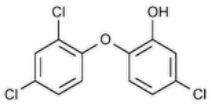
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Dec-2021
Document Type: USP Monographs
DocId: GUID-0FA6F91F-0918-4250-9CC8-3FEDB867C47C_5_en-US
DOI: https://doi.org/10.31003/USPNF_M85150_05_01
DOI Ref: i852i

Triclosan



$C_{12}H_7Cl_3O_2$ 289.54

Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-;

2,4,4'-Trichloro-2'-hydroxydiphenyl ether CAS RN®: 3380-34-5; UNII: 4NM5039Y5X.

DEFINITION

Triclosan contains NLT 97.0% and NMT 103.0% of triclosan ($C_{12}H_7Cl_3O_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-Dec-2021)

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

ASSAY

Change to read:

• **Procedure**

Standard solution: 0.4 mg/mL of USP Triclosan RS in ethyl acetate

Sample solution: 0.4 mg/mL of Triclosan in ethyl acetate

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 15-m; ▲coated with a 1.0-µm film of▲ (USP 1-Dec-2021) phase G3

Temperatures

Injection port: ▲▲ (USP 1-Dec-2021) 200°

Detector: 260°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
34	20	140	0
140	4	240	NLT 5

Carrier gas: Helium

Pressure: 6 psi

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of triclosan ($C_{12}H_7Cl_3O_2$) in the portion of Triclosan taken:

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

r_U = peak response of triclosan from the *Sample solution*

r_S = peak response of triclosan from the *Standard solution*

C_S = concentration of USP Triclosan RS in the *Standard solution* (mg/mL)

C_U = concentration of Triclosan in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the anhydrous basis

IMPURITIES

• **Organic Impurities**

Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Sample: *Sample solution*

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

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of all peak responses in the *Sample solution*

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 0.5%

Change to read:

• **Limit of 1,3,7-Trichlorodibenzo-*p*-dioxin, 2,8-Dichlorodibenzo-*p*-dioxin, 2,8-Dichlorodibenzofuran, and 2,4,8-Trichlorodibenzofuran**

Mobile phase: Acetonitrile, water, and glacial acetic acid (70: 30: 0.1)

Standard solution: Use USP Triclosan Related Compounds Mixture A RS

Sample solution: Transfer 2.0 g of Triclosan into a screw-capped centrifuge tube. Add 5 mL of 2 N potassium hydroxide, and shake for 10 min to dissolve. Add 3 mL of *n*-hexane, shake for 10 min, and allow the phases to separate. Transfer the organic layer to a suitable container, add another 3 mL of *n*-hexane to the aqueous layer, shake for 10 min, and allow the phases to separate. Transfer the organic layer to the previous extract, discard the aqueous layer, add 3 mL of 2 N potassium hydroxide to the combined organic layers, shake for 10 min, and allow the phases to separate. Discard the aqueous layer, add another 3 mL of 2 N potassium hydroxide to the combined organic layers, shake for 10 min, and allow the phases to separate. Transfer the organic layer to a suitable container, and evaporate with the aid of a stream of nitrogen to dryness. Dissolve the residue in 1.0 mL of methanol.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; ▲5-µm▲ (USP 1-Dec-2021) packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 15.0% from the 2,8-dichlorodibenzo-*p*-dioxin peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration of each impurity in the portion of Triclosan taken:

$$\text{Result} = (r_U/r_S) \times (C_S/W) \blacktriangle\times V\blacktriangle \text{ (USP 1-Dec-2021)}$$

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

r_S = peak response of the corresponding impurity in USP Triclosan Related Compounds Mixture A RS from the *Standard solution*

C_S = concentration of the corresponding impurity in USP Triclosan Related Compounds Mixture A RS in the *Standard solution* (µg/mL)

W = weight of Triclosan taken to prepare the *Sample solution* (g)

$\blacktriangle V$ = volume of the *Sample solution*, 1 mL▲ (USP 1-Dec-2021)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (ppm)
2,8-Dichlorodibenzofuran	0.59	0.25
2,8-Dichlorodibenzo-*p*-dioxin	0.71	0.5
2,4,8-Trichlorodibenzofuran	0.88	0.5
1,3,7-Trichlorodibenzo-*p*-dioxin	1.00	0.25

Change to read:

• **Limit of 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and 2,3,7,8-Tetrachlorodibenzofuran**

[**Caution—**2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and 2,3,7,8-tetrachlorodibenzofuran are extremely toxic substances. Exercise all necessary precautions in the conduct of this procedure.]

Stationary phase A: Transfer 10 g of silica gel to a suitable container, add 3 mL of 1 N sodium hydroxide, and mix.

Stationary phase B: Transfer 60 g of silica gel to a suitable container, add 74 mL of concentrated sulfuric acid, and mix.

Chromatographic column A: Transfer 5.1 g of *Stationary phase A*, 0.5 g of silica gel, 6.2 g of *Stationary phase B*, and 3.2 g of sodium sulfate to a glass chromatographic column having an internal diameter of 10 mm. Wash the column with 50 mL of *n*-hexane, and discard the eluate.

Chromatographic column B: Transfer 2.5 g of alumina and 2.5 g of sodium sulfate to a glass chromatographic column having an internal diameter of 6 mm. Wash the column with 30 mL of *n*-hexane, and discard the eluate.

Internal standard solution: 1.0 pg/µL each of ^{13}C-labeled 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and ^{13}C-labeled 2,3,7,8-tetrachlorodibenzofuran prepared as follows. Transfer quantities of ^{13}C-labeled 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and ^{13}C-labeled 2,3,7,8-tetrachlorodibenzofuran, in nonane, and dilute if necessary, with 2,2,4-trimethylpentane.

Sample solution: Transfer 30 g of Triclosan into a separatory funnel. Add 30 µL of *Internal standard solution*, and dissolve in 200 mL of 1 N sodium hydroxide. Extract with four 30-mL portions of *n*-hexane and combine the extracts. Wash the combined extracts with 20 mL of water, extract the washing with 15 mL of *n*-hexane, and add the extract to the other combined extracts. Add 3 g of anhydrous sodium sulfate to the combined extracts, allow to stand for 30 min, quantitatively transfer to an appropriate round-bottom flask, and distill, using a distillation apparatus with a Vigreux column, until about 1 mL remains. Transfer this solution to the top of *Chromatographic column A*, and elute with 50 mL of *n*-hexane. Collect the eluate on top of *Chromatographic column B*, and elute with 30 mL of a mixture of *n*-hexane and methylene chloride (98:2), discarding the eluate. Elute with 40 mL of a mixture of *n*-hexane and methylene chloride (50:50), collecting the eluates in a round-bottom flask. Distill the combined eluates, using a distillation apparatus with a Vigreux column, until 1 mL remains.

Further concentrate this solution with the aid of a stream of nitrogen to 50 µL, evaporate at room temperature to dryness, and dissolve in 10 µL of 2,2,4-trimethylpentane.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability* and *Mass Spectrometry ⟨736⟩*.)

Mode: GC

Detector: High-resolution mass spectrometer with an electron-impact ionization source

Column: 0.25-mm × 60-m; coated with ▲a 0.15-µm film of▲ (USP 1-Dec-2021) phase G48

Temperatures

Injection port: 280°

Column: See *Table 3*.

Table 3

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
80	0	80	1
80	20	220	0
220	2	270	NLT 20

Carrier gas: Helium

Injection volume: 1 µL

System suitability

Sample: *Internal standard solution*

Suitability requirements

Signal-to-noise ratio: NLT 50 at a mass-to-charge (m/z) ratio of 321.89

Analysis

Sample: *Sample solution*

Measure the peak responses at m/z ratios of 319.90, 321.89, 331.88, 333.93, 303.90, 305.90, 315.94, and 317.94.

Acceptance criteria: The peak response for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin at an m/z ratio of 319.90 is NMT the peak response of the associated internal standard at an m/z ratio of 331.88; the peak response for 2,3,7,8-tetrachlorodibenzofuran at an m/z ratio of 303.90 is NMT the peak response of the associated internal standard at an m/z ratio of 315.94.

Change to read:

• **Limit of Monochlorophenols and 2,4-Dichlorophenol**

Buffer: Dissolve 1.38 g of sodium phosphate, monobasic, anhydrous and 1.42 g of sodium phosphate, dibasic in 1 L of water.

Mobile phase: Acetonitrile and *Buffer* (50:50)

Standard solution: 0.5 µg/mL of USP Parachlorophenol RS and 0.1 µg/mL of USP 2,4-Dichlorophenol RS prepared as follows. Dissolve in acetonitrile a suitable amount each of USP Parachlorophenol RS and USP 2,4-Dichlorophenol RS in a suitable volumetric flask, and add an equal volume of water. Dilute appropriately a portion of this solution with a mixture of acetonitrile and water (50:50).

Sample solution: Transfer 250 mg of Triclosan into a 25-mL, low-actinic volumetric flask. Dissolve in 20 mL of acetonitrile, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: Coulometric electrochemical with electrode 1 set at 0.45 V and electrode 2 set at 0.75 V, both having a positive (oxidative) polarity

Column: 4.6-mm × 25-cm; ▲5-µm▲ (USP 1-Dec-2021) packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 9.0% for 2,4-dichlorophenol

Analysis

Samples: *Standard solution* and *Sample solution*

▲[NOTE—The relative retention times for parachlorophenol and 2,4-dichlorophenol are 0.7 and 1.0, respectively.]▲ (USP 1-DEC-2021)

Acceptance criteria: The peak responses for parachlorophenol and 2,4-dichlorophenol of the *Sample solution* are NMT the corresponding peaks of the *Standard solution*.

SPECIFIC TESTS

- **WATER DETERMINATION ⟨921⟩, *Method I*:** NMT 0.1%
- **COMPLETENESS OF SOLUTION ⟨641⟩**

Sample: 1.40 g/10 mL of acetone

Acceptance criteria: Meets the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.

Change to read:

- **USP REFERENCE STANDARDS ⟨11⟩**

USP 2,4-Dichlorophenol RS

▲2,4-Dichlorophenol.
$C_6H_4Cl_2O$ 163.00▲ (USP 1-Dec-2021)

USP Parachlorophenol RS

▲4-Chlorophenol.
C_6H_5ClO 128.56▲ (USP 1-Dec-2021)

USP Triclosan RS

USP Triclosan Related Compounds Mixture A RS

▲Contains a mixture of the following four compounds:
2,8-Dichlorodibenzofuran.
2,4,8-Trichlorodibenzofuran.
2,8-Dichlorodibenzodioxin.
1,3,7-Trichlorodibenzodioxin.▲ (USP 1-Dec-2021)

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

Topic/Question	Contact	Expert Committee
TRICLOSAN	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(3)

Current DocID: GUID-0FA6F91F-0918-4250-9CC8-3FEDB867C47C_5_en-US

DOI: https://doi.org/10.31003/USPNF_M85150_05_01

DOI ref: i852i