

Test Material: Tolclofos methyl

MRID: 48341917

Title: Validation of a Multi-Residue Method for the Determination of Tolclofos-methyl in Drinking Water.

MRID: 48341918

Title: Validation of a Multi-Residue Method for the Determination of Tolclofos-methyl in Surface Water.

MRID: 48809101

Title: Independent Laboratory Validation of Analytical Method VP-38290 Tolclofos –methyl: Determination of Tolclofos-methyl in Drinking Water.

EPA PC Code: 128905

OCSPP Guideline: 850.6100

For CDM Smith

Primary Reviewer: Lisa Muto

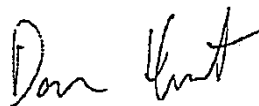
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Date: 5/6/14

Secondary Reviewer: Dan Hunt

Signature:



Date: 5/6/14

QC/QA Manager: Joan Gaidos

Signature:



Date: 5/6/14

Analytical method for tolclofos-methyl in water

- Reports:** MRID 48341917. Wolf, S. 2001. Validation of a Multi-Residue Method for the Determination of Tolclofos-methyl in Drinking Water. Report prepared by Environmental Chemistry & Pharamalytics Division, Itingen, Switzerland; sponsored by Sumitomo Chemical Company, Hyogo, Japan; and submitted by Valent U.S.A. Corporation, Walnut Creek, California. RCC Study No.: 833872. Sumitomo Chemical Company No.: QA-0075. Final report issued November 12, 2001.
- MRID 48341918. Wolf, S. 2001. Validation of a Multi-Residue Method for the Determination of Tolclofos-methyl in Surface Water. Report prepared by Environmental Chemistry & Pharamalytics Division, Itingen, Switzerland; sponsored by Sumitomo Chemical Company, Hyogo, Japan; and submitted by Valent U.S.A. Corporation, Walnut Creek, California. RCC Study No.: 835503. Sumitomo Chemical Company No.: QA-0076. Final report issued November 14, 2001.
- MRID 48809101. Golich-Moore, R. 2012. Independent Laboratory Validation of the Analytical Method VP-38290 Tolclofos –methyl: Determination of Tolclofos-methyl in Drinking Water. Report prepared by North Coast Laboratories, Ltd. (NCL), Arcata, California; sponsored and submitted by Valent U.S.A. Corporation, Walnut Creek, California. Laboratory Project ID: 120.024. Final report issued November 7, 2012.
- Document No.:** MRIDs 48341917, 48341918 & 48809101
- Guideline:** 850.6100
- Statements:** MRID 48341917.: The study was conducted in compliance with Swiss and OECD GLP (pp. 2-3). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 1i-5). The certification of the authenticity of the report is included with the Quality Assurance statement.
- MRID 48341918.: The study was conducted in compliance with Swiss and OECD GLP (pp. 2-3). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 1i-5). The certification of the authenticity of the report is included with the Quality Assurance statement.
- MRID 48809101. The study was conducted in accordance with the USEPA FIFRA GLP (40 CFR Part 160; p. 2). Signed and dated No Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 1i-3). A Certification of Authenticity was not provided.
- Classification:** This analytical method is classified as Acceptable. The LOQ is less than the lowest toxicological level of concern in water for Tolclofos-methyl noting that:
- Only three replicate samples were fortified at the LOQ and one sample at 10x LOQ in the ECM for the analytical method that was validated in the ILV

- The LOQ and LOD were not determined using scientifically acceptable procedures and
- The ILV required more than the maximum of three sample sets to validate the ECM.

PC Code: 128905

Reviewer:

Mohammed A. Ruhman
Senior Scientist, ERB5

Signature: 

Date: 08-01-2022

All page citations are specified with their MRID numbers.

Executive Summary

This analytical method, Valent Analytical Method VP-38290, is designed for the quantitative determination of tolclofos-methyl in water using GC/FPD (P-mode) and GC/MS (for confirmation). The method is quantitative for tolclofos-methyl at the stated LOQ of 0.1 µg/L using GC/FPD (not verified by the ILV); however, a minimum of five replicates were not used for confirmatory analysis using GC/MS. The lowest toxicological level of concern in water was not reported. The ILV was conducted using the confirmatory method of GC/MS only. An independent laboratory validation was not submitted using GC/FPD analysis. The independent laboratory was unsuccessful in validating the method using dechlorinated tap water and stated that the trace amount of residual chlorine in the water affected the recovery of tolclofos-methyl. The ILV was successful using well water on the fifth trial.

Table 1. Analytical Method Summary

Analyte(s) by Pesticide	MRID		EPA Review	Matrix	Method Date	Registrant	Analysis	Limit of Quantitation (LOQ)
	Environmental Chemistry Method	Independent Laboratory Validation						
Tolclofos- methyl	48341917 & 48341918	48809101		Water	11/12/2001 & 11/14/2001	Valent U.S.A Corporation	GC/FPD & GC/MS	0.1 µg/L

I. Principle of the Method

Water samples (1000 mL) were extracted via solid phase extraction (SPE; p. 17 of MRID 48341917; p. 17 of MRID 48341918). The SPE C18 column was pre-conditioned by passing methanol and distilled water (10 mL each) under suction via vacuum manifold. Samples were passed through the SPE C18 column at a flow rate of 5-10 mL/minute and the column was dried by suction of air through it for 1-2 minutes. Tolclofos-methyl was eluted with 2x 10 mL of dichloromethane and the combined dichloromethane eluates were filtered through 5-10 g of anhydrous sodium sulphate into a 50 mL round bottom flask. The sodium sulphate was rinsed with 10-20 mL of dichloromethane. The combined dichloromethane solution was evaporated to

about 1-2 mL via rotary evaporation at *ca.* 30-40°C under vacuum. The remaining solvent was removed under a gentle stream of nitrogen. The residue was reconstituted in 1.0 mL toluene for GC analysis.

Samples were analyzed for tolclofos-methyl by gas chromatography (DB-1, 30 m x 0.25 mm, 0.25- μ m column; deactivated fused silica, 1.5 m x 0.53 mm pre-column) with flame photometric detection (FPD) in P-mode (p. 18 of MRID 48341917; p. 18 of MRID 48341918). Injection volume was 2 μ L; samples were injected in duplicate.

Tolclofos-methyl in the samples was confirmed by gas chromatography (Rtx-1, 30 m x 0.25 mm, 0.25- μ m column) with negative electron impact tandem mass spectrometry (p. 19 of MRID 48341917; p. 19 of MRID 48341918). Four parent-to-daughter ions were monitored: the 301→265 was the quantitative transition; and the 301→267, 301→250 and 301→125 were monitored for additional identification. Injection volume was 1 μ L; samples were injected in duplicate.

In the ECMs, the LOQ and LOD were 0.1 μ g/L and 0.01 μ g/L, respectively (pp. 21-22 of MRID 48341917; pp. 21-22 of MRID 48341918). In the ILV, the LOQ and LOD were 0.1 μ g/L and 0.05 μ g/L, respectively (p. 13 of MRID 48809101).

II. Recovery Findings

ECM (MRID 48341917): Mean recoveries and relative standard deviations (RSD) were within guideline requirements (mean 70-120%; RSD \leq 20%) for analysis of tolclofos-methyl in drinking water at the LOQ and 10x LOQ (pp. 21-22; Table 1, p. 23). The recovery and identification of tolclofos-methyl was confirmed in selected samples by GC/MS.

ECM (MRID 48341918): Mean recoveries and relative standard deviations (RSD) were within guideline requirements (mean 70-120%; RSD \leq 20%) for analysis of tolclofos-methyl in surface water at the LOQ and 10x LOQ (pp. 21-22; Table 1, p. 23). The recovery and identification of tolclofos-methyl was confirmed in selected samples by GC/MS.

ILV (MRID 48809101): Mean recoveries and RSDs were within guideline requirements for analysis of tolclofos-methyl in drinking water from a well in McKinleyville, California at the LOQ and 10x LOQ (pp. 17, 23; Table 1, pp. 26-27 of MRID 48809101). Tolclofos-methyl in all samples was quantified by GC/MS; the method was validated with the fifth analysis of the second trial (Trial #2 Analysis #5).

Table 2. Initial Validation Method Recoveries for Tolclofos-methyl in Water*

Analyte	Fortification Level (μ g/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Drinking water (Itingen, Switzerland)						
FPD quantification						
Tolclofos-methyl	0.1 (LOQ)	5	81.8-93.4	87.7	4.2	4.8
	1.0	5	89.1-100.1	93.8	4.5	4.8
MS confirmation*						
Tolclofos-methyl	0.1 (LOQ)	3	96.5-99.7	98.6	1.8	1.9

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
	1.0	1	109.7	109.7	--	--
Surface water (River in Black Forrest, Germany)						
FPD quantification						
Tolclofos-methyl	0.1 (LOQ)	5	82.1-90.1	85.7	3.6	4.2
	1.0	5	100.4-107.4	103.1	2.9	2.8
MS confirmation*						
Tolclofos-methyl	0.1 (LOQ)	3	105.1-110.8	107.8	2.9	2.6
	1.0	1	107.9	107.9	--	--

Data were obtained from p. 21; Table 1, p. 23 of MRID 48341917 and p. 21; Table 1, p. 23 of MRID 48341918.

*Reviewer-calculated using data obtained from Table 1, p. 23 of MRID 48341917 and MRID 48341918. The mean recoveries and standard deviations from the MS confirmation were not calculated by study authors. The reviewer included these values since the ILV used GC/MS analysis, not GC/FPD analysis.

Table 3. Independent Validation Method Recoveries for Tolclofos-methyl in Water*

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Drinking water well (McKinleyville, California)						
MS quantification						
Tolclofos-methyl	0.10 (LOQ)	5	75.8-82.9	80.7	3.0	3.7
	1.0	5	92.6-98.2	96.5	2.4	2.5

Data were obtained from Table 1, pp. 26-27 of MRID 48809101.

III. Method Characteristics

In the ECMs, the LOQ (0.1 µg/L) was arbitrarily set as the lowest fortification level of the spiked samples that achieved acceptable performance data (pp. 21-22 of MRID 48341917; pp. 21-22 of MRID 48341918). The LOD of 0.01 µg/L was equivalent to the lowest concentration standard. No other justification or calculation was provided. No comparison was made to chromatogram background levels. For the ILV, the method LOQ was not independently determined, and the LOD was defined as approximately 0.5 x LOQ (pp. 13, 23 of MRID 48809101). The determinations of the LOD/LOQ were not based on scientifically acceptable procedures.

Table 4. Method Characteristics

	Tolclofos-methyl	
	Drinking water	Surface water
Limit of Quantitation (LOQ)	0.1 µg/L	0.1 µg/L
Limit of Detection (LOD)	0.01 µg/L	0.01 µg/L
Linearity (calibration curve r^2 and concentration range)	$r^2 = 0.9976^{1,3}$ & $0.9987^{2,3}$ (0.01-1.00 µg/mL)	$r^2 = 0.9968^1$ & 0.9986^2 (0.01-1.00 µg/mL)
Repeatable	Yes	Yes
Reproducible	Yes ⁴	No ILV provided.
Specific	Yes	Yes

Data were obtained from pp. 21-22; Tables 3-4, pp. 24-25 of MRID 48341917 and pp. 21-22; Tables 3-4, pp. 24-25 of MRID 48341918.

- 1 Calibration curve using GC/FPD analysis.
- 2 Calibration curve using GC/MS analysis.
- 3 ILV calibration curves displayed linearity, $r^2 = 1.000$, for drinking water in the concentration range of 0.05-5.00 $\mu\text{g}/\text{mL}$ (p. 16; Figure 1, pp. 30-32 of MRID 48809101).
- 4 ECM validated by ILV using only GC/MS analysis, not GC/FPD analysis. ECM validated with ILV Trial #2 Analysis #5.

IV. Method Deficiencies and Reviewer's Comments

1. The ILV was not performed on the same version of the analytical method that was used as the primary method of analysis in the ECM, with analysis by GC/FPD. Rather, the ILV was performed using the confirmatory method using GC/MS analysis. The reviewer notes that only three samples were analyzed at the LOQ and only one sample was analyzed at 10x LOQ in the ECM using the confirmatory method. A minimum of five spiked replicates samples should be analyzed at each concentration. An ILV was not submitted to validate the GC/FPD procedure of the ECM.
2. The reported LOQ in the ECMs and ILV were set at the lowest fortification level of the spiked samples that achieved acceptable performance data and was not based on scientifically acceptable procedures. No comparison was made to chromatogram background levels. Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples. The LOD was reported as 0.01 $\mu\text{g}/\text{L}$ in the ECM, which was equivalent to the lowest concentration standard, and as $\frac{1}{2}\text{LOQ}$ (0.05 $\mu\text{g}/\text{L}$) in the ILV, which were not based on scientifically acceptable procedures as defined in 40 CFR Part 136. Additionally, the lowest toxicological level of concern in water was not reported. An LOQ above toxicological levels of concern results in an unacceptable method classification.
3. The ILV required more than the maximum of three sample sets to validate the ECM. The ILV reported that the validation was performed and succeeded on the fifth analysis of the second trial (Trial #2 Analysis #5; p. 17; Table 1, pp. 26-27 of MRID 48809101).
4. ECMs were submitted for drinking water (regular tap water from a village in Switzerland; MRID 48341917) and surface water (MRID 48341918). The independent laboratory was unsuccessful in validating the method using tap water and dechlorinated tap water and indicated that even trace amount of residual chlorine in the water affected the recovery of tolclofos-methyl (MRID 48809101, pp. 10, 18). The ILV was successful using well water on the fifth trial. An ILV was not submitted using surface water.
5. The ILV made the following changes to the ECM procedure following communication with the sponsor: the extracts were analyzed using GC/MS rather than GC/FPD; the samples were analyzed by GC in single, rather than duplicate; a different analytical column was used; untreated well water was used in the study since chlorine was observed to interfere with the recovery results; extracts were analyzed after 8 days of storage, which was reported as the stability timeframe in the ECM; and sample sets were analyzed as one set, not intermixed with analysis of calibration standards (p. 18-19, 23 of MRID 48809101).

6. The ILV recommended several modifications to the ECM, including 1) more detail regarding the set-up and collection of the dichloromethane extraction to ensure reproducibility among technicians and laboratories, 2) more detail regarding stopping points during the extraction procedure since the extraction procedure required more than 8 hours to complete, 3) additional procedures for testing chlorinated tap water since chlorine caused very low yields of tolclofos-methyl, and 4) including an initial “conditioning” step during the analytical sequence to reduce exposure of tolclofos-methyl to active sites on the column (p. 18 of MRID 48809101). None of the recommendations were implemented or addressed by the ECM.
7. In the ILV, tolclofos-methyl in the samples was quantified by gas chromatography (Restek Rxi™-XLB, 30 m x 0.25 mm, 0.25- μ m column) with negative electron impact tandem mass spectrometry, not GC/FPD (p. 15 of MRID 48809101). Four parent-to-daughter ions were monitored: the 301→265 was the quantitative transition; and the 301→267, 301→250 and 301→125 were monitored for additional identification. Injection volume was 1 μ L, samples were injected in single.
8. The drinking water was not well-characterized in the ILV (pp. 12-13 of MRID 48809101). The water was described as from a well in McKinleyville, California and was not further characterized. The drinking and surface water in the ECMs were adequately characterized (p. 14 of MRID 48341917 and p. 14 of MRID 48341918).
9. A summary of the communication between the ILV and ECM was documented; however, the actual communication was not submitted (pp. 18-19 of MRID 48809101).
10. It was reported for the ILV that a single analyst completed a sample set consisting of 13 samples in *ca.* 10 hours (p. 17 of MRID 48809101).

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

Attachment 1: Chemical Names and Structures**Tolclofos-methyl [TM; V-10178; Rizolex]****IUPAC Name:** O-2,6-Dichloro-p-tolyl O,O-dimethyl phosphorothioate.**CAS Name:** O-(2,6-Dichloro-4-methylphenyl) O,O-dimethyl phosphorothioate.**CAS Number:** 57018-04-9.**SMILES String:** C1C(C(H)(H)H)=CC(Cl)=C(OP(=S)(OC(H)(H)H)OC(H)(H)H)C=1Cl
(EpiSuite 4.0).