Designation: D7598 – 09

Standard Test Method for Determination of Thiodiglycol in Water by Single Reaction Monitoring Liquid Chromatography/Tandem Mass Spectrometry[1]

This standard is issued under the fixed designation D7598; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This procedure covers the determination of thiodiglycol (TDG) in surface water by direct injection using liquid chromatography (LC) and detected with tandem mass spectrometry (MS/MS). TDG is qualitatively and quantitatively determined by this method. This method adheres to single reaction monitoring (SRM) mass spectrometry.

1.2 This test method has been developed in support of the National Homeland Security Research Center, US EPA by Region 5 Chicago Regional Laboratory.

1.3 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.4 The Detection Verification Level (DVL) and Reporting Range for TDG are listed in Table 1.

1.4.1 The DVL is required to be at a concentration at least 3 times below the reporting limit (RL) and have a signal/noise ratio greater than 3:1. Fig. 1 displays the signal/noise ratio at the DVL.

1.4.2 The RL is the concentration of the level 1 calibration standard as shown in Table 2. The reporting limit for this method is 100 µg/L.

1.5 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D1129 Terminology Relating to Water

D1193 Specification for Reagent Water

D2777 Practice for Determination of Precision and Bias of Applicable Test Methods of Committee D19 on Water

D3856 Guide for Good Laboratory Practices in Laboratories Engaged in Sampling and Analysis of Water

D3694 Practices for Preparation of Sample Containers and for Preservation of Organic Constituents

D5847 Practice for Writing Quality Control Specifications for Standard Test Methods for Water Analysis

E2554 Practice for Estimating and Monitoring the Uncertainty of Test Results of a Test Method in a Single Laboratory Using a Control Sample Program

2.2 *Other Documents:*

EPA publication SW-846 Test Methods for Evaluating Solid Waste, Physical/Chemical Methods[3]

TABLE 1 Detection Verification Level and Reporting Range

Analyte	DVL (µg/L)	Reporting Range (µg/L)
Thiodiglycol	20	100–10 000

3. Terminology

3.1 *Definitions:*

3.1.1 *detection verification level (DVL), n*—a concentration that has a signal/noise ratio greater than 3:1 and is at least 3 times below the reporting limit (RL).

3.1.2 *reporting limit (RL), n*—the concentration of the lowest-level calibration standard used for quantification.

3.2 *Abbreviations:*

3.2.1 *ND*—non-detect

4. Summary of Test Methods

4.1 This is a performance based method and modifications are allowed to improve performance.

4.2 For thiodiglycol analysis, samples are shipped to the lab between 0°C and 6°C and analyzed within 7 days of collection. In the lab, the samples are spiked with surrogate, filtered using a syringe driven Millex HV PVDF filter unit and analyzed directly by LC/MS/MS.

[1] This test method is under the jurisdiction of ASTM Committee D19 on Water and is the direct responsibility of Subcommittee D19.06 on Methods for Analysis for Organic Substances in Water.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from National Technical Information Service (NTIS), U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA, 22161 or at http://www.epa.gov/epawaste/hazard/testmethods/index.htm.

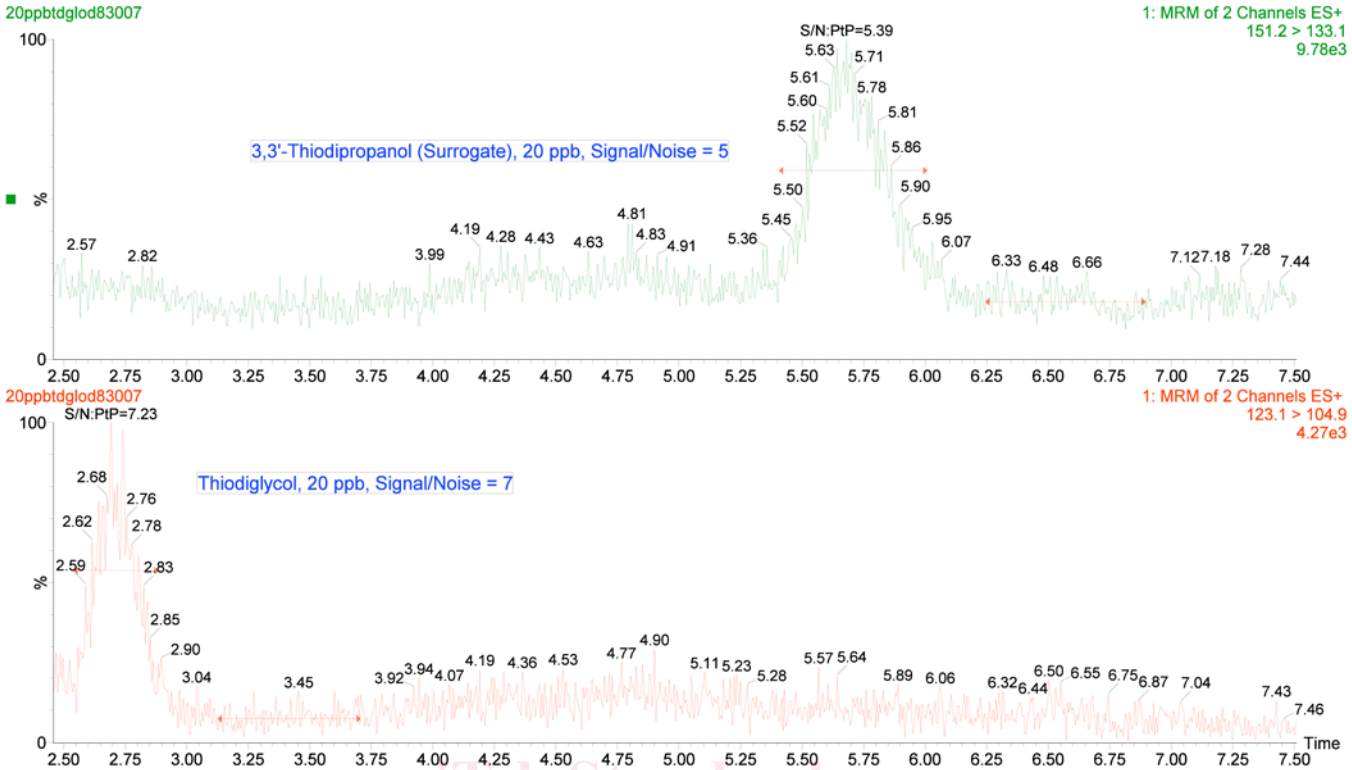

FIG. 1 Example SRM Chromatograms Signal/Noise at Detection Verification Level

TABLE 2 Concentrations of Calibration Standards (PPB)

Analyte/Surrogate	LV 1	LV 2	LV 3	LV 4	LV 5	LV 6	LV 7
Thiodiglycol	100	250	500	1000	2500	5000	10 000
3,3'-Thiodipropanol	100	250	500	1000	2500	5000	10 000

4.3 Thiodiglycol and 3,3'-thiodipropanol (surrogate) are identified by retention time and one SRM transition. The target analyte and surrogate are quantitated using the SRM transitions utilizing an external calibration. The final report issued for each sample lists the concentration of TDG and the 3,3'-thiodipropanol surrogate recovery.

5. Significance and Use

5.1 Thiodiglycol is a Schedule 2 compound under the Chemical Weapons Convention (CWC). Schedule 2 chemicals include those that are precursors to chemical weapons, chemical weapons agents or have a number of other commercial uses. They are used as ingredients to produce insecticides, herbicides, lubricants, and some pharmaceutical products. Schedule 2 chemicals can be found in applications unrelated to chemical weapons. Thiodiglycol is both a mustard gas precursor and degradant as well as an ingredient in water-based inks, ballpoint pen inks, dyes and some pesticides.[4]

[4] Additional information about CWC and thiodiglycol is available on the Internet at http://www.opcw.org (2009)

5.2 This method has been investigated for use with reagent and surface water.

6. Interferences

6.1 Method interferences may be caused by contaminants in solvents, reagents, glassware and other apparatus producing discrete artifacts or elevated baselines. All of these materials are demonstrated to be free from interferences by analyzing laboratory reagent blanks under the same conditions as samples.

6.2 All glassware is washed in hot water with a detergent, rinsed in hot water followed by distilled water. The glassware is then dried and heated in an oven at 250°C for 15 to 30 minutes. All glassware is subsequently cleaned with acetone, then methanol.

6.3 All reagents and solvents should be pesticide residue purity or higher to minimize interference problems.

6.4 Matrix interferences may be caused by contaminants that are co-extracted from the sample. The extent of matrix interferences can vary considerably from sample source depending on variations of the sample matrix.

7. Apparatus

7.1 *LC/MS/MS System*

7.1.1 *Liquid Chromatography (LC) System*—A complete LC system is needed in order to analyze samples.[5] A system that is capable of performing at the flows, pressures, controlled temperatures, sample volumes and requirements of the standard may be used.

7.1.2 *Analytical Column-SIELC*—Primesep SB 5 µm, 100 Å particle, 150 mm × 2.1 mm or equivalent.

7.1.3 *Tandem Mass Spectrometer (MS/MS) System*—A MS/MS system capable of MRM analysis.[6] A system that is capable of performing at the requirements in this standard may be used.

7.2 *Filtration Device*

7.2.1 *Hypodermic syringe*—A lock tip glass syringe capable of holding a Millex HV Syringe Driven Filter Unit PVDF 0.45 µm (Millipore Corporation, Catalog # SLHV033NS) or similar may be used.

7.2.1.1 A 25-mL lock tip glass syringe size is recommended since a 25-mL sample size is used in this test method.

7.2.2 *Filter*—Millex HV Syringe Driven Filter Unit PVDF 0.45 µm (Millipore Corporation, Catalog # SLHV033NS) or similar may be used.

8. Reagents and Materials

8.1 *Purity of Reagents*—High-performance liquid chromatography (HPLC) pesticide residue analysis and spectrophotometry grade chemicals shall be used in all tests. Unless indicated otherwise, it is intended that all reagents shall conform to the Committee on Analytical Reagents of the American Chemical Society.[7] Other reagent grades may be used provided they are first determined they are of sufficiently high purity to permit their use without affecting the accuracy of the measurements.

8.2 *Purity of Water*—Unless otherwise indicated, references to water shall be understood to mean reagent water conforming to Type 1 of Specification D1193. It must be demonstrated that this water does not contain contaminants at concentrations sufficient to interfere with the analysis.

8.3 *Gases*—Ultrapure nitrogen and argon.

8.4 Acetonitrile (CAS # 75-05-8).

8.5 Methanol (CAS # 67-56-1).

8.6 Acetone (CAS # 67-64-1).

8.7 Ammonium formate (CAS # 540-69-2).

8.8 Formic acid (64-18-6).

8.9 Thiodiglycol (CAS # 111-48-8).

8.10 3,3'-Thiodipropanol (CAS # 10595-09-2).

9. Hazards

9.1 Normal laboratory safety applies to this method. Analysts should wear safety glasses, gloves, and lab coats when working in the lab. Analysts should review the Material Safety Data Sheets (MSDS) for all reagents used in this method.

10. Sampling

10.1 *Sampling*—Grab samples must be collected in ≥25-mL pre-cleaned amber glass bottles with Teflon-lined caps demonstrated to be free of interferences. This test method requires a 25-mL sample size per analysis. Conventional sampling practices should be followed. Refer to Guide D3856 and Practices D3694.

10.2 *Preservation*—Store samples between 0°C and 6°C from the time of collection until analysis. Analyze the sample within 1 day of collection.

11. Preparation of LC/MS/MS

11.1 *LC Chromatograph Operating Conditions*[5]:

11.1.1 Injection volumes of all calibration standards and samples are 50 µL. The first sample analyzed after the calibration curve is a blank to ensure there is no carry-over. The gradient conditions for the liquid chromatograph are shown in Table 3.

11.1.2 *Temperatures*—Column, 30°C; Sample compartment, 15°C.

11.1.3 *Seal Wash*—Solvent: 50 % Acetonitrile/50 % Water; Time: 5 minutes.

11.1.4 *Needle Wash*—Solvent: 50 % Acetonitrile/50 % Water; Normal Wash, approximately 13 second wash time.

11.1.5 *Autosampler Purge*—Three loop volumes.

11.1.6 Specific instrument manufacturer wash/purge specifications should be followed in order to eliminate sample carry-over in the analysis of TDG.

11.2 *Mass Spectrometer Parameters*[6]:

11.2.1 In order to acquire the maximum number of data points per SRM channel while maintaining adequate sensitivity, the tune parameters may be optimized according to your instrument. Each peak requires at least 10 scans per peak for adequate quantitation. This standard contains only one target compound and one surrogate which are in different SRM experiment windows in order to optimize the number of scans and sensitivity. Variable parameters regarding retention times, SRM Transitions and cone and collision energies are shown in Table 4.

TABLE 3 Gradient Conditions for Liquid Chromatography

Time (min)	Flow (µL/min)	Percent CH_3CN	Percent Water	Percent 500 mmolar Ammonium Formate/2% Formic Acid
0	300	0	95	5
2.5	300	0	95	5
6	300	90	5	5
10	300	90	5	5
12	300	0	95	5
16	300	0	95	5

[5] A Waters Alliance High Performance Liquid Chromatography (HPLC) System was used to develop this test method. The multi-laboratory study included Agilent and Waters LC systems.

[6] A Waters Quattro micro API mass spectrometer was used to develop this test method. The multi-laboratory study included Agilent, Applied Biosystems, Varian and Waters mass spectrometers.

[7] *Reagent Chemicals, American Chemical Society Specifications*, American Chemical Society, Washington, DC. For Suggestions on the testing of reagents not listed by the American Chemical Society, see *Annual Standards for Laboratory Chemicals,* BDH Ltd., Poole, Dorset, U.K., and the *United States Pharmacopeia and National Formulary,* U.S. Pharmacopeial Convention, Inc. (USPC), Rockville, MD.

TABLE 4 Retention Times, SRM Ions, and Analyte-Specific Mass Spectrometer Parameters

Analyte	SRM Mass Transition (Parent > Product)	Retention Time (min)	Cone Voltage (Volts)	Collision Energy (eV)
Thiodiglycol	123.1 > 104.9	2.75	18	5
3,3'-Thiodipropanol	151.2 > 133.1	5.75	19	8

The instrument is set in the Electrospray (+) positive setting.
Capillary Voltage: 3.5 kV
Cone: Variable depending on analyte (Table 4)
Extractor: 2 Volts
RF Lens: 0.2 Volts
Source Temperature: 120°C
Desolvation Temperature: 300°C
Desolvation Gas Flow: 500 L/hr
Cone Gas Flow: 25 L/hr
Low Mass Resolution 1: 14.5
High Mass Resolution 1: 14.5
Ion Energy 1: 0.5
Entrance Energy: –1
Collision Energy: Variable depending on analyte (Table 4)
Exit Energy: 2
Low Mass Resolution 2: 15
High Mass resolution 2: 15
Ion Energy 2: 0.5
Multiplier: 650
Gas Cell Pirani Gauge: 3.3×10^{-3} Torr
Inter-Channel Delay: 0.02 seconds
Inter-Scan Delay: 0.1 seconds
Repeats: 1
Span: 0 Daltons
Dwell: 0.1 Seconds

12. Calibration and Standardization

12.1 The mass spectrometer must be calibrated per manufacturer specifications before analysis. In order that analytical values obtained using this test method are valid and accurate within the confidence limits of the test method, the following procedures must be followed when performing the test method.

12.2 *Calibration and Standardization*—To calibrate the instrument, analyze seven calibration standards containing the seven concentration levels of TDG and 3,3'-thiodipropanol prior to analysis as shown in Table 2. A calibration stock standard solution is prepared from standard materials or purchased as certified solutions. Stock standard solution A (Level 7) containing TDG and 3,3'-thiodipropanol is prepared at Level 7 concentration and aliquots of that solution are diluted to prepare Levels 1 through 6. The following steps will produce standards with the concentration values shown in Table 2. The analyst is responsible for recording initial component weights carefully when working with pure materials and correctly carrying the weights through the dilution calculations.

12.2.1 Prepare stock standard solution A (Level 7) by adding to a 100-mL volumetric flask individual methanol solutions of the following: 250 µL of TDG and 3,3'-thiodipropanol each at 4 g/L, dilute to 100 mL with water. The preparation of the Level 7 standard can be accomplished using different volumes and concentrations of stock solutions as is accustomed in the individual laboratory. Depending on stock concentrations prepared, the solubility at that concentration will have to be ensured.

12.2.2 Aliquots of Solution A are then diluted with water to prepare the desired calibration levels in 2-mL amber glass LC vials. The calibration vials must be used within 24 hours to ensure optimum results. Stock calibration standards are routinely replaced every six months if not previously discarded for quality control failure. Calibration standards are not filtered.

12.2.3 Inject each standard and obtain a chromatogram for each one. An external calibration is used monitoring the SRM transition of each analyte. Calibration software is utilized to conduct the quantitation of the target analyte and surrogate. The SRM transition of each analyte is used for quantitation and confirmation. This gives confirmation by isolating the parent ion, fragmenting it to the product ion, and also relating it to the retention time in the calibration standard.

12.2.4 The calibration software manual should be consulted to use the software correctly. The quantitation method is set as an external calibration using the peak areas in ppb or ppm units as long as the analyst is consistent. Concentrations may be calculated using the data system software to generate linear regression or quadratic calibration curves. Forcing the calibration through the origin is not recommended.

12.2.5 Linear calibration may be used if the coefficient of determination, r^2, is >0.98 for the analyte. The point of origin is excluded and a fit weighting of 1/X is used in order to give more emphasis to the lower concentrations. If one of the calibration standards other than the high or low point causes the r^2 of the curve to be <0.98, this point must be re-injected or a new calibration curve must be regenerated. If the low or high (or both) point is excluded, minimally a five point curve is acceptable but the reporting range must be modified to reflect this change.

12.2.6 Quadratic calibration may be used if the coefficient of determination, r^2, is >0.99 for the analyte. The point of origin is excluded and a fit weighting of 1/X is used in order to give more emphasis to the lower concentrations. If one of the calibration standards, other than the high or low, causes the curve to be <0.99 this point must be re-injected or a new calibration curve must be regenerated. If the low or high point is excluded, a six point curve is acceptable using a quadratic fit. An initial seven-point curve over the calibration range is suggested in the event that the low or high point must be excluded to obtain a coefficient of determination >0.99. In this event, the reporting range must be modified to reflect this change. Each calibration point used to generate the curve must have a calculated percent deviation less than 25 % from the generated curve.

12.2.7 The retention time window of the SRM transitions must be within 5 % of the retention time of the analyte in a midpoint calibration standard. If this is not the case, re-analyze the calibration curve to determine if there was a shift in retention time during the analysis and the sample needs to be re-injected. If the retention time is still incorrect in the sample, refer to the analyte as an unknown.