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Thimerosal Topical Aerosol

DEFINITION

Thimerosal Topical Aerosol is an alcoholic solution of Thimerosal mixed with suitable propellants in a pressurized container. It contains NLT 85.0% and NMT 115.0% of the labeled quantity of thimerosal ($C_9H_9HgNaO_2S$).

[Note—Thimerosal Topical Aerosol is sensitive to some metals.]

IDENTIFICATION

• **A.**

Sample: 10 mL of Topical Aerosol

Analysis: Spray the *Sample* into a suitable container, add 10 mL of water, and heat on a steam bath until the odor of alcohol is no longer perceptible. Cool, and pass hydrogen sulfide through the solution.

Acceptance criteria: No black discoloration or black precipitate is formed.

• **B.**

Sample: 15 mL of Topical Aerosol

Analysis: Spray the *Sample* into a suitable container, add 15 mL of water, heat on a steam bath until the odor of alcohol is no longer perceptible, and add 2 drops of bromine. Mix with 1.5 mL of 3 N hydrochloric acid, filter, evaporate the excess bromine with a current of air, and pass hydrogen sulfide through the filtrate.

Acceptance criteria: A black precipitate is formed.

ASSAY

• **Procedure**

The *Standard solutions* and *Sample solution* may be diluted with water, if necessary, to yield solutions of suitable concentration, adaptable to the linear or working range of the instrument.

Solution A: Dissolve 50 g of stannous chloride in 100 mL of hydrochloric acid on a steam bath, cool, dilute with water to 500 mL, and mix. Use within 3 months.

Standard stock solution A: 1.8 µg/mL of USP Thimerosal RS

Standard stock solution B: 2.0 µg/mL of USP Thimerosal RS

Standard stock solution C: 2.2 µg/mL of USP Thimerosal RS

Standard solution A: Pipet 20 mL of *Standard stock solution A* into a 100-mL volumetric flask. Add 5 mL of sulfuric acid, cool, add 3 mL of nitric acid, and mix. Add potassium permanganate crystals, while mixing, until the purple color persists for NLT 15 min. Add 200 mg of potassium persulfate, mix, and heat on a steam bath for 2 h. Cool, and dilute with water to volume.

Standard solution B: Pipet 20 mL of *Standard stock solution B* into a 100-mL volumetric flask. Add 5 mL of sulfuric acid, cool, add 3 mL of nitric acid, and mix. Add potassium permanganate crystals, while mixing, until the purple color persists for NLT 15 min. Add 200 mg of potassium persulfate, mix, and heat on a steam bath for 2 h. Cool, and dilute with water to volume.

Standard solution C: Pipet 20 mL of *Standard stock solution C* into a 100-mL volumetric flask. Add 5 mL of sulfuric acid, cool, add 3 mL of nitric acid, and mix. Add potassium permanganate crystals, while mixing, until the purple color persists for NLT 15 min. Add 200 mg of potassium persulfate, mix, and heat on a steam bath for 2 h. Cool, and dilute with water to volume.

Sample stock solution: Weigh a filled Topical Aerosol container, and record the weight. Place the container in a dry ice–alcohol bath, and cool for 60 min. Remove the container from the bath, and carefully remove the spray cap with wire cutters, taking precautions to save all pieces of the spray head and cap. With the aid of three 5-mL portions of water, transfer the contents of the container to a beaker previously chilled in the bath. Dry the rinsed empty container and all of its parts in an oven at 105° for 2 h, cool, and weigh. Calculate the weight of the container contents. Add a few boiling chips to the beaker, and carefully stir to help evaporate the propellant. After the bulk of the propellant has evaporated, place the beaker on a steam bath, evaporate the volatile solvents, and cool. Transfer the residual liquid with the aid of 35.0 mL of alcohol to a 50-mL volumetric flask, and dilute with water to volume. Dilute a portion of this solution quantitatively with water to obtain nominally 2 µg/mL of thimerosal.

Sample solution: Pipet 20 mL of *Sample stock solution* into a 100-mL volumetric flask. Add 5 mL of sulfuric acid, cool, add 3 mL of nitric acid, and mix. Add potassium permanganate crystals, while mixing, until the purple color persists for NLT 15 min. Add 200 mg of potassium persulfate, mix, and heat on a steam bath for 2 h. Cool, and dilute with water to volume.

Instrumental conditions

Mode: Flameless atomic absorption spectroscopy

Lamp: Mercury hollow-cathode

Blank solution: Pipet 20 mL of water into a 100-mL volumetric flask. Add 5 mL of sulfuric acid, cool, add 3 mL of nitric acid, and mix. Add potassium permanganate crystals, while mixing, until the purple color persists for NLT 15 min. Add 200 mg of potassium persulfate, mix, and heat on a steam bath for 2 h. Cool, and dilute with water to volume.

Analysis

Samples: *Standard solutions A, B,* and *C*, *Sample solution*, and *Blank solution*

Proceed with each of the *Samples* as follows. Separately pipet 3 mL into the scrubbing chamber of a suitable system designed for determination of mercury. Dilute with water to 150 mL, and add hydroxylamine hydrochloride solution (1 in 10) to reduce the excess permanganate. Add 5 mL of *Solution A*, and immediately attach the scrubbing chamber to the system. Concomitantly determine the absorbance of the vapor from each solution at an integration time of 15 s. Use the absorbance of the *Blank solution* to correct the absorbances of *Standard solutions A, B,* and *C*, and the *Sample solution*. Plot the corrected absorbances of the standards versus the respective concentrations of the *Standard stock solutions*, in µg/mL, and from the curve so obtained determine the concentration, *C*, in µg/mL, of the *Sample solution*.

Calculate the percentage of thimerosal ($C_9H_9HgNaO_2S$) in the Topical Aerosol taken:

$$\text{Result} = (C/C_U) \times 100$$

C = measured concentration of thimerosal in the *Sample solution* (µg/mL)

C_U = nominal concentration of thimerosal in the *Sample solution* (µg/mL)

Acceptance criteria: 85.0%–115.0%

SPECIFIC TESTS

• **Alcohol Determination,** *Method II*⟨611⟩

Analysis: Weigh, chill, and open 1 Topical Aerosol container, and remove the propellant as directed for the *Sample solution* in the *Assay*, continuing until the bulk of the propellant has evaporated. Determine the alcohol content of the sample thus prepared by the *Gas Chromatographic Method* (see *Method II* in *Alcohol Determination* ⟨611⟩), using methyl ethyl ketone as the internal standard in place of acetonitrile.

Acceptance criteria: 18.7%–25.3% (w/w) of C_2H_5OH

• **Other Requirements:** Meets the requirements for *Topical Aerosols* ⟨603⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant, pressurized containers, and avoid exposure to excessive heat.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
THIMEROSAL TOPICAL AEROSOL	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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