtering, stir the solution above the filter manually or with a mechanical stirrer, taking care not to physically damage the membrane filter. Transfer 50.0 mL of the clear filtrate to a tared 100-mL beaker, evaporate to dryness, and dry at 110° for 3 h.
  Acceptance criteria: The weight of the residue does not exceed 75 mg (1.5%).

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** The label states the type (Type A or Type B).
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Crospovidone RS

Gamma Cyclodextrin



$(C_6H_{10}O_5)_8$ 1297.12
Cyclooctaamylose;
Cyclomaltooctaose [17465-86-0].

DEFINITION

Gamma Cyclodextrin is composed of 8 alpha-(1–4) linked D-glycopyranosyl units. It contains NLT 98.0% and NMT 102.0% of cyclooctaamylose $(C_6H_{10}O_5)_8$, calculated on the dried basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B.** The retention time of the major peak from the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.

• **C.** It meets the requirements of the test for *Specific Rotation*.

ASSAY

• **PROCEDURE**

Mobile phase: Methanol and water (7:93)

System suitability solution: Prepare an aqueous solution containing 0.5 mg/mL each of USP Alpha Cyclodextrin RS, USP Beta Cyclodextrin RS, and USP Gamma Cyclodextrin RS.

Standard solution: 1.0 mg/mL of USP Gamma Cyclodextrin RS

Sample stock solution: Transfer 250 mg of Gamma Cyclodextrin to a 25-mL volumetric flask, and dissolve in water, with the aid of heat if necessary. Cool, and dilute with water to volume.

Sample solution: 1.0 mg/mL of Gamma Cyclodextrin, prepared from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: Refractive index

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

Temperature

Detector: 40°

Column: 30°

Flow rate: 1.5 mL/min

Injection size: 50 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for gamma cyclodextrin, alfadex, and betadex are 0.8, 1.0, and 1.9, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the gamma cyclodextrin and alfadex peaks

Tailing factors: 0.8–2.0 for the three cyclodextrins

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of gamma cyclodextrin $[(C_6H_{10}O_5)_8]$ in the portion of sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL) corrected for water found in *Specific Tests, Loss on Drying*

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

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

• **HEAVY METALS,** *Method II* **⟨231⟩:** NMT 5 ppm

• **RELATED COMPOUNDS**

Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

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

Sample solution: Use the *Sample stock solution*, prepared as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: For the *Sample solution*, the areas of any peaks corresponding to alfadex (alpha cyclodextrin) or to betadex (beta cyclodextrin) are not greater than the area of the corresponding peaks in the chromatogram of the *Standard solution* (0.5%); and the sum of the areas of all the peaks, excluding the principal peak, the peaks corresponding to alfadex or to betadex, and artifact peaks, is not greater than the area of the peak corresponding to gamma cyclodextrin in the chromatogram of the *Standard solution* (0.5%).

• **REDUCING SUBSTANCES**

Dextrose standard solution: 10.0 mg/mL of USP Dextrose RS, calculated on the anhydrous basis

Analysis: Transfer a quantity of Gamma Cyclodextrin, equivalent to 1.0 g on the dried basis, to a 500-mL conical flask. Dissolve in 10 mL of water, and add 25 mL of alkaline cupric citrate TS2. Cover the flask with aluminum foil, and boil the solution for 5 min. Cool in an ice bath to room temperature. Add 25 mL of 0.6 N acetic acid, 10 mL of 3 N hydrochloric acid, and 10 mL of 0.1 N iodine solution. [NOTE—The addition of these solutions must be in the order given.]

Titrate the solution with 0.1 N sodium thiosulfate VS, and determine the endpoint potentiometrically. Perform a blank determination (see *Titrimetry* ⟨541⟩*, Residual Titrations*). Calculate the difference in volumes required.

Create a calibration curve by similarly titrating 0.25, 0.5, 0.75, and 1.0 mL of *Dextrose standard solution*. Plot the amount, in mg, of dextrose in each titrated *Dextrose standard solution* versus the volume consumed, in mL, of 0.1 N sodium thiosulfate VS in the titration, and draw a straight line through the four points. From the line so obtained and the volume of 0.1 N sodium thiosulfate VS required in the titration of Gamma Cyclodextrin, determine the weight, *W*, in mg, of the reducing substances as dextrose in the portion of Gamma Cyclodextrin taken.

Calculate the percentage of the reducing substances in the portion of Gamma Cyclodextrin taken:

$$\text{Result} = (W/W_G) \times F \times 100$$

W = weight of the reducing substances as dextrose in the portion of Gamma Cyclodextrin taken (mg)
W_G = weight of Gamma Cyclodextrin taken (g)
F = conversion factor, 10^{-3} g/mg

Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

• **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** It meets the requirements of the tests for the absence of *Salmonella* species and *Escherichia coli*. The total aerobic microbial count does not exceed 1000 cfu/g, and the total combined molds and yeasts count does not exceed 100 cfu/g.

• **COLOR AND CLARITY OF SOLUTION**

Sample solution: Transfer a quantity of Gamma Cyclodextrin, equivalent to 2.5 g on the dried basis, into a 25-mL volumetric flask, dissolve in and dilute with water that has been previously boiled and cooled to room temperature to volume, and mix.

Analysis: Determine the absorbance of the *Sample solution* in a 1-cm cell at 420 nm, with a suitable spectrophotometer, after correcting for the blank.

Acceptance criteria: At 420 nm, the absorbance is not greater than 0.20, and the solution is clear.

• **LOSS ON DRYING ⟨731⟩:** Dry a sample at 105° for 2 h: it loses NMT 11.0% of its weight.

• **OPTICAL ROTATION,** *Specific Rotation* **⟨781S⟩**

Sample solution: 10 mg/mL

Analysis: Proceed as directed in the chapter.

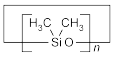
Acceptance criteria: +174° to +180°

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at room temperature.

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Alpha Cyclodextrin RS
USP Beta Cyclodextrin RS
USP Dextrose RS
USP Gamma Cyclodextrin RS

Cyclomethicone



$(C_2H_6OSi)_n$
Cyclopolydimethylsiloxane.
Cyclomethicone [69430-24-6].

» Cyclomethicone is a fully methylated cyclic siloxane containing repeating units of the formula:

$$[-(CH_3)_2SiO-]_n$$

in which *n* is 4, 5, or 6, or a mixture of them. It contains not less than 98.0 percent of $(C_2H_6OSi)_n$, calculated as the sum of cyclomethicone 4, cyclomethicone 5, and cyclomethicone 6, and not less than 95.0 percent and not more than 105.0 percent of the labeled amount of any one or more of the individual cyclomethicone components.

Packaging and storage—Preserve in tight containers.

Labeling—Label it to state, as part of the official title, the *n*-value of the Cyclomethicone. Where it is a mixture of 2 or 3 such cyclic siloxanes, the label states the *n*-value and percentage of each in the mixture.

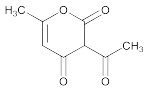
USP Reference standards ⟨11⟩**—**
USP Cyclomethicone 4 RS
USP Cyclomethicone 5 RS
USP Cyclomethicone 6 RS

Identification—Proceed as directed under ⟨197S⟩, except to use neat liquids. The IR absorption spectrum, determined in a 0.1-mm cell, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Cyclomethicone 4 RS, USP Cyclomethicone 5 RS, or USP Cyclomethicone 6 RS.

Limit of nonvolatile residue—Evaporate 2.0 g in an open, tared aluminum dish in a circulating air oven at 150° for 2 hours, allow to cool in a desiccator, and weigh: the weight of the residue so obtained does not exceed 3.0 mg, corresponding to not more than 0.15% (w/w).

Assay—The gas chromatograph is equipped with a thermal conductivity detector and a suitable recorder, and contains a 3.66-m × 3-mm column packed with 20% liquid phase G1 on 60- to 80-mesh packing S1A (see *Gas Chromatography* under *Chromatography* ⟨621⟩). The column is temperature-programmed at a rate of about 8° per minute from 125° to 320°, the injection port is maintained at a temperature of about 300°, and the detector block is maintained at a temperature of about 350°. Helium is used as the carrier gas, flowing at a rate of about 20 mL per minute. Separately inject about 1 µL of USP Cyclomethicone 4 RS, USP Cyclomethicone 5 RS, and USP Cyclomethicone 6 RS into the gas chromatograph, record the chromatograms, and note the retention times of the peaks. Similarly inject about 1 µL of Cyclomethicone, record the chromatogram, and measure the responses of the major peaks. Calculate the percentage of cyclomethicone 4, cyclomethicone 5, and cyclomethicone 6 by dividing 100 times the response of each peak at the retention time of the corresponding reference standard by the sum of all of the responses in the chromatogram. The percentages obtained from duplicate injections agree to within 1.0%. Calculate the percentage purity by adding the percentages of cyclomethicone 4, cyclomethicone 5, and cyclomethicone 6.

Dehydroacetic Acid



$C_8H_8O_4$ 168.15
Keto form: 2*H*-Pyran-2,4(3*H*)-dione, 3-acetyl-6-methyl-.
3-Acetyl-6-methyl-2*H*-pyran-2,4(3*H*)-dione [520-45-6].
Enol form: 2*H*-Pyran-2-one, 3-acetyl-4-hydroxy-6-methyl-.
3-Acetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one [771-03-9].

» Dehydroacetic Acid contains not less than 98.0 percent and not more than 100.5 percent of $C_8H_8O_4$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers. No storage requirements specified.

USP Reference standards ⟨11⟩**—**
USP Dehydroacetic Acid RS

Identification, *Infrared Absorption* ⟨197K⟩.

Heavy metals, *Method II* ⟨231⟩**:** not more than 0.001%.

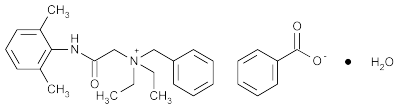
Loss on drying ⟨731⟩**:** Dry it at 80° for 4 hours: it loses not more than 1.0% of its weight.

Melting range, *Class I* ⟨741⟩**:** between 109° and 111°.

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

Assay—Transfer about 500 mg of Dehydroacetic Acid, accurately weighed, into a 250-mL conical flask, dissolve it in 75 mL of neutralized alcohol, add phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS to a pink endpoint that persists for not less than 30 seconds. Each mL of 0.1 N sodium hydroxide is equivalent to 16.82 mg of $C_8H_8O_4$.

Denatonium Benzoate



$C_{28}H_{34}N_2O_3 \cdot H_2O$ 464.60
Benzenemethanaminium, *N*-[2-[(2,6-dimethylphenyl)amino]-2-oxoethyl]-*N*,*N*-diethyl-, benzoate, monohydrate.
Benzyldiethyl[(2,6-xylylcarbamoyl)methyl]ammonium benzoate monohydrate [86398-53-0].
Anhydrous 446.59 [3734-33-6].

» Denatonium Benzoate, dried at 105° for 2 hours, contains one molecule of water of hydration or is anhydrous. When dried at 105° for 2 hours, it contains not less than 99.5 percent and not more than 101.0 percent of $C_{28}H_{34}N_2O_3$.

Packaging and storage—Preserve in tight containers.

Labeling—Label it to indicate whether it is hydrous or anhydrous.

USP Reference standards ⟨11⟩**—**
USP Denatonium Benzoate RS