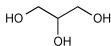


Glycerin



C₃H₈O₃ 92.10
1,2,3-Propanetriol.
Glycerol [56-81-5].

Change to read:

» Glycerin contains not less than 99.0 percent and not more than 101.0 percent of C₃H₈O₃, calculated on the anhydrous basis. • (RB 1-May-2009)

Packaging and storage—Preserve in tight containers.

USP Reference standards (11)—*USP Diethylene Glycol RS*. *USP Ethylene Glycol RS*. *USP Glycerin RS*.

Color—Its color, when viewed downward against a white surface in a 50-mL color-comparison tube, is not darker than the color of a standard made by diluting 0.40 mL of ferric chloride CS with water to 50 mL and similarly viewed in a color-comparison tube of approximately the same diameter and color as that containing the Glycerin.

Change to read:

Identification—[NOTE—Compliance is determined by meeting the requirements for *Identification A, B, and C*.•(RB 1-May-2009)]

A: *Infrared Absorption* (197F).

B: **Limit of diethylene glycol and ethylene glycol**—

Standard solution: 2.0 mg per mL of USP Glycerin RS, 0.050 mg per mL of USP Ethylene Glycol RS, 0.050 mg per mL of USP Diethylene Glycol RS, and 0.10 mg per mL of 2,2,2-trichloroethanol (internal standard) in methanol.

Sample solution: 50 mg per mL of Glycerin, accurately weighed, and 0.10 mg per mL of 2,2,2-trichloroethanol, accurately weighed (internal standard) in methanol.

Chromatographic system (see *Chromatography* (621))—The gas chromatograph is equipped with a flame-ionization detector, a 0.53-mm × 30-m fused-silica analytical column coated with 3.0-μm G43 stationary phase, and a deactivated split liner with glass wool. The injection port temperature is maintained at 220° and the detector temperature is maintained at 250°. The carrier gas is helium with a flow rate of about 4.5 mL per minute. The split flow ratio is about 10 : 1. The chromatograph is programmed as follows. Initially, the column temperature is equilibrated at 100° for 4 minutes, then increased at a rate of 50° per minute to 120°, and is maintained at 120° for 10 minutes, then increased at a rate of 50° per minute to 220°, and is maintained at 220° for 6 minutes. Chromatograph the *Standard solution*; record the peak responses directed for *Procedure*: the resolution, *R*, between diethylene glycol and glycerin is not less than 1.5. [NOTE—the relative retention times are about 0.3 for ethylene glycol, 0.6 for 2,2,2-trichloroethanol, 0.8 for diethylene glycol, and 1.0 for glycerin.]

Procedure—Inject about 1 μL of the *Sample solution* into the chromatograph, record the chromatogram, and measure the peak responses. If a peak at the retention times for the diethylene glycol or ethylene glycol is present in the *Sample solution*, the peak response ratio relative to 2,2,2-trichloroethanol is not more than the peak response ratio for diethylene glycol or ethylene glycol relative to 2,2,2-trichloroethanol in the *Standard solution*; not more than 0.10% each for diethylene glycol and ethylene glycol is found.

C: Examine the chromatograms obtained in *Identification test B*. The retention time of the glycerin peak in the chromatogram of the *Sample solution* corresponds to that obtained in the chromatogram of the *Standard solution*.• (RB 1-May-2009)

Specific gravity (841): not less than 1.249.

Residue on ignition (281)—Heat 50 g in an open, shallow 100-mL porcelain dish until it ignites, and allow it to burn without further application of heat in a place free from drafts. Cool, moisten the residue with 0.5 mL of sulfuric acid, and ignite to constant weight: the weight of the residue does not exceed 5 mg (0.01%).

Water, Method I (921): not more than 5.0%.

Chloride (221)—A 7.0-g portion shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (0.001%).

Sulfate (221)—A 10-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (about 0.002%).

Heavy metals (231)—Mix 4.0 g with 2 mL of 0.1 N hydrochloric acid, and dilute with water to 25 mL: the limit is 5 μg per g.

Limit of chlorinated compounds—Accurately weigh 5 g of Glycerin into a dry, round-bottom, 100-mL flask, add 15 mL of morpholine, and connect the flask by a ground joint to a reflux condenser. Reflux gently for 3 hours. Rinse the condenser with 10 mL of water, receiving the washing in the flask, and cautiously acidify with nitric acid. Transfer the solution to a suitable comparison tube, add 0.50 mL of silver nitrate TS, dilute with water to 50.0 mL, and mix: the turbidity is not greater than that of a blank to which 0.20 mL of 0.020 N hydrochloric acid has been added, the refluxing being omitted (0.003% of Cl).

Fatty acids and esters—Mix 50 g of Glycerin with 50 mL of freshly boiled water and 5 mL of 0.5 N sodium hydroxide VS, boil the mixture for 5 minutes, cool, add phenolphthalein TS, and titrate the excess alkali with 0.5 N hydrochloric acid VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* (541)): not more than 1 mL of 0.5 N sodium hydroxide is consumed.

Delete the following:

• **Diethylene glycol and ethylene glycol impurities**—

Internal standard solution—Transfer 100 mg of 2,2,2-trichloroethanol (internal standard), accurately weighed, to a 100-mL volumetric flask, dilute with methanol to volume, and mix.

Standard stock solution 1—Transfer 50 mg of USP Diethylene Glycol RS, accurately weighed, to a 100-mL volumetric flask, dilute with methanol to volume, and mix.

Standard stock solution 2—Transfer 50 mg of USP Ethylene Glycol RS, accurately weighed, to a 100-mL volumetric flask, dilute with methanol to volume, and mix.

Standard stock solution 3—Transfer 50 mg of USP Glycerin RS, accurately weighed, to a 100-mL volumetric flask, dilute with methanol to volume, and mix.

Standard solution—Transfer 5.0 mL each of *Standard stock solution 1*, *Standard stock solution 2*, and the *Internal standard solution* to a 100-mL volumetric flask, and dilute with methanol to volume, and mix.

Resolution solution—Transfer 500 mg of USP Glycerin RS to a 10-mL volumetric flask, add 0.5 mL each of *Standard stock solution 1* and *Standard stock solution 2*, dilute with methanol to volume, and mix.

Test solution—Transfer about 5 g of Glycerin to a 100-mL volumetric flask, add 5.0 mL of *Internal standard solution*, dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* (621))—The gas chromatograph is equipped with a flame-ionization detector, a 0.53-mm × 30-m fused-silica analytical column coated with 3.0-μm G43 stationary phase. The injection port temperature is maintained at 220° and the detector temperature is maintained at 250°. The carrier gas is helium, flowing at a rate of about 4.5 mL per minute. The

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split flow ratio is about 10 : 1. The chromatograph is programmed as follows. Initially, the column temperature is equilibrated at 100° for 4 minutes, then increased at a rate of 50° per minute to 120°, and is maintained at 120° for 10 minutes then increased at a rate of 50° per minute to 220°, and is maintained at 220° for 6 minutes. Chromatograph the *Standard solution*, and record the peak response ratio and retention times as directed for *Procedure*: the relative retention times are about 0.3 for ethylene glycol, 0.8 for diethylene glycol, and 1.0 for glycerin; the relative standard deviation for replicate injections for the diethylene glycol is not more than 10%; and the limit of quantitation of diethylene glycol and ethylene glycol is not more than 0.025%.

Procedure—Separately inject equal volumes (about 1 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the ethylene glycol and diethylene glycol peaks. Calculate the percentage of diethylene glycol and ethylene glycol in the portion of Glycerin taken by the formula:

$$100(C_S / C_U)(R_U / R_S)$$

in which C_S is the concentration, in mg per mL, of diethylene glycol (or ethylene glycol) in the *Standard solution*; C_U is the concentration, in mg per mL, of Glycerin in the *Test solution*; and R_U and R_S are the peak response ratios for diethylene glycol (or ethylene glycol) to the internal standard peak obtained from the *Test solution* and the *Standard solution*: NMT the limit of quantitation for each, is found (0.025%). •(RB 1-May-2009)

Add the following:**•Related compounds—**

System suitability solution: 0.5 mg per mL of USP Diethylene Glycol RS and USP Glycerin RS in water.

Sample solution: 50 mg per mL of Glycerin in water.

Chromatographic system (see *Chromatography* <621>)—The gas chromatograph is equipped with a flame-ionization detector, a 0.53-mm × 30-m fused-silica analytical column coated with 3.0-µm G43 stationary phase, and an inlet liner having an inverted cup or spiral structure. The chromatograph is programmed as follows. Initially, the column temperature is equilibrated at 100° until the time of injection; is increased at a rate of 7.5° per minute to 220°; and is maintained at 220° for 4 minutes. The injection port temperature is maintained at 220°, and the detector temperature is maintained at 250°. The carrier gas is helium. The split flow ratio is about 10 : 1, and the linear flow is maintained at about 38 cm per second. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure*: the resolution, R , between diethylene glycol and glycerin is not less than 7.0.

Procedure—Inject about 0.5 µL of the *Sample solution* into the chromatograph, record the chromatogram, and measure the responses for all of the peaks. Calculate the percentage of each impurity, excluding any solvent peaks, and diethylene glycol in the portion of Glycerin taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response of each individual impurity obtained from the *Sample solution*; and r_s is the sum of the responses of all the peaks obtained from *Sample solution*: not more than 0.1% of any individual impurity is found; and not more than 1.0% of total impurities is found. •(RB 1-May-2009)

Assay—

Sodium periodate solution—Dissolve 60 g of sodium metaperiodate in sufficient water containing 120 mL of 0.1 N sulfuric acid to make 1000 mL. Do not heat to dissolve the periodate. If the solution is not clear, pass through a sintered-glass filter. Store the solution in a glass-stoppered, light-resistant container. Test the suitability of this solution as follows. Pipet 10 mL into a 250-mL volumetric flask, dilute with water to volume, and mix. To about 550 mg of Glycerin dissolved in 50 mL of water add 50 mL of the diluted periodate solution with a pipet. For a blank, pipet 50 mL of the solution into a flask containing 50 mL of water. Allow the solutions to stand for 30 minutes, then to each add 5 mL of hydrochloric acid and 10 mL of potassium iodide TS, and rotate to mix. Allow to stand for 5 minutes, add 100 mL of water, and titrate with 0.1 N sodium thiosulfate, shaking continuously and adding 3 mL of starch TS as the endpoint is approached. The ratio of the volume of 0.1 N sodium thiosulfate required for the glycerin–periodate mixture to that required for the blank should be between 0.750 and 0.765.

Procedure—Transfer about 400 mg of Glycerin, accurately weighed, to a 600-mL beaker, dilute with 50 mL of water, add bromothymol blue TS, and acidify with 0.2 N sulfuric acid to a definite green or greenish yellow color. Neutralize with 0.05 N sodium hydroxide to a definite blue endpoint, free from green color. Prepare a blank containing 50 mL of water, and neutralize in the same manner. Pipet 50 mL of the *Sodium periodate solution* into each beaker, mix by swirling gently, cover with a watch glass, and allow to stand for 30 minutes at room temperature (not exceeding 35°) in the dark or in subdued light. Add 10 mL of a mixture of equal volumes of ethylene glycol and water, and allow to stand for 20 minutes. Dilute each solution with water to about 300 mL, and titrate with 0.1 N sodium hydroxide VS to a pH of 8.1 ± 0.1 for the specimen under assay and 6.5 ± 0.1 for the blank, using a pH meter. Each mL of 0.1 N sodium hydroxide, after correction for the blank, is equivalent to 9.210 mg of C₃H₈O₃.