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OFFICE OF PESTICIDE PROGRAMS
ENVIRONMENTAL CHEMISTRY LABORATORY
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January 16, 2007

MEMORANDUM

SUBJECT: XDE-742 in Soil (DP# 332342)

FROM: Joseph B. Ferrario, Branch Chief
OPP/BEAD/Environmental Chemistry Laboratory

1/12/07

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

The EFED Environmental Fate and Effect Division (EFED) have requested and Environmental Chemistry Method Review on XDE-742 and its metabolites in soil using the method submitted by Dow AgroScience LLC in accordance with the registration of the above mentioned analyte and its degradates, MRID No. 469084-53. The method and independent laboratory validation data was 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

2070874

Charles Kennedy
BEAD/Environmental Chemistry Laboratory

ERBA

ENVIRONMENTAL CHEMISTRY METHOD REVIEW REPORT

Data Requirement: PMRA Data Code: NA
EPA DP Barcode: - 332342
OECD Data Point: NA
EPA Guideline: ECM Method Review

Test material:
Common name: XDE-742

IUPAC Name: N-(5,7-dimethoxy[1,2,4] triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide

CAS Name: N-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide

CAS No: 422556-08-9

Primary Evaluator: Charles Kennedy **Date:** 12/4/06
Charles Kennedy, Chemist, EPA/OPP/BEAD/ECB

Peer Reviewer: Elizabeth Flynt **Date:** 12/4/06
Elizabeth Flynt, Chemist, EPA/OPP/BEAD/ECB

QA Officer: Christian Byrne **Date:** 12/4/06
Dr. Christian Byrne, EPA/OPP/BEAD/ECB

ANALYTICAL METHOD: M. J. Hastings, *Determination of Residues of XDE-742 and Its Metabolites in Soil and Sediment by Liquid Chromatography with Tandem Mass Spectrometry Detection*. Unpublished method created by Dow AgroSciences LCC, 9330 Zionsville Road, Indianapolis, Indiana 46268-1054. Method ID: GRM 05.05, Study ID: 041024, Method Effective Date: February 13, 2006.

EXECUTIVE SUMMARY

This method is applicable for the quantitative determination of residues of XDE-742 and its metabolites in soil. The method was submitted to EPA by Dow AgroSciences to support studies performed to seek registration for XDE-742 and its metabolites. The method was created by Dow AgroSciences in Indianapolis, Indiana and independently validated by PTRL Europe GmbH, Helmholtzstr. 22, Science Park, D-89081 Ulm, Germany 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, "*XDE-742: Independent Laboratory Validation of Dow AgroSciences LLC Analytical Method 05.05 – Determination of Residues of XDE-742 and Its Metabolites in Soil and Sediment by Liquid Chromatography with Tandem Mass Spectrometry Detection*". Based on the information and data which accompanied the method and ILV, ECB found this method to be acceptable for soil.

Method Summary: Residues of XDE-742 and its metabolites are extracted from the soil by sonicating with 1 N hydrochloric acid solution by shaking after the addition of methanol, to produce a methanol/1 N hydrochloric acid solution (90:10). A mixed XDE-742 and metabolites stable isotope internal standard solution is added to the extraction solvent and an aliquot of the extract is evaporated to dryness. The sample is reconstituted in 0.1 N hydrochloric acid and purified using a polymeric 96-well solid phase extraction (SPE) plate. The SPE plate is washed with a water/methanol solution (75:25) and eluted with an acetonitrile/methanol solution (50:50). The eluate is evaporated to dryness and the residues are reconstituted in water/methanol solution (90:10) containing 2 mM ammonium acetate. The purified extract is analyzed by high performance liquid chromatography with positive-ion electrospray (ESI) tandem mass spectrometry (LC/MS/MS).

The limits of quantitation (LOQ) and detection (LOD) were calculated for XDE-742 and its metabolites using the standard deviation from the 1.0 ng/g (LOQ) recovery results. The LOQ was calculated as ten times the standard deviation, and the LOD was calculated as three times the standard deviation.

The calculated LOQ supports the validated LOQ of 1.0 ng/g for soil. For soil, the calculated LOD's were in the range 0.25-0.31 ng/g which supports a method LOD of 0.3 ng/g.

The method was evaluated by determining the average recoveries and relative standard deviation at the LOD (0.3 ng/g), LOQ (1.0 ng/g), and 10 x LOQ (10.0 ng/g). For XDE-742 in soil, the individual recovery samples were between 83 and 119% with standard deviations less than or equal to 8.7% after one outlier was rejected after applying the Grubb's Test. For 5-OH-XDE-742 in soil, the individual recovery samples were between 82 and 116% with standard deviations less than or equal to 8.1%. For 7-OH-XDE-742 in soil the individual recovery samples were between 77 and 110% with standard deviations less than or equal to 7.2%. For 6-C1-7-OH-XDE-742 in soil, the individual recovery samples were between 84 and 112% with standard deviations less than or equal to 7.6% after one outlier was rejected. The method was found capable of quantifying XDE-742 and its metabolites in soil at the targeted LOQ of 1.0 ng/g.

METHOD ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

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 XDE-742 and its metabolites in soil.

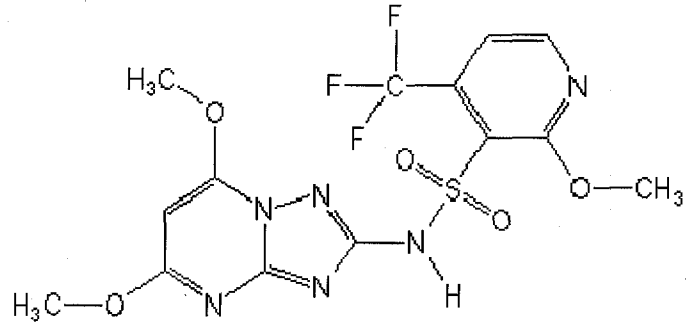
COMPLIANCE

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

XDE-742 is an herbicide in the sulfonamide family that is being developed by Dow AgroSciences LLC for the post-emergence control of grasses and broadleaf weeds in cereal crops. The mode of action is by the inhibition of the acetolactate synthase (ALS) enzyme.

TABLE A.1. Test Compound Nomenclature

Compound	XDE-742 **STRUCTURE:** 
Common name	XDE-742
Company name	XDE-742
IUPAC Name	N-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide

CAS Name	N-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
CAS. NO.	422556-08-9
End-use produce/EP	GF-1674, GF-1274

TABLE A.2. Physicochemical Properties of the Technical Grade Test Compound

Parameter	Value
Melting point/range	Not available
pH	Not available
Density (Relative/Specific Gravity) density std = water @ 4 °C	XDE-742 (pure active): 1.618
Water solubility (g/L) at 20 °C	pH 4.0 (buffered) = 0.0164 pH 6.1 (unbuffered) = 0.0626 pH 7 (buffered) = 3.2 pH 9 (buffered) = 13.7
Solvent solubility (g/L) at 20 °C	Methanol = 1.01 Acetone = 2.79 Xylene = 0.0352 Dichloroethane = 3.94 Ethyl Acetate = 2.17 n-Heptane < 0.001 1-Octanol = 0.73
Vapor pressure at 20 °C	< 1E-7 Pa
Dissociation Constant (pK_a) at 20 °C	4.670
Octanol/water distribution coefficient (Log D) at 20 °C	pH 4 = 1.080 pH 7 = -1.010 pH 9 = -1.600
UV/visible absorption spectrum	Not available

MATERIALS AND METHODS

B.1. Principle of Method

An analytical method (GRM 05.05) was developed for determination of XDE-742 and its metabolites (5-OH-XDE-742, 7-OH-XDE-742, 6-C1-7-OH-XDE-742) in 5 grams of soil. Soils were fortified as appropriate with the internal standards of XDE-742 and its metabolites. The soil samples were simultaneously extracted by sonicating with 1N hydrochloric acid solution by shaking, after the addition of methanol, to produce a methanol/1N hydrochloric acid solution (90:10). A mixed XDE-742 and metabolite

stable isotope internal standard solution is added to the extraction solvent and an aliquot of the extract is evaporated to dryness. The sample is reconstituted in 0.1N hydrochloric acid and purified using a polymeric 96 well solid phase extraction (SPE) plate. The SPE plate is washed with a water/methanol solution (75:25) and eluted with an acetonitrile/methanol solution (50:50). The eluate is evaporated to dryness and the residues are reconstituted in water/methanol solution (90:10) containing 2 mM ammonium acetate. The purified extract is analyzed by high performance liquid chromatography with positive-ion electrospray (ESI) tandem mass spectrometry (LC/MS/MS).

TABLE B.1.1.	**Summary Parameters for the Analytical Method Used for the Quantitation of XDE-742 and its Metabolites in Soil**
Method ID	(GRM 05.05)
Analyte(s)	XDE-742, 5-OH-XDE-742, 7-OH-XDE-742, 6-Cl-7-OH-XDE-742
Extraction solvent/technique	XDE-742 and its metabolites are extracted from the soil by sonicating with 1 N hydrochloric acid solution and shaking, after addition of methanol, to produce a methanol/1N hydrochloric acid solution (90:10).
Cleanup strategies	Off-line phase extraction (SPE) using polymeric SPE.
Instrument/Detector	XDE-742 is analyzed by liquid chromatography with positive-ion electrospray tandem mass spectrometry (LC/MS/MS). Chromatographic analysis was performed using a Phenomenex Synergi Hydro C18, 50 x 2 mm, 4-µm column coupled to a Spark Holland Symbiosis Pharma system and a MDS/SCIEX API 4000 LC/MS/MS.
Standardization method	Stable-isotope labeled internal standard using an 8 point calibration line.
Stability of standard solutions	XDE-742 and its metabolites have been shown to be stable in the standard solutions prepared in GRM 05.05 for at least 222 days when stored refrigerated (approximately 4 °C)
Retention time	XDE-742 (nominally 2.9 minutes), 5-OH-XDE-742 (nominally 2.0 minutes), 7-OH-XDE-742 (nominally 2.5 minutes), 6-Cl-7-OH-XDE-742 (nominally 3.0 minutes)

C. RESULTS AND DISCUSSION

C.1. Recovery Results Summary

TABLE C.1.1. Average Recovery Results from Method Validation of XDE-742 in Soil.

Matrix Soil	Fortification Level (ng/g)	Average Recovery (%)	Recovery Range (%)	SD (%)	RSD (%)	n
XDE-742	1	93	84-119	10.3	11.0	10
XDE-742	10	103	96-114	7.2	7.0	8
XDE-742	100	91	83-99	6.3	6.9	7
5-OH-XDE-742	1	94	82-115	9.6	10.2	10
5-OH-XDE-742	10	95	89-116	9.2	9.8	9
5-OH-XDE-742	100	93	82-102	8.1	8.7	7
7-OH-XDE-742	1	88	82-110	8.3	9.4	10
7-OH-XDE-742	10	88	77-108	8.7	9.8	9
7-OH-XDE-742	100	84	79-91	5.1	6.1	7
6-Cl-7-OH-XDE-742	1	100	84-112	9.2	9.2	10
6-Cl-7-OH-XDE-742	10	95	89-106	6.7	6.7	8
6-Cl-7-OH-XDE-742	100	92	85-104	7.3	7.9	7

C.1.2. Method Characteristics

TABLE C.1.2. Method Characteristics

Analyte	XDE-742, 5-OH-XDE-742, 7-OH-XDE-742, 6-C1-7-OH-XDE-742
Limit of Quantitation	1.0 ng/g. (soil)
Limit of Detection (LOD)	0.3 ng/g (soil)
Accuracy/Precision at LOQ	See above chart
Reliability of the Method/ [ILV]	An independent laboratory validation [ILV], (MRID No.469083-13), was conducted to verify the reliability of method (MRID No. 469084-53) for the determination of residues of XDE-742 and its metabolites in soil.
Linearity	For the linear regression analysis, the coefficient of determination (r^2) were greater or equal to 0.987 for all of the calibration curve determinations during the method validation.
Specificity	The method is specific for the determination of XDE-742 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)

Recovery Results Summary Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of XDE-742 and its Metabolites in Soil.

Results Soil LUFA 2.2	Fortification Level	XDE-742		5-OH-XDE-742		7-OH-XDE-742		6-Cl-7-OH-XDE-742	
		435 m/z ->435 m/z 195 m/z	82 m/z	421 m/z ->421 m/z 181 m/z	148 m/z	421 m/z ->421 m/z 181 m/z	138 m/z	455 m/z ->455 m/z 215 m/z	148 m/z
Average	LOQ	100%	100%	102%	103%	91%	88%	93%	102%
RSD	1.0 ng/g	3%	2%	6%	9%	7%	6%	7%	5%
Average	10 x LOQ	100%	97%	97%	100%	92%	94%	88%	97%
RSD	10.0 ng/g	2%	3%	5%	6%	5%	10%	5%	3%
Average	100 x LOQ	95%	96%	96%	94%	88%	93%	84%	85%
RSD	100.0 ng/g	3%	3%	3%	4%	6%	4%	5%	3%
Overall Mean		98%	98%	98%	99%	90%	92%	89%	95%
Overall RSD		3%	3%	5%	8%	6%	7%	7%	9%

Results Soil LUFA 3A	Fortification Level	XDE-742		5-OH-XDE-742		7-OH-XDE-742		6-Cl-7-OH-XDE-742	
		435 m/z ->435 m/z 195 m/z	82 m/z	421 m/z ->421 m/z 181 m/z	148 m/z	421 m/z ->421 m/z 181 m/z	138 m/z	455 m/z ->455 m/z 215 m/z	148 m/z
Average	LOQ	95%	94%	91%	86%	89%	98%	95%	94%
RSD	1.0 ng/g	3%	2%	4%	2%	4%	5%	2%	5%
Average	10 x LOQ	99%	94%	101%	92%	88%	87%	92%	96%
RSD	10.0 ng/g	3%	7%	3%	6%	10%	12%	7%	9%
Average	100 x LOQ	97%	96%	95%	99%	97%	95%	94%	93%
RSD	100.0 ng/g	7%	8%	7%	6%	4%	7%	8%	9%
Overall Mean		97%	95%	96%	92%	91%	93%	93%	94%
Overall RSD		5%	6%	6%	8%	8%	9%	6%	7%

D. CONCLUSION

This study provides a residue method for XDE-742 and its metabolites in soil. The method appears satisfactory with the data being used to support the original method by M. J. Hastings, *"Determination of Residues of XDE-742 and Its Metabolites in Soil and Sediment by Liquid Chromatography with Tandem Mass Spectrometry Detection"*. Based on the information and data which accompanied the method, ECB considers the method acceptable to support the registration studies.