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January 25, 2008

MEMORANDUM

SUBJECT: Etofenprox in Soil-Report No. ECM0238S1-S3 (DP# 343477)

FROM: Joseph B. Ferrario, Branch Chief
OPP/BEAD/Environmental Chemistry Laboratory *Joseph B. Ferrario 1/25/08*

TO: Cara Dzubow, Program Analyst
OPP/Environmental Fate and Effects Division
Information and Support Branch (7507C)

The Environmental Fate and Effect Division (EFED) has requested an Environmental Chemistry Method Review on Etofenprox and its metabolites in soil using the method submitted by Wildlife International Ltd. in accordance with the registration of the above mentioned analyte and its degradates, MRID No. 467797-16. The method and independent laboratory validation data were reviewed and the conclusions included in the attached Environmental Chemistry Method Review.

The following report includes an overview of the method and the method completeness, statements of adherence to EPA regulations, a presentation of results and a discussion of problems found in the registrant method. A statement of method acceptability is also included.

If you have questions concerning this report, please contact Charles Kennedy at (228) 688-2443 or Elizabeth Flynt at (228) 688-2410.

Attachments

cc: Christian Byrne, QA Officer
BEAD Environmental Chemistry Laboratory

Charles Kennedy
BEAD/Environmental Chemistry Laboratory

Etofenprox and Metabolites in Soil/128965, Mitsui Chemicals Inc./33657
ENVIRONMENTAL CHEMISTRY METHOD REVIEW REPORT

Data Requirement: PMRA Data Code: NA
EPA DP Barcode: D343477
OECD Data Point: NA
EPA Guideline: ECM Method Review

Test material:

Common name: Etofenprox

CAS: 1-[[2-(4-ethoxyphenyl)-2-methylpropyl]methyl]-3-phenoxybenzene

IUPAC Name: 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether

Primary Evaluator: Charles Kennedy **Date:** 11/26/2007
Charles Kennedy, Chemist, EPA/OPP/BEAD/ECB

Peer Reviewer: Elizabeth Flynt **Date:** 01/09/08
Elizabeth Flynt, Chemist, EPA/OPP/BEAD/ECB

QA Officer: Christian Byrne **Date:** 01/09/08
Dr. Christian Byrne, EPA/OPP/BEAD/ECB

ANALYTICAL METHOD: Jon A. MacGregor, B.S./Willard B. Nixon, Ph.D.,
November 11, 2005. *Analytical Method for the Determination of Etofenprox, α -CO and 4'-OH in Soil, Water and Sediment.* Unpublished method created by Wildlife
International, Ltd., 8598 Commerce Drive, Easton, MD 21601.

EXECUTIVE SUMMARY

This method is applicable for the overall quantitative determination of residues for Etofenprox and its metabolite in soil. The method was submitted to EPA by Mitsui Chemical Inc. of Minato-ku, Japan to support studies performed to seek registration for Etofenprox in soil. It was independently validated by PTRL West Inc., Hercules, California in accordance with EPA's Good Laboratory Practice Standards, Title 40, Code of the Federal Regulations Part 160. The independent laboratory validation that was submitted with this method was entitled, "*Independent Laboratory Validation of the Analytical Method for Determination of Etofenprox, α -CO and 4'-OH in Water and Soil*". Based on the information and data which accompanied the method and ILV, ECB found this method to be acceptable for soil.

Method Summary: An analytical method was developed to quantify Etofenprox and its two metabolites in soil using high-performance liquid chromatography electrospray

tandem mass spectrometry (LC-MS/MS). The soil sample was extracted by an ultrasonic disruption technique and centrifuged. An aliquot of sample extract was then passed through a silica SPE column, eluted and the eluate evaporated to dryness, and reconstituted in acetonitrile:water:formic acid. An aliquot of the final extract is transferred to an autosampler vial for LC/MS/MS analysis.

The lowest fortification level for which recovery data were obtained for the multiple extractions, was established as 0.0100 mg/kg (LOQ) and 0.100 mg/kg (10 x LOQ) for Etofenprox and its two metabolites. LOD values, by definition, are one-third of the LOQ values calculated for this study.

METHOD ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

This method lacks in full documentation. It does include an ILV. The accuracy and precision values for the initial method validation as well as the ILV are well within the required range.

It should be mentioned that the independent laboratory had a problem with the method which was corrected when the registrant told them that they should follow a vigorous pre rinsing of the glassware being used. No mention of this is made in the method. This doesn't warrant non-acceptance of the method but it is considered a shortcoming of this version of the method.

Additionally there is a lack of raw data area counts provided. Therefore it was impossible to check the calculations to convert raw area counts to analyte concentrations and recoveries using actual data. It is likely that the calculations for the validation were done correctly, but the reviewer can only speculate due to the lack of raw data. An ILV was performed and the raw data included make it possible to check those calculations. For the record ECB states the raw area counts should in the future be included with the methods created by this registrant. In this instance, due to the presence of the data in the ILV, ECB finds the method acceptable.

Under the conditions and parameters set in the Ecological Effects Test Guidelines, OPPTS 850.7100, Data Reporting for Environmental Chemistry Methods; "Public Draft." (U.S. Environmental Protection Agency Office of Prevention, Pesticides, and Toxic Substances (7101). U.S. Government Printing Office: Washington, DC, 1996, EPA-712-C-96-348), ECB finds this method acceptable for Etofenprox and its degradates, α -CO, and 4'-OH in soil.

COMPLIANCE

A signed and dated statement was given that this method was conducted in accordance with the requirements for Good Laboratory Practice. Also, a statement of non-confidentiality on the basis of the method falling within the scope of FIFRA Section 10(d)(1)(A)(B) or (C) was signed and dated along with information on the Quality Assurance inspection dates and signatures.

A. BACKGROUND INFORMATION

Etofenprox is an insecticide used to manage populations of aphids, bollworms, cutworms, leafhoppers and whiteflies on cereals, rice orchards, vegetables and tea crops.

Compound	Chemical Structure *(See Appendix A for chemical structure information)
Common name	Etofenprox
Company name	Etofenprox
IUPAC Name	2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether
CAS Name	1-[[2-(4-ethoxyphenyl)-2-methylproxy]methyl]-3-phenoxybenzene

Parameter	Value
Physical State	White crystalline powder
Vapor Pressure	2.4×10^{-4} mm Hg at 100°C
Melting Point	36.4 – 38.0°C
Solubility in Water	$<10^{-7}$ at 25°C
Specific Gravity	Solid (23.0°C): 1.157 g/mL Liquid (40.1°C): 1.067 g/mL
Stability to Heat	No loss during a least 3 months storage at 80°C. Partial degradation at 100°C

MATERIALS AND METHODS

B.1. Principle of Method

An analytical method for the determination of residues of Etofenprox and its two metabolites [α -CO and 4''-OH] is based on the extraction of a soil sample ultrasonic disruption, SPE clean-up and LC/MS/MS analysis. A 5 gram soil sample is transferred into a glass, screw-top bottle and the soil extracted with 50 mL of acetone by ultrasonic disruption for ~ 5 minutes. The bottle is centrifuged for ~ 5 minutes at 1500 rpm. A

Etofenprox and Metabolites in Soil/128965, Mitsui Chemicals Inc./33657
ENVIRONMENTAL CHEMISTRY METHOD REVIEW REPORT

1 mL aliquot of the centrifuged extract is quantitatively transferred to a prepared Si SPE column and eluted with 2 mL of additional acetone into a 15 mL glass tube. The acetone extract is evaporated to dryness using a nitrogen evaporator with a water bath at 40-50°C. The dried extract is reconstituted with 8 mL of acetonitrile:water:formic acid, 50:50:0.1 (v:v:v) and mixed well. An aliquot of the extract is transferred to an auto-sampler vial for LC/MS/MS analysis.

TABLE B.1.1.	Summary Parameters for the Analytical Method Used for the Quantitation of Etofenprox and its Metabolites in Soil
Project ID	Wildlife International Ltd. 236C-135
Analyte(s)	Etofenprox, α -CO, 4'OH
Extraction solvent/technique	Etofenprox and its metabolites are extracted from soil and sediment using ultrasonic disruption.
Instrument/Detector	LC/MS/MS.
Standardization method	The extracts were analyzed using a 7-point calibration curve prepared from standards.

C. RESULTS AND DISCUSSION

C.1. Recovery Results Summary

TABLE C.1.1. Mean Recovery Results from Method Validation of Etofenprox and Metabolites in Soil				
Substrate	Fortification Concentration	Etofenprox Recovery \pm SD RSD	α-CO Recovery \pm SD RSD	4'-OH Recovery \pm SD RSD
Soil (7 analysis)	0.0100 mg/Kg	102 \pm 2.94 2.84	84.0 \pm 4.81 5.73	106 \pm 2.55 2.40
Soil (5 analysis)	0.100 mg/Kg	99.5 \pm 1.92 1.93	77.9 \pm 3.82 4.90	95.6 \pm 1.16 1.21

C.1.2. Method Characteristics

TABLE C.1.2. Method Characteristics	
Analyte	Etofenprox, α -CO, 4'-OH
Limit of Quantitation	0.0100 mg/kg (parent and metabolites)
Limit of Detection (LOD)	0.00092 mg/kg – Etofenprox, 0.0015 mg/kg – α -CO, 0.00080 mg/kg – 4'-OH
Accuracy/Precision at LOQ	See above chart
Reliability of the Method/ [ILV]	An independent laboratory validation [ILV],

Etofenprox and Metabolites in Soil/128965, Mitsui Chemicals Inc./33657
ENVIRONMENTAL CHEMISTRY METHOD REVIEW REPORT

TABLE C.1.2. Method Characteristics	
	(MRID No.471328-45), was conducted to verify the reliability of method (MRID No. 467797-16) for the determination of residues of Etofenprox and its two metabolite residues in soil.
Linearity	For the linear regression analysis, the coefficient of determination (r^2) were greater or equal to 0.9985 for all of the soil calibration curve determinations during the method validation.
Specificity	The method is specific for the determination of Etofenprox and its metabolites by virtue of the chromatographic separation and selective detection system used. According to recently published guidelines, when detection is performed by tandem mass spectrometry methods, confirmation of the presence of the analyte should require the observation of a precursor ion plus one structurally significant product ion observed at the same retention time. Further confirmation is not necessary due to the highly specific nature of the MS/MS transitions monitored.

C.2. Independent Laboratory Validation (ILV)

Method Validation Recovery Summary for Etofenprox, α -CO and 4'-OH in Soil

Substrate	Fortification Concentration	Etofenprox Recovery/RSD	α-CO Recovery/RSD	4'-OH Recovery/RSD
Soil (LOQ)	0.0100 mg/Kg	88.0 \pm 12.2	84.0 \pm 7.2	87.0 \pm 15.2
Soil (10 x LOQ)	0.100 mg/Kg	97.0 \pm 5.7	108 \pm 18.1	93.0 \pm 10.9

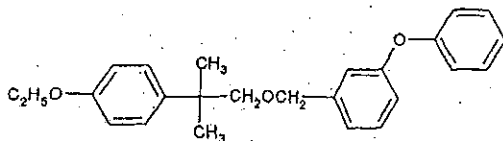
D. CONCLUSION

This study provides a residue method for Etofenprox and its metabolites in soil. Despite some minor deficiencies, ECB finds the method acceptable. The data provided support the method created by Jon A. MacGregor, B.S., Willard B. Nixon, Ph.D. "*Analytical Method Validation for the Determination of Etofenprox, α -CO and 4'-OH in Soil, Water and Sediment*".

Appendix A: Chemical Structure of Etofenprox and Metabolites

Etofenprox

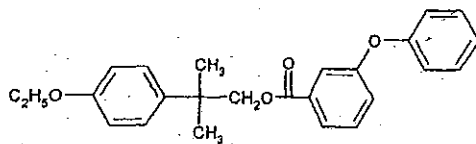
ISO Name: Etofenprox
Test Name: MTI-500
CAS Number: 80844-07-1
Structural Formula:



Molecular Weight: 376.47
Chemical Name: 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether
(IUPAC)
Appearance: White crystal
Lot Number: 9604
Purity: 99.9% by HPLC/UV (254 nm)
Expiration Date: December 2006

α -CO

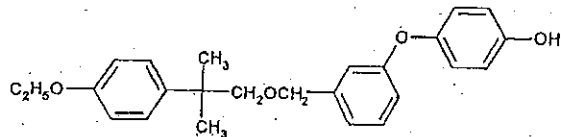
Test Name: α -CO
Structural Formula:



Molecular Weight: 390.48
Chemical Name: 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate
Appearance: White crystal
Lot Number: LS9911
Purity: 99.4% by HPLC/UV (254 nm)
Expiration Date: December 2008

4'-OH

Test Name: 4'-OH
Structural Formula:



Molecular Weight: 392.50
Chemical Name: 2-(4-ethoxyphenyl)-2-methylpropyl 3-(4-hydroxyphenoxy)benzyl ether
Appearance: White Crystals
Lot Number: 043-011222-1
Purity: 96.0% by HPLC/UV (254 nm)
Expiration Date: December 2008