

## Noncrystallizing Sorbitol Solution

» Noncrystallizing Sorbitol Solution is an aqueous solution containing not less than 45.0 percent of D-sorbitol (C<sub>6</sub>H<sub>14</sub>O<sub>6</sub>) (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 *Other Impurities*.

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

### Change to read:

**USP Reference standards** <11>—*USP Sorbitol RS*. •*USP Diethylene Glycol RS*. *USP Ethylene Glycol RS*.• (RB 1-Feb-2010)

### Change to read:

#### Identification—

**A:** Dissolve 1.4 g of Noncrystallizing Sorbitol 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), mix, add 6 mL of sulfuric acid, mix again, and gently heat the tube in a flame for about 30 seconds: a deep pink or wine-red color appears.

**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: 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 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- $\mu$ m 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  $\times$  15-m fused-silica capillary column, 0.25- $\mu$ m layer of phase G46

#### Temperature

**Detector:** 300°

**Injection port:** 240°

**Column:** See 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  $\mu$ L

**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 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 Noncrystallizing Sorbitol 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 Noncrystallizing Sorbitol 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, and the total combined molds and yeasts count is not more than 100 cfu per mL.

**pH** <791>: between 5.0 and 7.5, in a 14% (w/w) solution of Noncrystallizing Sorbitol Solution in carbon dioxide-free water.

**Water, Method 1** <921>: between 28.5% and 31.5%.

**Residue on ignition** <281>: not more than 0.1%, calculated on the anhydrous basis, determined on a 2-g portion, accurately weighed.

**Reducing sugars**—To an amount of Noncrystallizing Sorbitol 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**—Proceed as directed in the test for *Limit of nickel* under *Sorbitol Solution*. Not more than 1  $\mu$ g per g, calculated on the anhydrous basis, is found.

#### Assay—

*Mobile phase*, *Resolution solution*, *Standard preparation*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Sorbitol*.

*Assay preparation*—Accurately weigh about 0.20 g of Noncrystallizing Sorbitol Solution, and dissolve in and dilute with water to about 20 g. Accurately record the final solution weight, and mix thoroughly.

## 2 Sorbitol

*Procedure*—Proceed as directed in the *Assay* under *Sorbitol*. Calculate the percentage of D-sorbitol ( $C_6H_{14}O_6$ ) in the portion of Noncrystallizing Sorbitol Solution taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which  $C_S$  is the concentration, in mg per g, of USP Sorbitol RS in the *Standard preparation*;  $C_U$  is the concentration, in mg per g,

of Noncrystallizing Sorbitol Solution in the *Assay preparation*; and  $r_U$  and  $r_S$  are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.