Test Material: Folpet

MRID: 49122709

Title: Mende, P. Residue analysis of folpet in water: Method validation

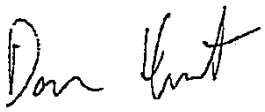
EPA PC Code: 081601

OCSPP Guideline: 850.6100

For CDM Smith

Primary Reviewer: Lisa Muto **Signature:** 

Date: 6/9/14

Secondary Reviewer: Dan Hunt **Signature:** 

Date: 6/9/14

QC/QA Manager: Joan Gaidos **Signature:** 

Date: 6/9/14

Analytical method for folpet in tap water

Reports: ECM: EPA MRID No. 49122709. Mende, P. 1994. Residue analysis of folpet in water: Method validation. Study Code: IFU94002/01-FOL. Report prepared by GAB Biotechnologie GmbH, Niefern-Oschelbronn, Germany; sponsored and submitted by Makhteshim Chemical Works Ltd., Beer Sheva, Israel; 27 pages. Final report issued June 16, 1994.
ILV: No ILV was provided.

Document No.: MRID 49122709

Guideline: 850.6100

Statements: ECM: The study was conducted in accordance with the 40 CFR Part 160, OECD and German GLP (p. 3). Signed and dated No Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4; Appendix 8, pp. 24-25). A Certification of Authenticity statement was not provided.
ILV: No ILV was provided.

Classification: This analytical method is classified as **Unaccepatable**. An ILV was not provided. In the ECM, only two replicates were analyzed in tap water at each fortification level. No samples were analyzed at the LOQ and 10× LOQ. The calculations for determining the LOQ and LOD were not provided. The matrix characterization and source of the tap water were not reported. Sample chromatograms were not provided for all fortification levels.

PC Code: 081601

Reviewer: He Zhong, Ph.D.
Biologist
EPA/OPP/EFED

Signature:
Date: 12-10-2014

Executive Summary

This analytical method, Study No. IFU94002/01-FOL, is designed for the quantitative determination of folpet in tap water using HPLC/UV. The method is quantitative for folpet at the stated LOQ of 0.06 µg/L. The lowest toxicological level of concern in water was not reported; however, the EPA Regional Screening Level for folpet in residential tap water is 17 µg/L. An independent laboratory validation (ILV) was not provided.

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						
Folpet	49122709	None provided		Water	06/16/1994	Makhteshim Chemical Works Ltd.	HPLC/UV	0.06 µg/L

I. Principle of the Method

Samples (200 mL) were extracted three times with dichloromethane (3 x 25 mL) by shaking for *ca*. 1 minute in a separatory funnel (pp. 8-9). The dichloromethane was reduced to dryness using vacuum rotary evaporation with a water bath at <50°C. The dry residue was reconstituted with 1 mL of toluene (for gas chromatograph analysis) or 1 mL of HPLC solvent. The toluene solvent was removed completely under a stream of nitrogen if the sample was to be used for HPLC analysis, and the residue was reconstituted with 1 mL of HPLC solvent.

Samples were analyzed for folpet by high performance liquid chromatography (HPLC; Shandon Hypersil C18, 250 mm x 4 mm i.d. column) using a mobile phase of acetonitrile:water (60:40, v:v) with 5 mM KH_2PO_4 (adjusted to pH 4.5 (20°C) with H_3PO_4) with photodiodearray UV detection (225 nm; p. 9). Injection volume was 50 µL.

In the ECM, the LOQ and LOD were 0.06 µg/L and 0.03 µg/L, respectively, for tap water (p. 6). No ILV was provided.

II. Recovery Findings

ECM (MRID 49122709): Mean recoveries and RSDs were within guideline requirements for analysis of folpet in tap water (pp. 12-13, 24). The tap water was not characterized (p. 7). Folpet was identified by co-chromatography with external standard using HPLC/UV.

ILV: No ILV was provided.

Table 2. Initial Validation Method Recoveries for Folpet in Water

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)*	Standard Deviation (%)*	Relative Standard Deviation (%)*
Tap water						
Folpet	0.02	2	86-87	87	1	1
	0.05	2	82-88	85	4	5
	0.1	2	94-98	96	3	3
	0.2	2	92-95	94	2	2
	0.5	2	95-97	96	1	1
	1.0	2	97-99	98	1	1

Data were obtained from p. 13 of the study report.
*Reviewer-calculated using data obtained from p. 13 of the study report (see DER Attachment 2). Mean recoveries, standard deviations and relative standard deviations were not reported by the study author.

Table 3. Independent Validation Method Recoveries for Folpet in Water

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Folpet	0.06 (LOQ)	No ILV provided.				
	0.6	No ILV provided.				

III. Method Characteristics

In the ECM, the LOQ and LOD were 0.06 µg/L and 0.03 µg/L, respectively, for tap water (p. 6). The LOQ and LOD were calculated from the results of the recovery experiments according to the guidelines of the "Deutsche Forschungsgeminschaft" (pp. 12, 14). Details of the calculations were provided. No ILV was provided.

Table 4. Method Characteristics

	Folpet
	Tap water
Limit of Quantitation (LOQ)	0.06 µg/L
Limit of Detection (LOD)	0.03 µg/L
Linearity (calibration curve r^2 and concentration range)	r^2 = 0.99996 (0.004-0.4 µg/mL)[1]
Repeatable	Yes[2]
Reproducible	Could not be determined[3]
Specific	Yes

Data were obtained from p. 6 and Appendix 1, p. 18 of the study report.
1 Reviewer-calculated calibration curve yielded similar linearity, r^2 value of 0.9996 (see DER Attachment 2).
2 Only 2 replicates were considered at each fortification level.
3 No ILV was provided.

IV. Method Deficiencies and Reviewer's Comments

1. An ILV report was not provided with the ECM; therefore, the method, Study No. IFU94002/01-FOL, could not be validated.

2. Only two replicates were analyzed in tap water at 0.02, 0.05, 0.10, 0.20, 0.50 and 1.00 µg folpet/L. No samples were analyzed at the LOQ and 10× LOQ. Fortifications at the LOQ and 10× LOQ is recommended by the OCSPP 850.6100 guidelines.

3. The reviewer could not determine if the determinations of the LOD in the ECM were based on scientifically acceptable procedures as defined in 40 CFR Part 136 since the calculations were not provided (p. 14). The study author only reported that the LOQ and LOD were calculated according to the DFG guidelines. Additionally, the lowest toxicological level of concern in water was not reported; however, the EPA Regional Screening Level (http://www.epa.gov////) for folpet in residential tap water is 17 µg/L. An LOQ above toxicological levels of concern results in an unacceptable method classification. Furthermore, the study author reported that this study satisfied a German guideline that requires pesticide LOQs to be ≤0.1 µg/L (p. 15).

4. Matrix characterization and source of the tap water were not reported (p. 7).

5. Sample chromatograms were not provided for all fortification levels.

6. Gas chromatography (capillary column DB-1, 50 mm x 0.32 mm i.d., 0.24 µm thickness or SE-4, 30 m x 0.32 mm i.d., 0.25 µm film thickness) with mass spectrometry (^{63}Ni electron capture detector) was also investigated for folpet identification; however, this method was not ideal due to folpet sensitivity towards active sites in the injector insert (pp. 10, 13, 15). The study author determined that HPLC/UV detection was much better than GC/MS for identification of folpet. The study author noted that sensitivity problems with GC/MS could be solved by use of direct injection combined with a short wide-bore capillary column; however, this solution was not tested in the submitted experiment.

7. The study author demonstrated the precision of the HPLC injections by injecting the tap water at 0.01 µg/mL eight times. The relative standard deviation of the recovery was 1.1% (n = 8; pp. 11, 14; Appendix 2, p. 19).

8. The extraction method which was used in this ECM for the extraction of folpet from drinking water differed from the water extraction methods which were reported in the submitted ECMs for folpet and its transformation products in drinking water (MRID 49122712; Sponsor Reference No.: R-27683) and for folpet and its transformation products in pond water and sediment (MRID 49122710; Sponsor Reference No.: R-25157).

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

Folpet, Folpan

IUPAC Name: N-(Trichloromethylthio)phthalimide
CAS Name: 2-[(Trichloromethyl)thio]-1H-isoindole-1,3(2H)-dione
CAS Number: 133-07-3
SMILES String: O=C(N(SC(Cl)(Cl)Cl)C(=O)c1cccc2)c12