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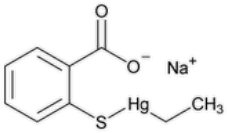
Thimerosal



$C_9H_9HgNaO_2S$ 404.81

Mercury, ethyl(2-mercaptobenzoato-*S*)-, sodium salt;

Ethyl (sodium *o*-mercaptobenzoato)mercury CAS RN®: 54-64-8.

DEFINITION

Thimerosal contains NLT 97.0% and NMT 102.0% of thimerosal ($C_9H_9HgNaO_2S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.**

Sample solution: 10 mg/mL

Analysis: To the *Sample solution* add a few drops of silver nitrate TS.

Acceptance criteria: A pale yellow precipitate is formed.

• **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 0.05% Trifluoroacetic acid, prepared by adding 1.0 mL of trifluoroacetic acid to 2 L of water

Mobile phase: Methanol and *Solution A* (60:40)

Standard stock solution: 250 µg/mL of USP Thimerosal RS in water

Impurity stock solution: 250 µg/mL of USP Thimerosal Related Compound A RS in methanol and water (90:10)

System suitability solution: 25 µg/mL each of USP Thimerosal RS and USP Thimerosal Related Compound A RS from *Standard stock solution* and *Impurity stock solution*, respectively, in water

Standard solution: 25 µg/mL of USP Thimerosal RS in water from *Standard stock solution*

Sample solution: 25 µg/mL of Thimerosal in water

[Note—Prepare both the *Standard solution* and *Sample solution* at a concentration of NMT ±10% of the specified concentration.]

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

Column: 2.1-mm × 10-cm; 2-µm packing L1

Autosampler temperature: 4°

Flow rate: 0.35 mL/min

Injection volume: 2.5 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times of thimerosal and thimerosal related compound A are 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 3.5 between the thimerosal and thimerosal related compound A peaks, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of thimerosal ($C_9H_9HgNaO_2S$) in the portion of Thimerosal taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Thimerosal RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: 97.0%–102.0% on the dried basis

IMPURITIES

• **Mercury Ions**

Iodide reagent: 332 mg/mL of potassium iodide. Prepare fresh daily. Keep the stopper in the flask, and protect from light.

Standard solution: 95 µg/mL of mercuric chloride

Sample stock solution: 5 mg/mL of Thimerosal

Sample solution A: 1 mg/mL of Thimerosal from *Sample stock solution*

Sample solution B: 1 mg/mL of Thimerosal from *Sample stock solution* and 9.5 µg/mL of mercuric chloride from *Standard solution*

Instrumental conditions

Mode: UV

Analytical wavelength: Determine the wavelength of maximum absorbance for the tetraiodomercurate ion at about 323 nm using the solution prepared by mixing 1.0 mL of the *Standard solution* and 5.0 mL of the *Iodide reagent*, and diluting with water to 10.0 mL.

Cell: 1 cm

Blank: Water

Analysis

Protect all solutions from light before determining their absorbances.

Samples: Label five 10-mL volumetric flasks C, D, E, F, and R. Transfer 5.0 mL of *Sample solution A* to flasks C and D, 5.0 mL of *Sample solution B* to flasks E and F, and 5.0 mL of water to flask R. Dilute flasks C and E with water to volume. Dilute flasks D, F, and R with *Iodide reagent* to volume.

Determine the absorbances of the solutions in flasks C, D, E, F, and R as A_C, A_D, A_E, A_F, and A_R, respectively.

Calculate the percentage of mercury ions in the portion of Thimerosal taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times (A_r/M_r) \times 100$$

A_U = absorbance of the *Sample solution* obtained by: $A_U = A_D - A_R - A_C$

A_S = absorbance of the *Standard solution* obtained by: $A_S = A_F - A_R - A_E - A_U$

C_S = concentration of mercuric chloride in *Sample solution B* (mg/mL)

C_U = concentration of Thimerosal in *Sample solution B* (mg/mL)

A_r = atomic weight of mercury, 200.59

M_r = molecular weight of mercuric chloride, 271.50

Acceptance criteria: NMT 0.70%

• **Organic Impurities**

Solution A: 0.05% Trifluoroacetic acid, prepared by adding 1.0 mL of trifluoroacetic acid to 2 L of water

Mobile phase: Methanol and *Solution A* (60:40)

Stock solution 1: 250 µg/mL of USP Thimerosal RS in water

Stock solution 2: 250 µg/mL of USP Thimerosal Related Compound A RS in methanol and water (90:10)

System suitability solution: 25 µg/mL each of USP Thimerosal RS and USP Thimerosal Related Compound A RS from *Stock solution 1* and *Stock solution 2*, respectively, in water

Standard solution: 0.25 µg/mL of USP Thimerosal Related Compound A RS from *Stock solution 2* in water

Sample solution: 250 µg/mL of Thimerosal in water

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

Column: 2.1-mm × 10-cm; 2-µm packing L1

Autosampler temperature: 4°

Flow rate: 0.35 mL/min

Injection volume: 2.5 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 3.5 between the thimerosal and thimerosal related compound A peaks, *System suitability solution*

Relative standard deviation: NMT 3%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Thimerosal taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of thimerosal related compound A from the *Standard solution*

C_S = concentration of USP Thimerosal Related Compound A RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: See *Table 1*. Disregard peaks less than 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Thiosalicylic acid[a]	0.36	0.10
Thimerosal	1.0	—
Thimerosal related compound A	1.3	0.10
Any other individual unspecified impurity	—	0.10
Total impurities	—	1.0

[a] 2-Sulfanylbenzoic acid.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry to constant weight under vacuum over phosphorus pentoxide.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards ⟨11⟩**

USP Thimerosal RS

USP Thimerosal Related Compound A RS

2,2'-Disulfanediyldibenzoic acid.

$C_{14}H_{10}O_4S_2$ 306.35

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

Topic/Question	Contact	Expert Committee
THIMEROSAL	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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