Analytical method for triallate and its metabolite TCPSA in water

Reports:	ECM: EPA MRID No.: 50432501. Wu, X. 2016. Validation of the Analytical Method for the Determination of Triallate and TCPSA in Aqueous Matrices by LC-MS/MS. Report prepared by Smithers Viscient, Wareham Massachusetts, and sponsored and submitted by Gowan Company, Yuma, Arizona; 115 pages. Smithers Viscient Study No. 12791.6265. Final report issued December 19, 2016. ILV: EPA MRID No. 50352202. MacGregor, J.A., E.S. Bodle, and R.L. VanHoven. 2017. INDEPENDENT LABORATORY VALIDATION OF A METHOD FOR THE DETERMINATION OF TRIALLATE AND TCPSA IN AQUEOUS MATRICES BY LC/MS/MS. Report prepared by Wildlife International (now doing business as EAG), Easton, Maryland, sponsored and submitted by Gowan Company, Yuma, Arizona; 113 pages. Project No. 334C-134. Final report issued July 21, 2017.
Document No.:	MRIDs 50432501 & 50352202
Guideline:	850.6100
Statements:	ECM: The study was conducted in accordance with USEPA FIFRA (40 CFR 160) and OECD Good Laboratory Practice (GLP) standards (p. 3 of MRID 50432501). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). Authenticity statement was included with the GLP statement (p. 4). ILV: The study was conducted in accordance with USEPA FIFRA GLP standards (p. 3 of MRID 50352202). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). An authenticity statement was not included.
Classification:	This analytical method is classified as **Unacceptable**. The LOD was not reported in the ILV. The specificity of the method for TCPSA was not supported by the ECM and ILV representative chromatograms. The TCPSA confirmation analysis was not independently validated. ECM linearity was not satisfactory for triallate.
PC Code:	078802
Final EPA Reviewer:	A'ja Duncan, Chemist Signature: Duncan, Aja Digitally signed by Duncan, Aja Date: 2018.09.10 15:36:54 -04'00' Date: 9/10/18
CDM/CSS-Dynamac JV Reviewers:	Lisa Muto, Environmental Scientist Signature: Lisa Muto Date: 6/21/18 Kathleen Ferguson, Ph.D., Environmental Scientist Signature: Kathleen P. Ferguson Date: 6/21/18

This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel. The CDM/CSS-Dynamac Joint Venture role does not include establishing Agency policies.

Executive Summary

The analytical method, Smithers Viscient Study No. 12791.6265, is designed for the quantitative determination of triallate and its metabolite TCPSA in water at the LOQ of 0.100 µg/L using LC/MS/MS. The LOQ is less than the lowest toxicological level of concern (14 µg/L; USEPA, 2014) in water for the two analytes. The ECM and ILV validated the method using ground and surface water matrices; however, the ECM matrices were not well-characterized. The ILV validated the ECM method for the quantitation and confirmation analyses of triallate and the quantitation analysis of TCPSA in two water matrices in the first trial with insignificant modifications to the analytical instruments. The ECM method for the confirmation analyses of TCPSA in two water matrices was validated in the second trial with modifications to sample processing and analytical parameters. These modifications did not warrant the submission of an updated ECM since a confirmatory method is not usually required when LC/MS and GC/MS is the primary method; however, based on ILV communications, the ECM should have been updated to indicate that the TCPSA confirmation analysis is used to confirm the identity of TCPSA, not quantitative results of the primary analysis. All ECM and ILV data regarding repeatability, accuracy, and precision were satisfactory for both analytes, based on the quantitation ion results; however, specificity of the method for TCPSA was not supported by the ECM and ILV representative chromatograms due to the fact that the LOQ peak was broad, small, and not well-distinguished from the baseline noise. ECM linearity was unsatisfactory for triallate. The LOD was not reported in the ILV.

Table 1. Analytical Method Summary

Analyte(s) by Pesticide[1]	MRID		EPA Review	Matrix	Method Date (dd/mm/yyyy)	Registrant	Analysis	Limit of Quantitation (LOQ)
	Environmental Chemistry Method	Independent Laboratory Validation						
Triallate	50432501	50352202		Water[1,2]	19/12/2016	Gowan Company	LC/MS/MS	0.100 µg/L
TCPSA								

1 In the ECM, the ground water was obtained from a laboratory well, reconstituted for hardness based on U.S. EPA 1975 hard water specifications, and filtered (Amberlite XAD-7 resin column) prior to use; surface water (pH 6.10 and 6.36 mg/L dissolved oxygen content), obtained from Taunton River, Taunton, Massachusetts. Water characterization was incomplete or absent.

2 In the ILV, the ground water (well; pH 8.03-8.15 and hardness 144-145 mg equiv. $CaCO_3$/L) obtained from EAG Laboratories aquatic testing facility and surface water (lake; pH 7.00 and hardness 64.0 mg equiv. $CaCO_3$/L) obtained from Tuckahoe Lake, Ridgely, Maryland, were used in the study.

I. Principle of the Method

Samples (5.00 mL) were transferred to 10-mL glass vials and fortified, as necessary, with mixed fortification solutions of triallate and TCPSA in acetonitrile (pp. 18, 21-25 of MRID 50432501). The sample volumes were adjusted to 10 mL with acetonitrile. The samples for triallate and TCPSA primary analysis on the T3 column were further diluted into the calibration standard range with acetonitrile:purified reagent water (50:50, v:v); samples for TCPSA confirmatory analysis on the HILIC column were further diluted into the calibration standard range with acetonitrile:purified reagent water (90:10, v:v). All samples were then centrifuged at 13,000 rpm for 5 minutes; the supernatant was transferred to HPLC vials and analyzed by LC/MS/MS.

Samples were analyzed for both analytes using an Agilent 1200 HPLC system coupled to an AB Sciex API 5000 mass spectrometer with an ESI Turbo V source (pp. 25-28 of MRID 50432501). The LC/MS conditions for triallate consisted of a XBridge C18 column (2.1 x 50 mm, 2.5-µm; column temperature 40°C), a mobile phase of (A) water with 0.1% formic acid and (B) acetonitrile with 0.1% formic acid [percent A:B (v:v) at 0.00-0.50 min. 75:25, 4.00-6.00 min. 0:100, 6.10-7.50 min. 75:25] and MS/MS detection in positive ion mode (ionization temperature 500°C). Injection volume was 100 µL. Two ion transitions were monitored (quantitation and confirmatory, respectively) as follows: *m/z* 304.1→86.1 and *m/z* 304.1→142.8 for triallate. Retention times were 3.86-3.88 minutes for triallate in both matrices. The LC/MS conditions for primary analysis of TCPSA consisted of a Atlantis® T3 column (4.6 x 100 mm, 3-µm; column temperature 40°C), a isocratic mobile phase at 50:50, v:v, of (A) water with 0.1% formic acid and (B) acetonitrile with 0.1% formic acid. The LC/MS conditions for confirmatory analysis of TCPSA consisted of Atlantis® HILIC silica column (3.0 x 100 mm, 3-µm; column temperature 40°C), a isocratic mobile phase at 10:90, v:v, of (A) water with 0.1% formic acid and (B) acetonitrile with 0.1% formic acid. MS/MS detection was conducted in negative ion mode (ionization temperature 500°C). Injection volume was 100 µL for primary and confirmatory analyses. One ion transition was monitored for TCPSA primary and confirmatory analysis: *m/z* 224.8→79.8. Retention times were 1.63-1.66 and 2.02-2.03 minutes for TCPSA for primary and confirmatory analysis, respectively.

In the ILV, the ECM was performed as written, except for modifications for the TCPSA confirmatory analysis processing and analytical parameters and a few minor modifications of analytical instruments (pp. 14-17; Tables 1-3, pp. 23-25 of MRID 50352202). For the TCPSA confirmatory analysis, the second dilution was performed with 100% acetonitrile and the HPLC isocratic mobile phase was adjusted to 5:95, v:v, of (A) water with 0.1% formic acid and (B) acetonitrile with 0.1% formic acid; also, matrix-matched calibration standards were used for the surface water analysis. An Agilent 1200 HPLC System coupled to an AB Sciex API 5000 Turbo-V Ion Spray mass spectrometer was used. The LC/MS conditions were the same, except for the modification of the HPLC isocratic mobile phase of TCPSA confirmatory analysis. Two ion transitions were monitored for triallate (quantitation and confirmatory, respectively) as follows: *m/z* 304.1→85.8 and *m/z* 304.1→142.8. One ion transition was monitored for TCPSA primary and confirmatory analysis: *m/z* 224.8→79.8. Retention times were *ca*. 4.9 and 5.8 minutes for triallate analysis in ground and surface water, respectively, and were *ca*. 1.9-2.0 and 2.0-3.1 minutes for TCPSA analysis in ground and surface water, respectively. No significant modifications were made by the ILV.

The Limit of Quantification (LOQ) was 0.100 µg/L for triallate and TCPSA in water in the ECM and ILV (pp. 29-30, 35-38 of MRID 50432501; p. 11 of MRID 50352202). The Limit of Detection

(LOD) was 0.00104-0.0215 µg/L for triallate and 0.0151-0.103 µg/L for TCPSA in surface and ground water matrices in the ECM; the LOD was not reported in the ILV.

II. Recovery Findings

ECM (MRID 50432501): Mean recoveries and relative standard deviations (RSDs) were within guideline requirements (mean 70-120%; RSD ≤20%) for analysis of triallate and its metabolite TCPSA in two water matrices at fortification levels of 0.100 µg/L (LOQ) and 1.00 µg/L (10×LOQ; Tables 1-8, pp. 41-48). Performance data (recovery results) from primary and confirmatory analyses were comparable. Ground water was obtained from a laboratory well, reconstituted for hardness based on U.S. EPA 1975 hard water specifications, and filtered (Amberlite XAD-7 resin column) prior to use; surface water (pH 6.10 and 6.36 mg/L dissolved oxygen content), obtained from Taunton River, Taunton, Massachusetts (p. 16). Water characterization was incomplete or absent.

ILV (MRID 50352202): Mean recoveries and RSDs were within guideline requirements for analysis of triallate and its metabolite TCPSA in two water matrices at fortification levels of 0.100 µg/L (LOQ) and 1.00 µg/L (10×LOQ), except for the confirmation ion analysis of TCPSA in ground water at the LOQ (mean 155% and RSD 66%; Tables 4-11, pp. 26-33). This deviation did not affect the validity of the study since a confirmatory method is not usually required when LC/MS and GC/MS is the primary method; statistics for this sample set were reviewer-calculated based on all five recovery values in the study report. Performance data (recovery results) from primary and confirmatory analyses were comparable, except for TCPSA in ground water at the LOQ. Ground water (well; pH 8.03-8.15 and hardness 144-145 mg equiv. $CaCO_3$/L) obtained from EAG Laboratories aquatic testing facility and surface water (lake; pH 7.00 and hardness 64.0 mg equiv. $CaCO_3$/L) obtained from Tuckahoe Lake, Ridgely, Maryland, were used in the study (p. 12; Appendices IV-V, pp. 100-101). The ECM method for the quantitation and confirmation analyses of triallate and the quantitation analysis of TCPSA in two water matrices was validated in the first trial with insignificant modifications to the analytical instruments (pp. 11, 16-17; Appendix VI, pp. 109-112). The ECM method for the confirmation analyses of TCPSA in two water matrices was validated in the second trial with modifications to sample processing and analytical parameters. These modifications did not warrant the submission of an updated ECM since a confirmatory method is not usually required when LC/MS and GC/MS is the primary method; however, based on ILV communications, the ECM should have been updated to indicate that the TCPSA confirmation analysis is used to confirm the identity of TCPSA, not quantitative results of the primary analysis.

Table 2. Initial Validation Method Recoveries for Triallate and TCPSA in Water[1,2]

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)[2]
	Ground Water					
	Quantitation ion					
Triallate	0.100 (LOQ)	5	97.2-109	105	5.42	5.17
	1.00	5	95.5-116	108	9.34	8.69
TCPSA	0.100 (LOQ)	5	84.0-112	95.5	10.7	11.2
	1.00	5	93.9-116	105	9.59	9.15
	Confirmation ion or analysis					
Triallate	0.100 (LOQ)	5	96.3-108	103	4.76	4.61
	1.00	5	94.3-116	106	8.34	7.89
TCPSA	0.100 (LOQ)	5	76.7-99.3	88.9	9.74	11.0
	1.00	5	84.6-107	93.4	9.15	9.80
	Surface Water					
	Quantitation ion					
Triallate	0.100 (LOQ)	5	110-118	114	3.63	3.19
	1.00	5	106-115	109	3.63	3.34
TCPSA	0.100 (LOQ)	5	92.6-107	99.1	5.35	5.39
	1.00	5	106-117	111	4.22	3.81
	Confirmation ion or analysis					
Triallate	0.100 (LOQ)	5	99.2-111	106	4.95	4.66
	1.00	5	100-107	104	2.51	2.42
TCPSA	0.100 (LOQ)	5	90.0-104	97.6	5.12	5.24
	1.00	5	110-118	113	2.95	2.61

Data (uncorrected recovery results, p. 30) were obtained from Tables 1-8, pp. 41-48 of MRID 50432501.

1 The ground water was obtained from a laboratory well, reconstituted for hardness based on U.S. EPA 1975 hard water specifications, and filtered (Amberlite XAD-7 resin column) prior to use; surface water (pH 6.10 and 6.36 mg/L dissolved oxygen content), obtained from Taunton River, Taunton, Massachusetts (p. 16). Water characterization was incomplete or absent.

2 Two ion transitions were monitored (quantitation and confirmatory, respectively) as follows: *m/z* 304.1→86.1 and *m/z* 304.1→142.8 for triallate. One ion transition was monitored for TCPSA primary and confirmatory analysis: *m/z* 224.8→79.8; different analytical columns were used for primary and confirmatory analyses.

Table 3. Independent Validation Method Recoveries for Triallate and TCPSA in Water[1,2]

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)[2]
	Ground Water					
	Quantitation ion					
Triallate	0.100 (LOQ)	5	97.6-112	107	5.52	5.16
	1.00	5	107-112	109	2.00	1.83
TCPSA	0.100 (LOQ)	5	82.2-103	87.8	8.80	10.0
	1.00	5	101-122	109	7.89	7.24
	Confirmation ion or analysis					
Triallate	0.100 (LOQ)	5	99.8-111	107	4.36	4.07
	1.00	5	105-115	111	4.04	3.64
TCPSA	0.100 (LOQ)	5[3]	104-339	**155**	103	**66**
	1.00	5	73.7-85.7	82.1	4.98	6.07
	Surface Water					
	Quantitation ion					
Triallate	0.100 (LOQ)	5	104-108	106	1.64	1.55
	1.00	5	104-110	108	2.88	2.68
TCPSA	0.100 (LOQ)	5	80.1-98.1	91.3	6.89	7.55
	1.00	5	83.5-96.0	91.7	6.26	6.82
	Confirmation ion or analysis					
Triallate	0.100 (LOQ)	5	100-109	104	3.29	3.16
	1.00	5	97.3-112	107	6.33	5.92
TCPSA	0.100 (LOQ)	5	83.3-117	97.5	12.8	13.1
	1.00	5	109-126	114	6.89	6.04

Data (uncorrected recovery results, pp. 17-19) were obtained from Tables 4-11, pp. 26-33 of MRID 50352202.

1 The ground water (well; pH 8.03-8.15 and hardness 144-145 mg equiv. $CaCO_3$/L) obtained from EAG Laboratories aquatic testing facility and surface water (lake; pH 7.00 and hardness 64.0 mg equiv. $CaCO_3$/L) obtained from Tuckahoe Lake, Ridgely, Maryland, were used in the study (p. 12; Appendices IV-V, pp. 100-101).

2 Two ion transitions were monitored (quantitation and confirmatory, respectively) as follows: *m/z* 304.1→85.8 and *m/z* 304.1→142.8 for triallate. One ion transition was monitored for TCPSA primary and confirmatory analysis: *m/z* 224.8→79.8; different analytical columns were used for primary and confirmatory analyses.

3 Mean, standard deviation, and relative standard deviation were reviewer-calculated based on all five recovery values in the study report; the study author omitted one recovery value (339%) from the statistics since it was deemed to be an outlier.

III. Method Characteristics

The LOQ was 0.100 µg/L for triallate and TCPSA in water in the ECM and ILV (pp. 29-30, 35-38 of MRID 50432501; p. 11 of MRID 50352202). In the ECM, the LOQ was defined as the lowest fortification level, and blank values should not be >30% of the LOQ; no calculations or comparisons to background levels were reported to justify the LOQ for the method in the ECM. In the ILV, the LOQ was reported from the ECM without justification. The LOD was 0.00104-0.0215 µg/L for triallate and 0.0151-0.103 µg/L for TCPSA in surface and ground water matrices in the ECM; the LOD was not reported in the ILV. The LOD was calculated in the ECM using the following equation:

$LOD = (3x(SN_{ctl})/(Resp_{LS}) \times Conc_{LS}$

Where, LOD is the limit of detection of the analysis, SN_{ctl} is the mean signal to noise in height of the control samples (or Blanks), $Resp_{LS}$ is the mean response in height of the two low calibration standards, and $Conc_{LS}$ is the concentration of the low calibration standard.

Table 4. Method Characteristics

Analyte[1]			**Triallate**	**TCPSA**
Limit of Quantitation (LOQ)	ECM		0.100 µg/L	
	ILV			
Limit of Detection (LOD)	ECM	Ground	0.00370 µg/L (Q) 0.00104 µg/L (C)	0.0151 µg/L (Q) 0.0624 µg/L (C)
		Surface	0.0215 µg/L (Q) 0.00167 µg/L (C)	0.0351 µg/L (Q) 0.103 µg/L (C)
	ILV		**Not reported**	
Linearity (calibration curve r^2 and concentration range)	ECM	Ground	r^2 = **0.9946** (Q) r^2 = **0.9940** (C)	r^2 = 0.9954 (Q) r^2 = 0.9962 (C)
		Surface	r^2 = **0.9948** (Q) r^2 = 0.9950 (C)	r^2 = 0.9990 (Q) r^2 = **0.9934** (C)
	ILV[1]	Ground	r^2 = 0.9990 (Q)	r^2 = 0.9987 (Q)
		Surface	**Not reported**	
	Range		0.005-0.500 µg/L	
Repeatable	ECM[2]		Yes at LOQ and 10×LOQ (poorly characterized ground and surface water matrices).	
	ILV[3,4]		Yes at LOQ and 10×LOQ (characterized ground and surface water matrices).	Yes at LOQ and 10×LOQ, except for LOQ C (mean **155**%, RSD **66**%; characterized ground water matrices).[5] Yes at LOQ and 10×LOQ (characterized surface water matrices).
Reproducible			Yes at LOQ and 10×LOQ	
Specific	ECM		Yes, matrix interferences were < 14% of the LOQ (based on peak area).	**No**, LOQ peak was small, broad, and barely resolved from the baseline.[6] Matrix interferences were < 6% of the LOQ (based on peak area).
	ILV		Only quantitation analysis chromatograms were provided.	

Analyte[1]		**Triallate**	**TCPSA**
		Yes, matrix interferences were < 11% of the LOQ (based on peak area).	Yes in surface water: matrix interferences were < 10% of the LOQ (based on peak area). LOQ peak was broad. **No** in ground water: matrix interferences were *ca*. 66% of the LOQ (based on peak area).[7] LOQ peak was broad and small compared to baseline noise.

Data were obtained from pp. 29-31, 35-38 (LOQ/LOD); p. 32 (correlation coefficients); Tables 1-8, pp. 41-48 (recovery data); Figures 1-47, pp. 57-103 (chromatograms) of MRID 50432501; p. 11 (LOQ); Tables 4-11, pp. 26-33 (recovery data); Figures 1-2, pp. 34-35 (calibration curves); Figures 3-8, pp. 36-41 (chromatograms) of MRID 50352202; and DER Attachment 2. Q = Quantitation ion transition; C = Confirmation ion transition or analysis.

1 Correlation coefficients (r^2) values were reviewer-calculated from r values provided in the study report (Figures 1-2, pp. 34-35 of MRID 50352202; DER Attachment 2). Only one calibration curve per analyte was presented: the quantitation ion from the ground water analysis. Solvent standards were used for all analyses, except the TCPSA confirmation ion analysis in surface water (pp. 13-14). The reviewer limited the calculated r^2 to 4 significant figures although 7 significant figures were reported in the ECM for r.

2 In the ECM, the ground water was obtained from a laboratory well, reconstituted for hardness based on U.S. EPA 1975 hard water specifications, and filtered (Amberlite XAD-7 resin column) prior to use; surface water (pH 6.10 and 6.36 mg/L dissolved oxygen content), obtained from Taunton River, Taunton, Massachusetts (p. 16 of MRID 50432501). Water characterization was incomplete or absent.

3 In the ILV, the ground water (well; pH 8.03-8.15 and hardness 144-145 mg equiv. $CaCO_3$/L) obtained from EAG Laboratories aquatic testing facility and surface water (lake; pH 7.00 and hardness 64.0 mg equiv. $CaCO_3$/L) obtained from Tuckahoe Lake, Ridgely, Maryland, were used in the study (p. 12; Appendices IV-V, pp. 100-101 of MRID 50352202).

4 The ILV validated the ECM method for the quantitation and confirmation analyses of triallate and the quantitation analysis of TCPSA in two water matrices in the first trial with insignificant modifications to the analytical instruments (pp. 11, 16-17; Appendix VI, pp. 109-112 of MRID 50352202). The ECM method for the confirmation analyses of TCPSA in two water matrices was validated in the second trial with modifications to sample processing and analytical parameters. These modifications did not warrant the submission of an updated ECM since a confirmatory method is not usually required when LC/MS and GC/MS is the primary method

5 A confirmatory method is not usually required when LC/MS and GC/MS is the primary method; therefore, the deviation of repeatability and precision in the confirmation analysis does not affect the validity of the method.

6 Based on Figure 16, p. 72; Figure 22, p. 78; Figure 40, p. 96; and Figure 46, p. 102 of MRID 50432501.

7 Based on Figure 7, p. 40 of MRID 50352202. The reviewer noted that the study author quantified the residues in the controls as <LOQ in Table 6, p. 28 (See Reviewer Comment #1).

Linearity is satisfactory when $r^2 \geq 0.995$.

IV. Method Deficiencies and Reviewer's Comments

1. The specificity of the method for TCPSA was not supported by the ECM and ILV representative chromatograms. In the ILV, chromatograms from the surface water analysis were acceptable, even though the LOQ peak was broad; however, chromatograms from the ground water analysis showed that matrix interferences were *ca*. 66% (based on peak area) and the LOQ peak was broad and small compared to baseline noise (Figure 7, p. 40 of MRID 50352202). In the ILV, only chromatograms from the quantitation analysis were provided for review. In the ECM, the LOQ peak of TCPSA was small, broad, and barely resolved from the baseline in both water matrices (Figure 16, p. 72; Figure 22, p. 78; Figure 40, p. 96; and Figure 46, p. 102 of MRID 50432501).

2. In the ILV, the LOD was not reported. Also, the calibration curves and correlation coefficients were not provided for the surface water sets. Solvent standards were used for all analyses, except the TCPSA confirmation ion analysis in surface water for which matrix-matched standards were used (pp. 13-14). All linearity data should be provided to assess the accuracy of the recovery data.

3. Performance data was not satisfactory for the ILV confirmation ion analysis of TCPSA in ground water (mean 155%, RSD 66%; Tables 4-11, pp. 26-33 of MRID 50352202). OCSPP guideline requirements state that the mean recovery is 70-120% and the RSD is ≤20%. This guideline deviation is not substantial since a confirmatory method is not typically required where GC/MS and/or LC/MS methods are used as the primary method(s) to generate study data.

   The reviewer noted that matrix-matched calibration standards were used for the ILV confirmation ion analysis of TCPSA in surface water, which had acceptable recovery results (p. 14; Tables 4-11, pp. 26-33 of MRID 50352202).

4. In the ECM, the linearity was not satisfactory for triallate, r^2 = 0.9946-0.9948 (Q) in both matrices and 0.9940 (C) in ground water (p. 32 of MRID 50432501). Linearity is satisfactory when $r^2 \geq 0.995$. However, in the case of the ILV confirmation ion analysis, the reviewer noted that a confirmatory method is not typically required where GC/MS and/or LC/MS methods are used as the primary method(s) to generate study data.

5. With respect to TCPSA matrix interferences in ground water, the reviewer noted that the study author quantified the residues in the controls as <LOQ for the quantitation analysis and as *ca*. 35.6% (mean) for the confirmation analysis (Tables 6-7, pp. 28-29 of MRID 50352202). The reviewer quantified the residues in the controls for the quantitation analysis as *ca*. 66%, based on the control chromatogram peak area of 2641.4 counts and the LOQ chromatogram peak area of 4032.9 counts (Figure 7, p. 40 of MRID 50352202).

6. The ILV communication log indicates that the ECM should be updated to indicate that the TCPSA confirmation analysis is used to confirm the identity of TCPSA, not quantitative results of the primary analysis. TCPSA confirmation analysis in the method with the HILIC column was extremely difficult for the ILV to validate, based on the ILV communication log information (Appendix VI, pp. 109-112 of MRID 50352202). Jon MacGregor of the ILV discussed this issue with the Gowan Study Monitors (Emily Foley, Premjit Halamkar, and Adam Pilkington), as intermediaries for the originating laboratory, Smithers Viscient. However, after continued failure, Jon MacGregor had a phone/teleconference call with the ECM study author (Xiania Wu), as well as others, to discuss the TCPSA confirmation analysis in the method with the HILIC column. It was decided that the HILIC column was very sensitive, but it successfully confirmed the identity of TCPSA.

   Although there was direct communication between the ECM and ILV staff, this collusion was not required to validate the primary analysis of the method. Since it was required for the TCPSA confirmation analysis with the HILIC column, this lack of independence indicates that the ECM should be updated to marginalize the TCPSA confirmation analysis.

7. In the ECM, the water matrices were not well-characterized (p. 16 of MRID 50432501).

8. The reported limit of quantitation (LOQ) was determined as the lowest level of method validation (LLMV). This means that the concentrations can reliably quantified at the LOQ (i.e., LLMV), but whether lower concentrations may also be reliably quantified is uncertain. (pp. 29-30, 35-38 of MRID 50432501; p. 11 of MRID 50352202). In the ECM, the LOQ was defined as the lowest fortification level, and blank values should not be >30% of the LOQ; no calculations or comparisons to background levels were reported to justify the LOQ for the method in the ECM. In the ILV, the LOQ was reported from the ECM without justification. The LOD was calculated in the ECM using the following equation: LOD = $(3x(SN_{ctl})/(Resp_{LS})$ x $Conc_{LS}$, where, LOD is the limit of detection of the analysis, SN_{ctl} is the mean signal to noise in height of the control samples (or Blanks), $Resp_{LS}$ is the mean response in height of the two low calibration standards, and $Conc_{LS}$ is the concentration of the low calibration standard.

   The reviewer noted that the LOD for the confirmation analysis of TCPSA in surface water was >LOQ, 0.103 µg/L (p. 31 of MRID 50432501). Further work could have been done to explore the actual LOQ.

9. It was reported for the ILV that one sample set of 13 samples required *ca*. 3 working days) including LC/MS/MS analysis time (Appendix VI, p. 109 of MRID 50352202).

V. References

U.S. Environmental Protection Agency. 2012. Ecological Effects Test Guidelines, OCSPP 850.6100, Environmental Chemistry Methods and Associated Independent Laboratory Validation. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-001.

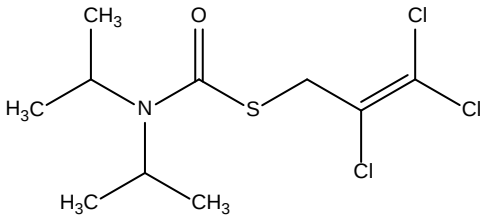
USEPA.2014. Registration Review Problem Formulation for Triallate. DP barcode 437990. U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention, Environmental Fate and Effects Division. Memorandum to the Pesticide Re-Evaluation Division. Aug. 21, 2014.

40 CFR Part 136. Appendix B. Definition and Procedure for the Determination of the Method Detection Limit-Revision 1.11, pp. 317-319.

DER Attachment 1: Chemical Names and Structures

Triallate

IUPAC Name: S-2,3,3-Trichloroallyl diisopropyl(thiocarbamate)
CAS Name: S-(2,3,3-trichloro-2-propen-1-yl) N,N-bis(1-methylethyl)carbamothioate
CAS Number: 2303-17-5
SMILES String: CC(C)N(C(C)C)C(=O)SCC(Cl)=C(Cl)Cl



TCPSA

IUPAC Name: Sodium 2,3,3-trichloro-2-propene-1-sulfonate
CAS Name: Not reported
CAS Number: Not reported
SMILES String: Not found