Sorbitan Sesquioleate

» Sorbitan Sesquioleate is a partial oleate ester of Sorbitol and its mono- and dianhydrides. It yields, upon saponification, not less than 74.0 percent and not more than 80.0 percent of fatty acids, and not less than 22.0 percent and not more than 28.0 percent of polyols (w/w).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Isosorbide RS
USP 1,4-Sorbitan RS
$C_6H_{12}O_5$ 164.16

Identification—It responds to *Identification* tests *A* and *B* under *Sorbitan Monooleate*.

Acid value ⟨401⟩: not more than 14.

Hydroxyl value ⟨401⟩: between 182 and 220.

Iodine value ⟨401⟩: between 65 and 75.

Saponification value ⟨401⟩: between 143 and 165.

Water, *Method I* ⟨921⟩: not more than 1.0%.

Residue on ignition ⟨281⟩: not more than 1.4%.

Heavy metals, *Method II* ⟨231⟩: 0.001%.

Assay for fatty acids—Proceed as directed for *Assay for fatty acids* under *Sorbitan Monooleate*.

Assay for polyols—Proceed as directed for *Assay for polyols* under *Sorbitan Monooleate*.

Sorbitan Trioleate

» Sorbitan Trioleate is the triester of Oleic Acid and Sorbitol and its mono- and dianhydrides. It yields, upon saponification, not less than 85.5 percent and not more than 90.0 percent of fatty acids, and not less than 13.0 percent and not more than 19.0 percent of polyols (w/w).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Isosorbide RS
USP 1,4-Sorbitan RS
$C_6H_{12}O_5$ 164.16

Identification—It responds to *Identification* tests *A* and *B* under *Sorbitan Monooleate*.

Acid value ⟨401⟩: not more than 17.

Hydroxyl value ⟨401⟩: between 50 and 75.

Iodine value ⟨401⟩: between 77 and 85.

Saponification value ⟨401⟩: between 169 and 183.

Water, *Method I* ⟨921⟩: not more than 0.7%.

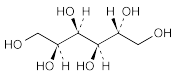
Residue on ignition ⟨281⟩: not more than 0.25%.

Heavy metals, *Method II* ⟨231⟩: 0.001%.

Assay for fatty acids—Transfer about 8.6 g of Sorbitan Trioleate, accurately weighed, to a 500-mL conical flask, cautiously add 100 mL of alcohol and 3.5 g of potassium hydroxide, then add a few glass beads, and mix. Proceed as directed for *Assay for fatty acids* under *Sorbitan Monooleate*, beginning with "Connect a suitable condenser."

Assay for polyols—Proceed as directed for *Assay for polyols* under *Sorbitan Monooleate*.

Sorbitol



$C_6H_{14}O_6$ 182.17
D-Glucitol [50-70-4].

DEFINITION
Sorbitol contains NLT 91.0% and NMT 100.5% of D-sorbitol, calculated on the anhydrous basis. The amounts of total sugars, other polyhydric alcohols, and any hexitol anhydrides, if detected, are not included in the requirements, nor in the calculated amount under *Other Impurities* in *General Notices*.

IDENTIFICATION
• **A.**
Sample solution: 1 g of Sorbitol in 75 mL of water
Analysis: Transfer 3 mL of *Sample solution* to a 15-cm test tube, and add 3 mL of freshly prepared catechol solution (1 in 10), and mix. Add 6 mL of sulfuric acid, then gently heat the tube in a flame for 30 s.
Acceptance criteria: A deep pink or wine-red color appears.
• **B.** The retention time of the major peak of the *Sample solution* corresponds to that from the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **PROCEDURE**
Mobile phase: Use degassed water.
System suitability solution: Prepare a solution containing 4.8 mg/g of each USP Sorbitol RS and mannitol
Standard solution: 4.8 mg/g of USP Sorbitol RS
Sample solution: Dissolve 0.10 g of Sorbitol in water, and dilute with water to 20 g. Record the final solution weight, and mix thoroughly.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: Refractive index
Column: 7.8-mm × 10-cm; packing L34
Temperature
Column: 50 ± 2°
Detector: 35°
Flow rate: 0.7 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for mannitol and sorbitol are about 0.6 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between sorbitol and mannitol, *System suitability solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage, on the anhydrous basis, of D-sorbitol in the portion of Sorbitol taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Sorbitol RS in the *Standard solution* (mg/g)
C_U = concentration of Sorbitol in the *Sample solution* (mg/g)
W = percentage obtained in the test for *Water Determination*

Acceptance criteria: 91.0%–100.5% on the anhydrous basis

IMPURITIES

- **LIMIT OF NICKEL**

  Sample solution: Dissolve 20.0 g of Sorbitol in diluted acetic acid, and dilute with diluted acetic acid to 150 mL.

  Blank solution: 150 mL of diluted acetic acid

  Standard solutions: Prepare three solutions by adding 0.5, 1.0, and 1.5 mL of nickel standard solution TS to 20.0 g of Sorbitol dissolved in diluted acetic acid, and dilute with the same solvent to 150 mL.

  Instrumental conditions

  (See *Spectrophotometry and Light-Scattering* ⟨851⟩.)

  Mode: Atomic absorption spectrophotometry

  Analytical wavelength: 232.0 nm

  Lamp: Nickel hollow-cathode

  Flame: Air–acetylene

  Analysis

  Samples: *Standard solutions* and *Sample solution*

  To each sample add 2.0 mL of a saturated ammonium pyrrolidinedithiocarbamate solution (containing 10 g/L of ammonium pyrrolidinedithiocarbamate) and 10.0 mL of methyl isobutyl ketone, and shake for 30 s. Protect from bright light. Allow the two layers to separate, and use the methyl isobutyl ketone layer. Set the instrument to zero using the organic layer from the *Blank solution*. Concomitantly determine the absorbances of the organic layer from the *Samples* at least three times each. Record the average of the steady readings for each of the *Standard solutions* and the *Sample solution*. Between each measurement, aspirate the organic layer from the *Blank solution*, and ascertain that the reading returns to zero. Plot the absorbances of the *Standard solutions* and the *Sample solution* versus the added quantity of nickel. Extrapolate the line joining the points on the graph until it meets the concentration axis. The distance between this point and the intersection of the axes represents the concentration of nickel in the *Sample solution*.

  Acceptance criteria: NMT 1 ppm

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%, determined on a 1.5-g portion

- **REDUCING SUGARS**

  [NOTE—The amount determined in this test is not included in the calculated amount under *Other Impurities* in the *General Notices*.]

  Sample solution: Dissolve 3.3 g of Sorbitol in 3 mL of water with the aid of gentle heat. Cool, and add 20.0 mL of cupric citrate TS and a few glass beads. Heat so that boiling begins after 4 min, and maintain boiling for 3 min. Cool rapidly, and add 40 mL of diluted acetic acid, 60 mL of water, and 20.0 mL of 0.05 N iodine VS. With continuous shaking, add 25 mL of a mixture of 6 mL of hydrochloric acid and 94 mL of water.

  Analysis: When the precipitate has dissolved, titrate the excess of iodine with 0.05 N sodium thiosulfate VS using 2 mL of starch TS, added toward the end of the titration, as an indicator.

  Acceptance criteria: NLT 12.8 mL of 0.05 N sodium thiosulfate VS is required, corresponding to NMT 0.3% of reducing sugars, as glucose.

- **CHLORIDE AND SULFATE,** *Chloride* ⟨221⟩ (if labeled for use in preparing parenteral dosage forms)

  Sample: 1.5 g

  Acceptance criteria: The *Sample* shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (NMT 0.0050%).

- **CHLORIDE AND SULFATE,** *Sulfate* ⟨221⟩ (if labeled for use in preparing parenteral dosage forms)

  Sample: 1.0 g

  Acceptance criteria: The *Sample* shows no more sulfate than corresponds to 0.10 mL of 0.020 N sulfuric acid (NMT 0.01%).

SPECIFIC TESTS

- **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** The total aerobic count using the *Plate Method* is NMT 1000 cfu/g, and the total combined molds and yeasts count is NMT 100 cfu/g.
- **pH ⟨791⟩:** 3.5–7.0, in a 10% (w/w) solution in carbon dioxide-free water
- **WATER DETERMINATION,** *Method I* ⟨921⟩**:** NMT 1.5%
- **CLARITY AND COLOR OF SOLUTION** (if labeled for use in preparing parenteral dosage forms)

  Sample: 10.0 g

  Analysis: Dissolve the *Sample* in 100.0 mL of carbon dioxide-free water.

  Acceptance criteria: The solution is clear and colorless.
- **BACTERIAL ENDOTOXINS TEST ⟨85⟩** (if labeled for use in preparing parenteral dosage forms)**:** NMT 4 USP Endotoxin Units/g for parenteral dosage forms having a concentration of less than 100 g/L of sorbitol, and NMT 2.5 USP Endotoxin Units/g for parenteral dosage forms having a concentration of 100 g/L or more of sorbitol

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. No storage requirements are specified.
- **LABELING:** Sorbitol intended for use in preparing parenteral dosage forms is so labeled.
- **USP REFERENCE STANDARDS ⟨11⟩**

  USP Endotoxin RS

  USP Sorbitol RS

Noncrystallizing Sorbitol Solution

DEFINITION

Noncrystallizing Sorbitol Solution is an aqueous solution containing NLT 45.0% of D-sorbitol ($C_6H_{14}O_6$) (w/w). The amounts of total sugars, other polyhydric alcohols, and any hexitol anhydrides, if detected, are not included in the requirements nor in the calculated amount under *General Notices, 5.60.10. Other Impurities in USP and NF Articles*.

IDENTIFICATION

- **A. PROCEDURE**

  Sample solution: Dissolve 1.4 g of Noncrystallizing Sorbitol Solution in 75 mL of water.

  Analysis: Transfer 3 mL of *Sample solution* to a 15-cm test tube. Add 3 mL of freshly prepared catechol solution (1 in 10), and mix. Add 6 mL of sulfuric acid, mix again, and gently heat the tube in a flame for 30 s.

  Acceptance criteria: A deep pink or wine-red color appears.
- **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. LIMIT OF DIETHYLENE GLYCOL AND ETHYLENE GLYCOL**

  Diluent: Acetone and water (96:4)

  Standard solution: 0.08 mg/mL of USP Diethylene Glycol RS and 0.08 mg/mL of USP Ethylene Glycol RS in *Diluent*.

  Sample solution: Transfer 2.0 g of Noncrystallizing Sorbitol Solution to a 25-mL volumetric flask. Add 1.0 mL of *Diluent* to the flask, and mix on a vortex mixer for 3 min. Add the remaining *Diluent* to the flask to volume in three equal portions. Mix on a vortex mixer for about 3 min after each addition of *Diluent*. Pass a portion of the supernatant layer obtained through a 0.45-µm nylon filter. Discard the first 2 mL of the filtrate, and collect the rest of the filtrate for analysis.

  [NOTE—Acetone is used to precipitate sorbitol.]

  Chromatographic system

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

  Mode: GC

  Detector: Flame ionization

  Column: 0.32-mm × 15-m fused-silica capillary column; 0.25-µm layer of phase G46