Sorbitol Sorbitan Solution

(Title for this monograph—to become official August 1, 2010) (Prior to August 1, 2010, the current practice of labeling the article of commerce with the name Anhydrized Liquid Sorbitol may be continued. Use of the name Sorbitol Sorbitan Solution will be permitted as of August 1, 2005, but the use of this name will not be mandatory until August 1, 2010. The 60-month extension will provide the time needed by the manufacturers and users to make necessary changes.)

» Sorbitol Sorbitan Solution is a water solution containing, on the anhydrous basis, not less than 25.0 percent of D-sorbitol ($C_6H_{14}O_6$) and not less than 15.0 percent of 1,4-sorbitan ($C_6H_{12}O_5$). The amounts of total sugars, other polyhydric alcohols, and any other hexitol anhydrides, if detected, are not included in the requirements or in the calculated amount under *Other Impurities.*

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

Labeling—The labeling indicates the percentage content, on the anhydrous basis, of D-sorbitol and 1,4-sorbitan.

Change to read:

USP Reference standards ⟨11⟩**—***USP Sorbitol RS. USP 1,4-Sorbitan RS.* •*USP Diethylene Glycol RS. USP Ethylene Glycol RS.*• (RB 1-Feb-2010)

Change to read:

Identification—

A: Prepare a solution containing 1.4 g of Sorbitol Sorbitan Solution in 75 mL of water. Transfer 3 mL of this 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, then gently heat the tube in a flame for about 30 seconds: a deep pink or wine-red color appears.

B: The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* 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 Sorbitol Sorbitan Solution to a 25-mL volumetric flask. Add 1.0 mL of *Diluent* to the flask, and vortex the flask for 3 minutes. Add the remaining *Diluent* to the flask to volume in three equal portions. Vortex the flask for about 3 minutes 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

Temperature

Detector: 300°

Injection port: 240°

Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
70	—	70	2
70	50	300	5

Carrier gas: Helium

Flow rate: 3.0 mL/minute

Injection size: 1.0 µL

Injection type: Split injection. The split ratio is about 10 : 1. [NOTE—A split liner, deactivated with glass wool, is used.]

System suitability

Sample: *Standard solution*

[NOTE—Diethylene glycol elutes after ethylene glycol in the chromatogram.]

Suitability requirements

Resolution: Not less than 30 between ethylene glycol and diethylene glycol

Analysis

Samples: *Standard solution* and *Sample solution*

Based on the *Standard solution*, identify the peaks of ethylene glycol and diethylene glycol. Compare the peak areas of ethylene glycol and diethylene glycol in the *Standard solution* and the *Sample solution.*

Acceptance criteria

Diethylene glycol: The peak area of diethylene glycol in the *Sample solution* is not more than the peak area of diethylene glycol in the *Standard solution*, corresponding to not more than 0.10% of diethylene glycol in Sorbitol Sorbitan Solution.

Ethylene glycol: The peak area of ethylene glycol in the *Sample solution* is not more than the peak area of ethylene glycol in the *Standard solution*, corresponding to not more than 0.10% of ethylene glycol in Sorbitol Sorbitan Solution.

• (RB 1-Feb-2010)

Microbial enumeration tests ⟨61⟩ and **Tests for specified microorganisms** ⟨62⟩**—**The total aerobic microbial count using the *Plate Method* is not more than 1000 cfu per mL. The total combined molds and yeasts count is not more than 100 cfu per mL.

pH ⟨791⟩**:** between 4.0 and 7.0, in a 14% (w/w) solution of Sorbitol Sorbitan Solution in carbon dioxide-free water.

Water, *Method I* ⟨921⟩**:** not more than 31.5%.

Residue on ignition ⟨281⟩**:** not more than 0.20%, calculated on the anhydrous basis. Determine on a 2-g portion, accurately weighed.

Reducing sugars—To an amount of Sorbitol Sorbitan Solution, equivalent to 3.3 g, on the anhydrous basis, add 3 mL of water, 20.0 mL of cupric citrate TS, and a few glass beads. Heat so that boiling begins after 4 minutes, and maintain boiling for 3 minutes. 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. When the precipitate has dissolved, titrate the excess of iodine with 0.05 N sodium thiosulfate VS using 2 mL of starch TS, added towards the end of the titration, as an indicator. Not less than 12.8 mL of 0.05 N sodium thiosulfate VS is required, corresponding to not more than 0.3% of reducing sugars, on the anhydrous

basis, as glucose. The amount determined in this test is not included in the calculated amount under *Other Impurities.*

Limit of nickel—

Test solution—Dissolve 20.0 g of Sorbitol Sorbitan Solution in diluted acetic acid, and dilute with diluted acetic acid to 100.0 mL. Add 2.0 mL of a saturated solution of ammonium pyrrolidine dithiocarbamate (about 10 g of ammonium pyrrolidine dithiocarbamate per L) and 10.0 mL of methyl isobutyl ketone, and shake for 30 seconds. Protect from bright light. Allow the two layers to separate, and use the methyl isobutyl ketone layer.

Blank solution—Prepare as directed for the *Test solution,* except to omit the use of Sorbitol Sorbitan Solution. Quantities should be increased five fold to ensure that a sufficient volume of *Blank solution* is available.

Standard solutions—Prepare as directed for the *Test solution,* except to prepare three solutions by adding 0.5 mL, 1.0 mL, and 1.5 mL of nickel standard solution TS.

Procedure—Set the instrument to zero using the *Blank solution.* Concomitantly determine the absorbances of the *Standard solutions* and the *Test solution* at least three times each, at the wavelength of maximum absorbance at 232.0 nm, with a suitable atomic absorption spectrophotometer (see *Spectrophotometry and Light-Scattering* ⟨851⟩) equipped with a nickel hollow-cathode lamp and an air–acetylene flame. Record the average of the steady readings for each of the *Standard solutions* and the *Test solution.* Between each measurement, aspirate the *Blank solution,* and ascertain that the reading returns to zero. Plot the absorbances of the *Standard solutions* and the *Test 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 *Test solution.* Not more than 1 µg per g, calculated on the anhydrous basis, is found.

Assay—

Mobile phase—Use degassed water.

Resolution solution—Dissolve sorbitol, 1,4-sorbitan, isosorbide, and mannitol in water to obtain a solution having concentrations of about 10 mg per g, 4 mg per g, 4 mg per g, and 1 mg per g, respectively.

Standard preparation—Dissolve accurately weighed quantities of USP Sorbitol RS and USP 1,4-Sorbitan RS in water to obtain a solution having concentrations of about 10 mg per g and 4 mg per g, respectively.

Assay preparation—Dissolve about 0.40 g of Sorbitol Sorbitan Solution, accurately weighed, in water, and dilute with water to about 20 g. Accurately record the final solution weight, and mix thoroughly.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a refractive index detector that is maintained at a constant temperature of about 35°, and a 7.8-mm × 10-cm column that contains packing L34. The column temperature is maintained at about 50°, controlled within ±2°, and the flow rate is about 0.6 mL per minute. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between the 1,4-sorbitan and isosorbide is not less than 2.0. Chromatograph the *Standard preparation,* and record the peak responses for 1,4-sorbitan and sorbitol as directed for *Procedure:* the relative retention times are about 0.35 for 1,4-sorbitan, 0.43 for isosorbide, 0.7 for mannitol, and 1.0 for sorbitol; and the relative standard deviation for replicate injections is not more than 2.0% for each analyte.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Separately calculate the percentages, on the anhydrous basis, of 1,4-sorbitan and D-sorbitol in the portion of Sorbitol Sorbitan Solution taken by the formula:

$$[10{,}000(C_S / C_U)(r_U / r_S)]/(100 - W)$$

in which C_S is the concentration, in mg per g, of the appropriate USP Reference Standard in the *Standard preparation;* C_U is the concentration, in mg per g, of the Sorbitol Sorbitan Solution in the *Assay preparation;* r_U and r_S are the peak responses of the corresponding analyte obtained from the *Assay preparation* and the *Standard preparation,* respectively; and W is the percentage obtained in the test for *Water.*