US EPA ARCHIVE DOCUMENT

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

Penoxsulam/XDE-638/PC Code 119031/Dow AgroSciences LLC
DACO 7.2.1, 7.2.2, and 7.2.3/OPPTS 860.1340/OECD IIA 4.2.5, 4.2.6 and 4.3
Residue Analytical Method/Independent Laboratory Validation - Rice Commodities

Primary Evaluator	William Cutchin, Chemist SIMB/HED	Date: 7/19/04
Reviewer	Richard Loranger, BSS RAB2/HED	Date: 7/22/04 for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874	

STUDY REPORTS

45830714 Hastings, M. (2002) Validation Report for Method GRM 01.25 - Determination of Residues of XDE-638 in Rice and Rice Processed Products by Liquid Chromatography with Tandem Mass Spectrometry: Lab Project Number: 010097. Unpublished study prepared by Dow AgroSciences LLC. 41 p.

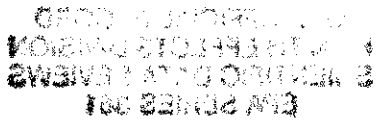
45830715 Chickering, C. (2002) Independent Laboratory Validation of Dow AgroSciences LLC Method GRM 0.125 - Determination of XDE-638 in Rice and Rice Processed Products by Liquid Chromatography with Tandem Mass Spectrometry Detection: Lab Project Number: 020038: 47421. Unpublished study prepared by ABC Laboratories and Dow AgroSciences LLC. 67 p.

EXECUTIVE SUMMARY

Dow AgroSciences LLC has proposed an LC/MS/MS method, GRM 01.25, for the enforcement of tolerances for residues of penoxsulam in/on rice commodities. This method was used for the quantitation of residues in rice commodities (forage, grain, straw, hulls, bran, and polished rice) from the rice field trial and processing studies with penoxsulam submitted in conjunction with DP Barcode D288152.

Briefly, samples of rice matrices are homogenized/extracted with acetonitrile/water, shaken for 60 minutes, and centrifuged. An aliquot of the supernatant is diluted with water and cleaned-up on a mixed-mode polymeric-anion exchange solid phase extraction (SPE) plate. Residues are eluted with ACN:formic acid (99.9:0.1, v:v), evaporated to dryness, and redissolved in mobile phase. Residues are quantitated by LC/MS/MS using a C8 column, a gradient mobile phase of ACN/methanol and water, each containing 0.1% acetic acid, and electrospray ionization in the positive ion mode. Residues are quantified using external standards. The validated limit of quantitation (LOQ) and calculated limit of detection (LOD) for penoxsulam were 0.01 and 0.002 ppm, respectively, in/on rice forage, straw, grain, hulls, bran, and polished rice.

RRC 7/29/04



Adequate method recoveries were obtained for rice commodities at the LOQ (0.01 ppm) and up to 100x the LOQ. Concurrent method validation data were also submitted in conjunction with rice field trial and processing studies (MRID 45830719).

A successful independent laboratory validation (ILV) of the LC/MS/MS method has been completed with rice grain and straw. Although extraction efficiency data were submitted, penoxsulam residues in the samples examined were too low to allow determination of the ability of the residue analytical method to extract aged residues. However, because the extraction procedures of the method are very similar to those used in the metabolism study, no additional extraction efficiency data will be required. The LC/MS/MS method has been submitted to ACB/BEAD for regulatory method validation.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the residue analytical method data are classified as scientifically acceptable. The laboratory that conducted the ILV for the method recommended some changes/clarifications to the method procedures. Unless ACB concludes differently, the modifications recommended by the ILV laboratory will need to be made to the method prior to its acceptance as a tolerance enforcement method; any additional changes recommended by ACB will also need to be incorporated.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would impact the validity of the study.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

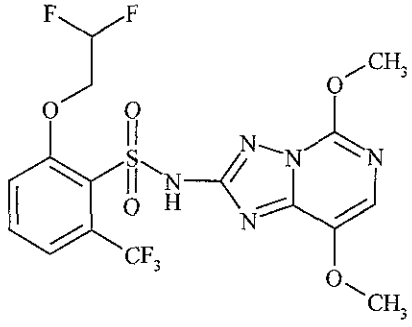
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Melting point/range	Not available		
pH	Not available		
Density	Not available		
Water solubility	pH	Solubility (mg/L)	45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		45830720
Dissociation constant, pK_a	5.1		45830720

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.			
Parameter	Value		Reference
Octanol/water partition coefficient, Log(K_{OW})	pH	Log(K_{OW})	45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Samples of rice commodities from the crop field trial and processing studies associated with the proposed use of penoxsulam on rice (PP#3F06542) were analyzed for residues of penoxsulam using the proposed LC/MS/MS enforcement method for plant commodities.

B.1.1. Principle of the Method

The method principles are discussed in Section B.2.1. below.

B.2. Enforcement Method

The proposed enforcement method is an LC/MS/MS method entitled, "Determination of Residues of XDE-638 in Rice and Rice Processed Products by Liquid Chromatography with Tandem Mass Spectrometry," Dow AgroSciences Method GRM 01.25.

B.2.1. Principle of the Method

The LC/MS/MS method quantitates residues of penoxsulam *per se* in/on rice raw agricultural and processed commodities. Briefly, samples of rice matrices are extracted with acetonitrile/water, and the extracts are purified by solid-phase extraction (SPE). Residues are quantitated by LC/MS/MS using a C8 column, a gradient mobile phase of acetonitrile/methanol and water, each containing 0.1% acetic acid, and electrospray ionization in the positive ion mode.

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Method Used for the Quantitation of Penoxsulam Residues in Rice Matrices.	
Method ID	Dow AgroSciences Method GRM 01.25
Analyte(s)	Penoxsulam
Extraction solvent/technique	Rice matrices are homogenized with acetonitrile:water (8:2, v:v) for one minute and then shaken for at least one hour; the extract is isolated by centrifugation.
Clean-up strategies	An aliquot of the extract is diluted with water and cleaned-up on a mixed-mode polymeric-anion exchange 96-well solid phase extraction plate. Residues are eluted with acetonitrile:formic acid (100.0:0.1, v:v), evaporated to dryness, and redissolved in acetonitrile:methanol:water:acetic acid (15:15:70:0.1, v:v:v:v).

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Method Used for the Quantitation of Penoxsulam Residues in Rice Matrices.	
Instrument/Detector	HPLC utilizing a C8 column and gradient mobile phase of water and acetonitrile:methanol (1:1, v:v), each containing 0.1% acetic acid, with tandem mass spectrometry (MS/MS) detection using electrospray ionization operating in the positive ion mode. The ion transition monitored is m/z 484.0 to m/z 195.0.
Standardization method	External calibration standards of penoxsulam are prepared in acetonitrile:methanol:water (15:15:70, v:v:v) containing 0.1% acetic acid.
Stability of std solutions	No information or data concerning the stability of the standard solutions were included in the method. The method does specify appropriate stopping points for the method and states that sample extracts should be stored refrigerated.
Retention times	5.1-5.2 minutes (based on representative chromatograms)

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

The LC/MS/MS method used for data collection for rice commodities is the same as the proposed enforcement method; the enforcement method results are discussed in Section C.2 below. Adequate concurrent method validation data were submitted for residues of penoxsulam in/on rice forage, straw, grain, hulls, bran, and polished rice in conjunction with the rice field trial and processing studies (refer to the 860.1500 and 860.1520 DERs for MRID 45830719).

C.2. Enforcement Method

Method validation data for penoxsulam in rice commodities have been submitted (MRID 45830714) for the proposed LC/MS/MS method. Untreated samples of rice forage, straw, grain, hulls, bran, and polished rice were fortified with 0.01-1.00 ppm penoxsulam. Adequate recoveries were obtained for the rice commodities; method validation recoveries are reported in Table C.2.1.

The fortification levels of the validation studies for the rice commodities represent the method LOQ (0.01 ppm), 10x the LOQ (0.10 ppm), and 100x the LOQ (1.00 ppm) which adequately cover the expected residue levels for rice raw agricultural and processed commodities. A sample of each rice matrix was also fortified at the LOD (0.002 ppm), but recoveries were not calculated or included in the method validation means. Quantitated residues in these samples were 0.002-0.003 ppm which demonstrated detection of residues at the calculated LOD.

The petitioner stated that residue confirmation is conducted by comparison of retention times and peak area ratios with those of the standards; however, no limits for these comparisons were provided. Because the LC/MS/MS method monitors a specific ion transformation, a confirmatory method is not required.

TABLE C.2.1. Recovery Results from Method Validation of Rice Matrices using the Enforcement Analytical Method.[1]

Matrix	Spiking Level (ppm)	Recoveries Obtained	Mean Recovery ± SD [CV]
Rice grain	0.01	103, 104, 104, 104, 104, 104, 105	103 ± 1.6 [1.5]
	0.10	103, 105	
	1.00	100, 101	
Rice straw	0.01	103	102 ± 1.0 [1.0]
	0.10	102	
	1.00	101	
Rice forage	0.01	104, 104, 104, 105, 106, 106, 106, 107	104 ± 3.4 [3.3]
	0.10	102, 105	
	1.00	95, 99	
Rice hulls	0.01	104	101 ± 4.2 [4.1]
	0.10	96	
	1.00	102	
Rice bran	0.01	93	86 ± 6.4 [7.4]
	0.10	82	
	1.00	82	
Polished rice	0.01	105	101 ± 4.5 [4.5]
	0.10	101	
	1.00	96	

[1] Calibration standards were prepared in acetonitrile:methanol:water (15:15:70, v:v:v, each containing 0.1% acetic acid); fortification solutions were prepared in acetonitrile.

TABLE C.2.2. Characteristics for the Enforcement Analytical Method Used for the Quantitation of Penoxsulam Residues in Rice Matrices.

Analyte	Penoxsulam
Equipment ID	Zorbax SB C8 column and LC/MS/MS with electrospray interface (PE SCIEX API 3000)
Limit of quantitation (LOQ)	0.01 ppm
Limit of detection (LOD)	0.002 ppm
Accuracy/Precision	Percent recoveries and coefficients of variance (CVs) indicate acceptable accuracy/precision for residues of penoxsulam in/on rice raw agricultural and processed commodities at the LOQ (0.01 ppm), 10x the LOQ, and 100x the LOQ. Recovery ranges (and CVs) for penoxsulam were 100-105% (1.5) from rice grain, 101-103% (1.0) from rice straw, 95-107% (3.3) from rice forage, 96-104% (4.1) from rice hulls, 82-93% (7.4) from rice bran, and 96-105% (4.5) from polished rice. See Table C.2.1 above.
Reliability of the Method/[ILV]	An independent laboratory method validation (ILV) of LC/MS/MS method GRM 01.25 was conducted using rice grain and straw. The recovery values obtained with the initial trial (grain) and second trial (straw) indicate that the LC/MS/MS method is reliable at the method LOQ (0.01 ppm), 2x the LOQ, and 10x the LOQ for rice grain, and at the method LOQ (0.01 ppm), 2x the LOQ, and 100x the LOQ for rice straw; see Section C.3 below.

TABLE C.2.2. Characteristics for the Enforcement Analytical Method Used for the Quantitation of Penoxsulam Residues in Rice Matrices.	
Linearity	The instrument response was linear (coefficient of determination, r^2, was 1.0000) for penoxsulam standards, prepared in acetonitrile:methanol:water (15:15:70, v:v:v, each containing 0.1% acetic acid), in the range of 0.002-1.0 ppm.
Specificity	No matrix interference was observed in the control sample chromatograms (rice grain), and the analyte peak was well-defined and symmetrical. High specificity of the mass spectrometric determination method was demonstrated for penoxsulam.

An extraction efficiency study was conducted with the method validation using samples of radiolabeled rice grain, straw, and immature forage obtained from a rice metabolism study (refer to the DER for MRID 45830712). We note that the petitioner did not specify whether radiolabeled samples were from plants treated with [triazolopyrimidine-2-^{14}C]penoxsulam or plants treated with [phenyl-U-^{14}C]penoxsulam, and did not identify from which harvest interval the immature rice forage samples were obtained (in the metabolism study, immature forage samples were collected 0, 3, 7, 14, and 30 days following treatment). In the metabolism study, residues were extracted with acetonitrile:water (80:20, v:v) three times. The residue method uses a single-step extraction including homogenization with acetonitrile:water (80:20, v:v) and shaking for at least one hour on a flat-bed shaker. The extractability using triplicate extraction was compared with two single-extraction procedures to determine whether the triplicate extraction procedure is required. The first single-step extraction procedure included 60-second homogenization followed by shaking at low speed for 60 minutes, and the second single-step extraction procedure used only shaking for 60 minutes at low speed. Optimum residue levels were extracted from rice forage with the single-step procedure using homogenization and shaking; recoveries are reported below in Table C.2.3.

It appeared that the results reported for the metabolism-method extraction were not those from the actual metabolism study, but were generated as part of the extraction efficiency study. However, because the petitioner did not include any raw data to support the extraction efficiency study, the study reviewer could not verify this. The actual results from the rice metabolism study are included in Table C.2.3.

Because of the low levels of penoxsulam residues in the samples examined, the ability of the residue analytical method to extract aged residues of penoxsulam from rice commodities cannot be determined from these data. However, because the extraction procedures of the method are very similar to those used in the metabolism study, no additional extraction efficiency data will be required. The petitioner should note for future submissions that more details regarding the samples used in extraction efficiency studies should be provided in the reports, and that samples bearing residues above the LOQ should be used if at all possible. In addition, any submitted extraction efficiency study should be supported by raw data.

TABLE C.2.3. Extraction Efficiency; Single-Step Extraction Versus Triplicate Extraction Procedures.

Extraction Procedure	Penoxsulam Residue Extracted (ppm)		
	Rice Forage	Rice Grain	Rice Straw
Metabolism Method: Triplicate acetonitrile/water extraction, shaken for 30 minutes	0.003, 0.004	ND,[1] ND	ND, ND
Single acetonitrile/water extraction, shaken for 60 minutes, 1.5-g sample size	0.004, 0.004	ND, ND	ND, ND
Single acetonitrile/water extraction, homogenized, shaken for 60 minutes, 1.5-g sample size	0.005, 0.006	ND, ND	ND, ND
Residue Method: Single acetonitrile/water extraction, homogenized, shaken for 60 minutes, 5-g sample size, larger solvent amount (100 mL)	0.004, 0.005	ND, ND	ND, ND
Metabolism study results:[2] [triazolopyrimidine-2-^{14}C]penoxsulam treatment	0.006	<0.001	0.003
[phenyl-U-^{14}C]penoxsulam treatment	0.023	<0.001	0.001

[1] ND = not detected; <0.002 ppm.
[2] Refer to the DER for MRID 45830712. The reported results are from rice forage samples from the 30-day posttreatment interval; much higher levels of penoxsulam were observed in forage samples from shorter posttreatment intervals.

C.3. Independent Laboratory Validation

An independent laboratory validation study (ILV; MRID 45830715) was conducted for LC/MS/MS method GRM 01.25 by ABC Laboratories, Inc. (Columbia, MO). Untreated samples of homogenized rice grain and straw, provided by the petitioner, were fortified with penoxsulam at 0.01 (LOQ), 0.02, and 0.10 (grain) or 1.00 (straw) ppm. Fortified and unfortified (control) samples were analyzed using the proposed enforcement method as described in Table B.2.1.

Adequate recoveries were obtained from rice grain with the first method trial; however, the first method trial failed for rice straw due to cross-contamination of control and blank samples from adjacent fortified samples during concentration in the collection plate. Adequate recoveries were obtained from rice straw with the second method trial, with one method modification. Samples of rice straw in the second trial were transferred from the collection plate into individual tubes prior to evaporation to minimize cross-contamination of the samples. Recoveries of penoxsulam from the ILV study are reported in Table C.3.1. No detectable residues of penoxsulam (<0.002 ppm) were observed in one unfortified sample of rice grain and four unfortified samples of rice straw; detectable penoxsulam residues were observed in one rice grain sample, at 0.002 ppm.

The ILV laboratory reported that the initial injection of rice straw samples fortified at 1.0 ppm resulted in average recoveries of 115% and noted that the 1.0-ppm fortification level is equivalent to the highest point in the calibration curve defined in the method. The ILV laboratory noted that the method does not specifically state that fortifications at or above the standard curve should be diluted to the mid-range (we note that the method does specify that samples expected to contain residues above the standard curve should be diluted). The laboratory diluted the 1.0-ppm fortification samples 5x and reran them; these results are reported in Table C.3.1. Based on these results, the laboratory recommended that information concerning the dilution of samples with residue values at or above the standard curve (0.002-1.0 ppm) be

included in the methodology. The laboratory also experienced difficulties profiling the 96-well SPE plate as written and suggested that the method be reworded to more thoroughly reflect how this profile should be performed. In addition, the laboratory recommended that the method allow the alternative of doing the analysis, under scaled up conditions, using conventional SPE columns.

The laboratory reported that one set of 30 samples required one person ~12 hours for preparation of the samples for LC/MS/MS analysis, using a 96-well SPE plate and without automated SPE clean-up.

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of Penoxsulam in Rice Grain and Straw.

Matrix	Spiking Level (ppm)	Recoveries Obtained	Mean Recovery ± SD [CV]
Rice grain	0.01	80, 92, 95, 100, 117	97 ± 10.2 [10.5]
	0.02	87, 92	
	0.10	88, 102, 102, 104, 108	
Rice straw; second trial	0.01	103, 107, 109, 113, 119	107 ± 5.9 [5.6]
	0.02	105, 112	
	1.00[1]	99, 101, 101, 102, 108	

[1] The samples fortified at 1.0 ppm were diluted 5x and re-injected; the actual recoveries from undiluted samples were not provided.

D. CONCLUSIONS

Adequate method validation data have been submitted for the proposed LC/MS/MS enforcement method, GRM 01.25, for residues of penoxsulam in/on rice commodities (grain, forage, straw, hulls, bran, and polished rice). A successful ILV has been completed with rice grain and straw. Because the extraction procedures of the proposed enforcement method are similar to those used in the rice metabolism study, radiovalidation data will not be required. The LC/MS/MS method has been submitted to ACB for regulatory agency validation (PMV).

In conjunction with the rice field trial and processing studies, adequate concurrent method validation data were submitted for the LC/MS/MS method used for data collection for residues of penoxsulam in/on rice forage, straw, grain, hulls, bran, and polished rice. The proposed LC/MS/MS enforcement method was used for data collection for residues of penoxsulam in/on rice commodities.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04).
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Template Version April 2003

Primary Evaluator	William Cutchin, Chemist SIMB/HED	Date: 7/19/04
Reviewer	Richard Loranger, BSS RAB2/HED	7/22/04 for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874	

STUDY REPORT

45830719 McCormick, R.; Rutherford, L.; Schelle, L. (2002) Magnitude of Residue of XDE-638 in Rice and Rice Processed Products: Lab Project Number: 010063. Unpublished study prepared by Dow AgroSciences LLC. 135 p.

EXECUTIVE SUMMARY

In rice processing studies conducted in MS and CA, mature rice grain was harvested 62 or 92 days following a single broadcast application of the 2 lbs ai/gal suspension concentrate formulation (MS trial) or the 0.11% G formulation (CA trial), respectively, at 0.18 lb ai/A (2x the application rate used in the crop field trials; see 860.1500 DER for MRID 45830719). The suspension concentrate formulation was applied as a broadcast foliar spray to rice at the 32 BBCH growth stage, using water containing a crop oil concentrate. The G formulation was applied directly to flooded rice, ~40 days after seeding, when the permanent flood was established.

Residues of penoxsulam were nondetectable (<0.002 ppm) in/on rice grain treated with the suspension concentrate or G formulation, and residues were nondetectable in hulls, bran, and polished rice processed from treated rice grain. Processing factors could not be determined because the residue levels were nondetectable in both the RAC and processed commodities. The maximum theoretical concentration factor for rice is 8x (OPPTS 860.1520, Table 1), based on concentration factors of 5x for hulls and 7.7x for bran (OPPTS 860.1520, Table 3).

The petitioner did not address the issue of conducting field trials on rice at higher rates, to potentially generate samples containing detectable or quantifiable residues; however, in the rice metabolism study (refer to the DER for MRID 45830712), it was noted that phytotoxic effects were observed in plants treated at 150 g ai/ha, which is equivalent to 0.13 lb ai/A.

Residues of penoxsulam in/on rice grain and its processed commodities were quantitated using the proposed LC/MS/MS enforcement method (GRM 01.25). The reported limit of detection (LOD) and limit of quantitation (LOQ) were 0.002 ppm and 0.01 ppm, respectively, for all rice

matrices. This method is adequate for data collection based on acceptable concurrent method recovery and method validation data (refer to the DER for MRID 45830714).

The maximum storage intervals from sample collection to analysis were 58 days (1.9 months) for rice grain and 135 days (4.4 months) for rice processed commodities. The available storage stability data (refer to the DER for MRID 45830717) demonstrate that residues of penoxsulam were stable under frozen conditions for up to 210 days (6.9 months) in rice grain and 197 days (6.5 months) in rice hulls, bran, and polished rice. These data are adequate to support the storage conditions and intervals of samples from the submitted rice processing study.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the rice processing study residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would impact the validity of the study.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

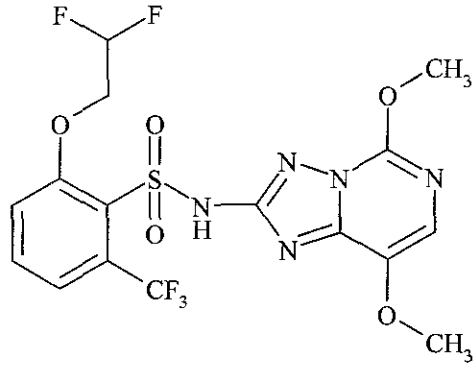
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Melting point/range	Not available		
pH	Not available		
Density	Not available		
Water solubility	pH	Solubility (mg/L)	MRID 45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	MRID 45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		MRID 45830720
Dissociation constant, pK_a	5.1		MRID 45830720

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.			
Parameter	Value		Reference
Octanol/water partition coefficient, Log(K_{ow})	pH	Log(K_{ow})	MRID 45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

TABLE B.1.2. Study Use Pattern.								
Location: City, State; Year	EP[1]	Application						Tank Mix Adjuvants
		Timing	Rate (lb ai/A)	RTI[2] (days)	Treat. No.	Method	Total Rate (lb ai/A)	
Greenville, MS; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 31 inches tall	0.18	N/A	1	Foliar broadcast spray	0.18	Crop oil concentrate (2.5%)
Fresno, CA; 2001	0.11% G	22 BBCH; 16 inches tall	0.18	N/A	1	Broadcast to flooded rice	0.18	None

[1] EP = End-use Product
[2] RTI = Retreatment Interval; N/A = not applicable; only one application was made.

B.2. Processing Procedures

A processing flowchart was not provided.

Rice grain samples were shipped frozen to STAR-Coastal (location not provided) for processing into hull, bran, and polished rice. The grain was dried to 12% moisture and cleaned in a grain cleaner to remove foreign particles. The hulls were then removed from the cleaned grain using a rice huller. The remaining brown rice (hulled grain) was milled to obtain polished rice and bran. Processing of rice grain into hulls, bran and polished rice was completed within 10 days of harvest. No material balance information or any additional details concerning the processing procedures were provided.

B.3. Analytical Methodology

Samples of rice grain and processed hulls, bran, and polished rice were analyzed for residues of penoxsulam using Dow AgroSciences Method GRM 01.25, the proposed enforcement method. A complete description of the method is provided in the DER for MRID 45830714.

Briefly, samples of rice grain and its processed commodities were extracted with ACN:water (8:2; v:v) and centrifuged. An aliquot of the supernatant was diluted with water and purified by solid-phase extraction. Residues were eluted with ACN:formic acid (99.9:0.1, v:v), evaporated

to dryness, and redissolved in ACN:methanol:water (15:15:70, v:v:v) mobile phase containing 0.1% acetic acid for analysis by LC/MS/MS. The reported LOD was 0.002 ppm, and the LOQ was 0.01 ppm for all rice matrices.

C. RESULTS AND DISCUSSION

In two trials, mature rice grain was harvested 62 or 92 days following a single broadcast application of the 2 lbs ai/gal suspension concentrate or 0.11% G formulation, respectively, at 0.18 lb ai/A (2x the field trial application rate). The suspension concentrate formulation was applied as a broadcast foliar spray to rice at the 32 BBCH growth stage using ground equipment in 11.4 gal/A water with a crop oil concentrate (2.5%). The G formulation was applied directly to flooded rice, ~40 days after seeding, when the permanent flood was established. The maximum theoretical concentration factor for rice is 8x (OPPTS 860.1520, Table 1).

Residues of penoxsulam in/on rice grain and its processed commodities were quantitated using the proposed LC/MS/MS enforcement method (GRM 01.25). Concurrent method validation data are presented in Table C.1. The reported LOD and LOQ were 0.002 ppm and 0.01 ppm, respectively, for all rice matrices; however, the lowest level of validation in the concurrent method recovery analyses was 0.015 ppm for each commodity. Adequate method validation data on rice matrices (including processed commodities) at the LOQ level were provided for the enforcement method (see the DER for MRID 45830714). This method is adequate for data collection based on acceptable concurrent and method validation recovery data.

Residues data from the study are presented in Table C.3. Residues of penoxsulam were nondetectable (<0.002 ppm) in/on rice grain (RAC) and hulls, bran, and polished rice processed from rice treated with either the suspension concentrate or G formulation. Processing factors could not be determined because the residue levels were nondetectable in both the RAC and processed commodities. Apparent residues of penoxsulam were reported as nondetectable in/on two samples each of untreated rice grain, hulls, bran, and polished rice.

The petitioner did not address the issue of conducting field trials on rice at higher rates, to potentially generate samples containing detectable or quantifiable residues; however, in the rice metabolism study (refer to the DER for MRID 45830712), it was noted that phytotoxic effects were observed in plants treated at 150 g ai/ha, which is equivalent to 0.13 lb ai/A.

Sample storage conditions and intervals are summarized in Table C.2. Bulk samples of rice grain were frozen at the field sites within 4 hours of sampling and were shipped frozen to STAR-Coastal for processing. Rice grain samples were processed within 10 days of harvest, and the frozen processed hull, bran, and polished rice samples were shipped overnight to Dow AgroSciences for analysis. The maximum storage intervals from sample collection to analysis were 58 days (1.9 months) for rice grain and 135 days (4.4 months) for rice processed commodities. The available storage stability data (refer to the DER for MRID 45830717) demonstrate that residues of penoxsulam are stable under frozen conditions for up to 210 days (6.9 months) in rice grain and 197 days (6.5 months) in rice hulls, bran, and polished rice. These

data are adequate to support the storage conditions and intervals of samples from the submitted rice processing studies.

TABLE C.1. Summary of Concurrent Recoveries of Penoxsulam from Rice.

Matrix	Analyte	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev
Rice, grain	Penoxsulam	0.015	2	93, 96	96 ± 3
		0.15	1	99	
Rice, hulls	Penoxsulam	0.015	2	109, 110	112 ± 3
		0.075	2	111, 116	
Rice, bran	Penoxsulam	0.015	2	107, 108	109 ± 3
		0.15	1	112	
Polished rice	Penoxsulam	0.015	2	105, 116	110 ± 6
		0.15	1	109	

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temp. (°C)	Actual Storage Duration from Collection (Processing) to Analysis [1]	Limit of Demonstrated Storage Stability
Rice, grain	-20	28-58 days (0.9-1.9 months)	210 days[2]
Rice, hulls		95-135 days (3.1-4.4 months)	197 days in rice hulls, bran, and polished rice[2]
Rice, bran		95-135 days (3.1-4.4 months)	
Polished rice		95-135 days (3.1-4.4 months)	

[1] Rice grain was processed within 10 days of harvest.
[2] Refer to the DER for MRID 45830717.

TABLE C.3. Residue Data from Rice Processing Study with Penoxsulam.

RAC	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Penoxsulam Residues (ppm) [1]	Processing Factor
Rice Treated with the 2 lbs ai/gal Suspension Concentrate					
Rice	Grain (RAC)	0.18	62	ND	--
	Hulls			ND	No processing factor could be calculated because residues in the RAC and processed commodities were nondetectable.
	Bran			ND	
	Polished Rice			ND	
Rice Treated with the 0.11% G					
Rice	Grain (RAC)	0.18	92	ND	--
	Hulls			ND	No processing factor could be calculated because residues in the RAC and processed commodities were nondetectable.
	Bran			ND	
	Polished Rice			ND	

[1] Residues in the RAC and processed commodities were reported as nondetectable (ND); the reported LOD and LOQ were 0.002 and 0.01 ppm, respectively, in all rice matrices.

D. CONCLUSIONS

The submitted rice processing data reflect the use of penoxsulam as a suspension concentrate or G formulation to rice at 0.18 lb ai/A. Application of the suspension concentrate formulation was made to rice at the 32 BBCH growth stage, and application of the G formulation was made ~40 days after seeding, when the permanent flood was established. Residues of penoxsulam were nondetectable (<0.002 ppm) in/on rice grain (RAC) and hulls, bran, and polished rice processed from rice treated with either the suspension concentrate or G formulation. An acceptable method was used for quantitation of residues in/on rice grain and its processed commodities.

The petitioner did not address the issue of conducting field trials on rice at higher rates, to potentially generate samples containing detectable or quantifiable residues; however, in the rice metabolism study (refer to the DER for MRID 45830712), it was noted that phytotoxic effects were observed in plants treated at 150 g ai/ha, which is equivalent to 0.13 lb ai/A.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Template Version April 2003

Penoxsulam/XDE-638/PC Code 119031/Dow AgroSciences LLC
DACO 7.4.1/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3
Crop Field Trials - Rice

Primary Evaluator	William Cutchin, Chemist SIMB/HED	Date: 7/19/04 William Cutchin
Reviewer	Richard Loranger, BSS RAB2/HE	7/27/04 Michael A Doherty for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874	

STUDY REPORT

45830719 McCormick, R.; Rutherford, L.; Schelle, L. (2002) Magnitude of Residue of XDE-638 in Rice and Rice Processed Products: Lab Project Number: 010063. Unpublished study prepared by Dow AgroSciences LLC. 135 p.

EXECUTIVE SUMMARY

Dow AgroSciences LLC has submitted crop field trial data depicting the magnitude of the residue of penoxsulam in/on rice forage, straw, and grain following treatment with either a suspension concentrate (SC) or granular (G) formulation. A total of 16 rice field trials were conducted in Regions 4 (AR, LA, MS; 11 trials), 5 (MO; 1 trial), 6 (TX; 2 trials), and 10 (CA; 2 trials) during the 2001 growing season.

In separate plots at each field trial, a single application of the 2 lbs ai/gal suspension concentrate or 0.11% G formulation was made to rice plants at 0.090 lb ai/A. Application of the suspension concentrate formulation was made to rice at the 30-32 BBCH (Biologische Bundesanstalt, Bundessortenamt and Chemical) growth stage to target a 60-day PHI; the suspension concentrate formulation was applied as a foliar broadcast spray in water with crop oil concentrate (2.5%). Application of the G formulation was made to rice ~40 days after seeding, when the permanent flood was established (21-23 BBCH); the G formulation was applied directly (broadcast) to flooded rice. Samples of mature rice grain and straw were collected from both plots at each trial site. To evaluate residue decline, samples of immature rice forage were collected 0, 1, 3, 7, 14, and 21 days following treatment at two field trial sites.

Residues of penoxsulam in/on rice forage, straw, and grain were quantitated using the proposed LC/MS/MS enforcement method (GRM 01.25). The reported limit of detection (LOD) and limit of quantitation (LOQ) were 0.002 ppm and 0.01 ppm, respectively, for all rice matrices. This method is adequate for data collection based on acceptable concurrent method recovery and method validation data (refer to the DER for MRID 45830714).

The maximum storage intervals of crop samples from harvest-to-analysis were 68-101 days (2.2-3.3 months) for rice grain, straw, and immature forage. The available storage stability data (refer to the DER for MRID 45830717) demonstrate that residues of penoxsulam are stable for up to 210 days (6.9 months) of freezer storage in rice forage, straw, and grain. These data are adequate to support the storage conditions and intervals of samples from the submitted rice field trials.

Residues of penoxsulam were less than the method LOQ (<0.01 ppm) to 0.013 ppm in/on rice grain samples and <0.01 0.484 ppm in/on rice straw samples harvested 47-97 days following a single application of the suspension concentrate formulation at 0.088-0.093 lb ai/A. Residues of penoxsulam were less than the method LOQ (<0.01 ppm) in/on rice grain and straw samples harvested 64-101 days following a single application of the G formulation at 0.09 lb ai/A.

The petitioner collected samples of immature rice forage at multiple posttreatment intervals in two field trials (one suspension concentrate treatment and one G treatment) to evaluate residue decline. The residue decline data indicate that residues of penoxsulam in/on immature rice forage decrease with increasing sampling intervals. The petitioner stated that the half-life of penoxsulam residues in rice forage was less than 1 day for both formulations. We note that residue levels were much higher in samples treated with the suspension concentrate formulation than in samples treated with the G formulation.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the rice field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would impact the validity of the study.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated

as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

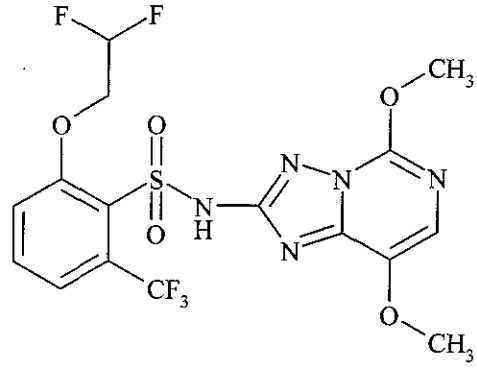
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Melting point/range	Not available		
pH	Not available		
Density	Not available		
Water solubility	pH	Solubility (mg/L)	MRID 45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	MRID 45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		MRID 45830720
Dissociation constant, pK_a	5.1		MRID 45830720
Octanol/water partition coefficient, $Log(K_{OW})$	pH	$Log(K_{OW})$	MRID 45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

TABLE B.1.1 Soil Characterization.

Trial Identifier: City, State; Year	Soil characteristics			
	Type	%OM	pH	CEC
Shoffner, AR; 2001	Silt loam	Not Applicable		
Newark, AR; 2001	Silt loam			
Proctor, AR; 2001	Silty clay loam			
Heth, AR; 2001	Clay			
Stuttgart, AR; 2001	Silt loam			
Tillar, AR; 2001	Silt loam			
Fresno, CA; 2001	Loam			
Live Oak, CA; 2001	Clay loam			
Washington, LA; 2001	Sandy loam			
Bunkie, LA; 2001	Clay			
Ville Platte, LA; 2001	*Silt loam*			
Bernie, MO; 2001	Silt loam			
Greenville, MS; 2001	Clay			
Walls, MS; 2001	Silty clay loam			
Brookshire, TX; 2001	Sandy loam			
East Bernard, TX; 2001	Clay loam			

Average monthly maximum and minimum temperatures and monthly rainfall, along with historical averages, were provided for the study period (not available electronically). All plots were flooded using typical production practices for rice production. The actual temperatures and rainfall were within typical environmental conditions for rice production. The petitioner noted that at the two CA sites, there was no rainfall between application and harvest; all other sites received at least some rainfall between application and harvest.

TABLE B.1.2. Study Use Pattern.

Trial ID: City, State; Year	EP[1]	Application					Tank Mix Adjuvants[3]
		Treat. No. and Crop Stage at Application	Rate (lb ai/A)	RTI[2] (days)	Method (GPA)	Total Rate (lb ai/A)	
Shoffner, AR; 2001	2 lbs ai/gal suspension concentrate	30-32 BBCH; 27-29 inches tall	0.090	N/A	Foliar broadcast (14.9 gal/A)	0.090	COC (2.5%)
	0.11% G	21-22 BBCH; 8-9 inches tall	0.09		Broadcast	0.09	None
Newark, AR; 2001	2 lbs ai/gal suspension concentrate	30-32 BBCH; 20-22 inches tall	0.093	N/A	Foliar broadcast (15.4 gal/A)	0.093	COC (2.5%)
	0.11% G	22 BBCH; 12 inches tall	0.09		Broadcast	0.09	None
Proctor, AR; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 26 inches tall	0.091	N/A	Foliar broadcast (18.3 gal/A)	0.091	COC (2.5%)
	0.11% G	23 BBCH; 10 inches tall	0.09		Broadcast	0.09	None
Heth, AR; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 25 inches tall	0.090	N/A	Foliar broadcast (18.1 gal/A)	0.090	COC (2.5%)
	0.11% G	23 BBCH; 12 inches tall	0.09		Broadcast	0.09	None
Stuttgart, AR; 2001	2 lbs ai/gal suspension concentrate	30-32 BBCH; 12-14 inches tall	0.090	N/A	Foliar broadcast (11.7 gal/A)	0.090	COC (2.5%)
	0.11% G	27-29 BBCH; 10-14 inches tall	0.09		Broadcast	0.09	None
Tillar, AR; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 22 inches tall	0.090	N/A	Foliar broadcast (10.9 gal/A)	0.090	COC (2.5%)
	0.11% G	32 BBCH; 22 inches tall	0.09		Broadcast	0.09	None
Fresno, CA; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 24 inches tall	0.090	N/A	Foliar broadcast (18.1 gal/A)	0.090	COC (2.5%)
	0.11% G	22 BBCH; 16 inches tall	0.09		Broadcast	0.09	None
Live Oak, CA; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 24 inches tall	0.091	N/A	Foliar broadcast (20.2 gal/A)	0.091	COC (2.5%)
	0.11% G	23 BBCH; 17 inches tall	0.09		Broadcast	0.09	None
Washington, LA; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 29 inches tall	0.090	N/A	Foliar broadcast (16.4 gal/A)	0.090	COC (2.5%)
	0.11% G	22 BBCH; 6 inches tall	0.09		Broadcast	0.09	None
Bunkie, LA; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 30 inches tall	0.093	N/A	Foliar broadcast (15.8 gal/A)	0.093	COC (2.5%)
	0.11% G	22 BBCH; 6 inches tall	0.09		Broadcast	0.09	None

TABLE B.1.2. Study Use Pattern.

Trial ID: City, State; Year	EP[1]	Application					Tank Mix Adjuvants[3]
		Treat. No. and Crop Stage at Application	Rate (lb ai/A)	RTI[2] (days)	Method (GPA)	Total Rate (lb ai/A)	
Ville Platte, LA; 2001	2 lbs ai/gal suspension concentrate	30-34 BBCH; 30 inches tall	0.091	N/A	Foliar broadcast (14.4 gal/A)	0.091	COC (2.5%)
	0.11% G	21 BBCH; 10 inches tall	0.09		Broadcast	0.09	None
Bernie, MO; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 24 inches tall	0.091	N/A	Foliar broadcast (18.3 gal/A)	0.091	COC (2.5%)
	0.11% G	23 BBCH; 10 inches tall	0.09		Broadcast	0.09	None
Greenville, MS; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 31 inches tall	0.088	N/A	Foliar broadcast (11.2 gal/A)	0.088	COC (2.5%)
	0.11% G	21 BBCH; 12 inches tall	0.09		Broadcast	0.09	None
Walls, MS; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 23 inches tall	0.091	N/A	Foliar broadcast (18.4 gal/A)	0.091	COC (2.5%)
	0.11% G	23 BBCH; 10 inches tall	0.09		Broadcast	0.09	None
Brookshire, TX; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 23-26 inches tall	0.090	N/A	Foliar broadcast (19.0 gal/A)	0.090	COC (2.5%)
	0.11% G	30 BBCH; 22-24 inches tall	0.09		Broadcast	0.09	None
East Bernard, TX; 2001	2 lbs ai/gal suspension concentrate	32 BBCH; 28-32 inches tall	0.089	N/A	Foliar broadcast (14.4 gal/A)	0.089	COC (2.5%)
	0.11% G	25 BBCH; 13-15 inches tall	0.09		Broadcast	0.09	None

[1] EP = End-use Product
[2] RTI = Retreatment Interval; N A = not applicable; only one application was made.
[3] COC = Crop oil concentrate.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Region	Rice		
	Submitted	Requested	
		Canada	US
1			
1A			
2			
3			
4	11		11
5	1		1
5A			
5B			
6	2		2
7			
7A			
8			
9			
10	2		2
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
Total	16	0	16

B.2. Analytical Methodology

Duplicate samples of mature rice grain and straw were collected from each site, and duplicate samples of immature rice forage were collected at multiple sampling intervals from two trial plots. Samples of rice grain, straw, and immature forage were analyzed for residues of penoxsulam using Dow AgroSciences Method GRM 01.25, the proposed enforcement method. A complete description of the method is provided in the DER for MRID 45830714.

Briefly, samples of rice matrices were extracted with ACN:water (8:2; v:v) and centrifuged. An aliquot of the supernatant was diluted with water and purified by solid-phase extraction.

Residues were eluted with ACN:formic acid (99.9:0.1, v:v), evaporated to dryness, and redissolved in ACN:methanol:water (15:15:70, v:v:v, each phase containing 0.1% acetic acid) for analysis by LC/MS/MS. The reported LOD was 0.002 ppm, and the LOQ was 0.01 ppm for all rice matrices.

C. RESULTS AND DISCUSSION

The petitioner conducted a total of 16 rice field trials in Regions 4 (AR, LA, MS; 11 trials), 5 (MO; 1 trial), 6 (TX; 2 trials), and 10 (CA; 2 trials) during the 2001 growing season. The number and location of field trials are adequate with respect to geographic representation of residue data for rice.

The 16 rice field trials consisted of two plots treated with two different formulations of penoxsulam. A single application of the 2 lbs ai/gal suspension concentrate or 0.11% G formulation was made to rice plants at ~0.090 lb ai/A. Application of the suspension concentrate formulation was made to rice at the 30-32 BBCH growth stage to target a 60-day PHI; the suspension concentrate formulation was applied in 10.9-20.2 gal/A water with crop oil concentrate (2.5%) as a foliar broadcast spray using ground equipment (backpack or tractor mounted sprayer). Application of the G formulation was made to rice ~40 days after seeding, when the permanent flood was established; the G formulation was applied directly (broadcast) to flooded rice by hand or using a spreader.

Samples of mature rice grain and straw were collected from both treated plots (and the control plot) at each trial site. Samples of immature rice forage were collected 0, 1, 3, 7, 14, and 21 days following treatment from the plot treated with the suspension concentrate formulation at one field trial site (Greenville, MS) and from the plot treated with the G formulation at a different field trial site (Fresno, CA) to evaluate residue decline.

Residues of penoxsulam in/on rice forage, straw, and grain were quantitated using the proposed LC/MS/MS enforcement method (GRM 01.25). Concurrent method validation data are presented in Table C.1. The reported LOD and LOQ were 0.002 ppm and 0.01 ppm, respectively, for all rice matrices; however, the lowest level of validation in the concurrent method recovery analysis was 0.015 ppm for each commodity. Adequate method validation data on rice at the LOQ level were provided for the enforcement method (see the DER for MRID 45830714). This method is adequate for data collection based on acceptable concurrent and method validation recovery data.

Residues of penoxsulam in/on rice commodities are presented in Table C.3; a summary of residue data in rice RAC (grain and straw) is presented in Table C.4. Residues of penoxsulam were less than the method LOQ (<0.01 ppm) to 0.013 ppm in/on rice grain samples and <0.01-0.484 ppm in/on rice straw samples harvested 47-97 days following a single application of the suspension concentrate formulation at 0.088-0.093 lb ai/A. Residues of penoxsulam were less than the method LOQ (<0.01 ppm) in/on rice grain and straw samples harvested 64-101 days following a single application of the G formulation at 0.09 lb ai/A.

The petitioner collected samples of immature rice forage at multiple posttreatment intervals in two field trials (one suspension concentrate treatment and one G treatment) to evaluate residue decline. Average penoxsulam residues from the suspension concentrate trial decreased from 2.11 ppm on Day 0 to 0.012 ppm on Day 21 in rice forage, and average penoxsulam residues from the G trial decreased from 0.114 ppm on Day 0 to <0.01 ppm (LOQ) on Day 21 in rice forage. The petitioner stated that the half-life of penoxsulam residues in rice forage was less than 1 day for both formulations. We note that residue levels were much higher in samples treated with the suspension concentrate formulation than in samples treated with the G formulation.

Apparent residues of penoxsulam were nondetectable (<0.002 ppm) in/on 16 samples of untreated rice grain, 15 samples of untreated rice straw, and 11 samples of untreated rice forage; detectable residues were observed in/on one sample of rice straw and one sample of rice forage, each at 0.003 ppm.

Sample storage conditions and intervals are summarized in Table C.2. Duplicate samples of mature rice grain and straw were collected from each site, and duplicate samples of immature rice forage were collected at multiple sampling intervals from two trial plots. Samples were frozen at the field sites within four hours of collection and were shipped frozen to Dow AgroSciences (Indianapolis, IN), where samples were stored frozen until analysis. The maximum storage intervals of crop samples from harvest to analysis were 68-101 days (2.2-3.3 months) for rice grain, straw, and immature forage. The available storage stability data (refer to the DER for MRID 45830717) demonstrate that residues of penoxsulam are stable for up to 210 days (6.9 months) of freezer storage in rice forage, straw, and grain. These data are adequate to support the storage conditions and intervals of samples from the submitted rice field trials.

TABLE C.1. Summary of Concurrent Recoveries of Penoxsulam from Rice Matrices.

Matrix	Analyte	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev
Rice, grain	Penoxsulam	0.015	7	93, 96, 97, 100, 102, 110, 117	102 ± 8
		0.15	4	97, 98, 99, 117	
Rice, straw	Penoxsulam	0.015	9	91, 91, 92, 92, 96, 97, 98, 99, 100	96 ± 3
		0.15	4	95, 97, 98, 102	
		0.3	2	94, 96	
Rice, immature forage	Penoxsulam	0.015	6	99, 101, 103, 109, 111, 121	100 ± 9
		0.03	2	93, 99	
		1.5	2	88, 91	
		4.5	2	94, 95	

TABLE C.2. Summary of Storage Conditions.			
Matrix (RAC)	Storage Temp. (°C)	Actual Storage Duration from Harvest to Analysis	Limit of Demonstrated Storage Stability
Rice, grain	-20	9-77 days (0.3-2.5 months)	210 days (6.9 months) in rice grain, straw, and forage [1]
Rice, straw		10-68 days (0.3-2.2 months)	
Rice, immature forage		79-101 days (2.6-3.3 months)	

[1] Refer to the DER for MRID 45830717.

TABLE C.3. Residue Data from Crop Field Trials with Penoxsulam.						
Trial ID: City, State; Year	Region	Crop; Variety	Total Rate (lb ai/A)	Commodity or Matrix	PHI (days)	Penoxsulam Residues (ppm) [1]
	Rice	**Treated with the 2 lb/gal Suspension Concentrate Formulation**				
Shoffner, AR; 2001	4	Rice; Wells	0.090	Grain	58	ND, ND
				Straw	58	0.044, 0.096
Newark, AR; 2001	4	Rice; Cocodrie	0.093	Grain	60	ND, ND
				Straw	60	ND, *0.002*
Proctor, AR; 2001	4	Rice; Cocodrie	0.091	Grain	47	ND, ND
				Straw	47	0.061, 0.122
Heth, AR; 2001	4	Rice; Wells	0.090	Grain	58	ND, ND
				Straw	58	0.016, 0.016
Stuttgart, AR; 2001	4	Rice; Cocodrie	0.090	Grain	73	ND, ND
				Straw	73	*0.002, 0.004*
Tillar, AR; 2001	4	Rice; Cocodrie	0.090	Grain	64	ND, ND
				Straw	64	ND, *0.003*
Fresno, CA; 2001	10	Rice; M-202	0.090	Grain	69	0.012, 0.012
				Straw	69	0.441, 0.484
Live Oak, CA; 2001	10	Rice; M-202	0.091	Grain	57	0.012, 0.013
				Straw	57	0.188, 0.201
Washington, LA; 2001	4	Rice; Cypress	0.090	Grain	60	ND, ND
				Straw	60	*0.003, 0.004*
Bunkie, LA; 2001	4	Rice; Cocodrie	0.093	Grain	59	ND, ND
				Straw	59	0.017, 0.024
Ville Platte, LA; 2001	4	Rice; Wells	0.091	Grain	97	ND, ND
				Straw	97	0.029, 0.046
Bernie, MO; 2001	5	Rice; Cocodrie	0.091	Grain	66	ND, ND
				Straw	66	0.055, 0.108

TABLE C.3. Residue Data from Crop Field Trials with Penoxsulam.

Trial ID: City, State; Year	Region	Crop; Variety	Total Rate (lb ai/A)	Commodity or Matrix	PHI (days)	Penoxsulam Residues (ppm) [1]
Greenville, MS; 2001	4	Rice; Lemont	0.088	Forage	0	2.01, 2.22
					1	0.739, 0.837
					3	0.191, 0.228
					7	0.083, 0.126
					14	0.015, 0.011
					21	*0.008*, 0.014
				Grain	62	ND, ND
				Straw	62	ND, ND
Walls, MS; 2001	4	Rice; Wells	0.091	Grain	58	ND, ND
				Straw	58	ND, *0.006*
Brookshire, TX; 2001	6	Rice; Cocodrie	0.090	Grain	57	ND, ND
				Straw	57	0.029, 0.055
East Bernard, TX; 2001	6	Rice; Cocodrie	0.089	Grain	61	ND, ND
				Straw	61	*0.006*, *0.008*
Rice Treated with the 0.11% G Formulation						
Shoffner, AR; 2001	4	Rice; Wells	0.09	Grain	85	ND, ND
				Straw	85	ND, *0.002*
Newark, AR; 2001	4	Rice; Cocodrie	0.09	Grain	85	ND, ND
				Straw	85	ND, ND
Proctor, AR; 2001	4	Rice; Cocodrie	0.09	Grain	75	ND, ND
				Straw	75	ND, ND
Heth, AR; 2001	4	Rice; Wells	0.09	Grain	86	ND, ND
				Straw	86	ND, ND
Stuttgart, AR; 2001	4	Rice; Cocodrie	0.09	Grain	83	ND, ND
				Straw	83	ND, ND
Tillar, AR; 2001	4	Rice; Cocodrie	0.09	Grain	64	ND, ND
				Straw	64	ND, ND
Fresno, CA; 2001	10	Rice; M-202	0.09	Forage	0	0.094, 0.134
					1	0.030, 0.058
					3	0.016, 0.019
					7	*0.007*, 0.012
					14	*0.003*, *0.004*
					21	*0.002*, *0.002*
				Grain	92	ND, *0.002*
				Straw	92	*0.002*, *0.005*
Live Oak, CA; 2001	10	Rice; M-202	0.09	Grain	86	ND, ND
				Straw	86	ND, *0.004*

TABLE C.3. Residue D ata from Crop Field Trials with Penoxsulam.

Trial ID: City, State; Year	Regi	Crop; Variety	Total Rate (lb ai/A)	Commodity or Matrix	PHI (days)	Penoxsulam Residues (ppm) [1]
Washington, LA; 2001	4	Rice; Cypress	0.09	Grain	80	ND, ND
				Straw	80	ND, ND
Bunkie, LA; 2001	4	Rice; Cocodrie	0.09	Grain	78	ND, ND
				Straw	78	ND, ND
Ville Platte, LA; 2001	4	Rice; Wells	0.09	Grain	101	ND, ND
				Straw	101	ND, ND
Bernie, MO; 2001	5	Rice; Cocodrie	0.09	Grain	90	ND, ND
				Straw	90	ND, ND
Greenville, MS; 2001	4	Rice; Lemont	0.09	Grain	84	ND, ND
				Straw	84	ND, ND
Walls, MS; 2001	4	Rice; Wells	0.09	Grain	70	ND, ND
				Straw	70	ND, *0.008*
Brookshire, TX; 2001	6	Rice; Cocodrie	0.09	Grain	65	ND, ND
				Straw	65	ND, *0.002*
East Bernard, TX; 2001	6	Rice; Cocodrie	0.09	Grain	81	ND, ND
				Straw	81	ND, ND

[1] Nondetectable residues are rep rted as ND, and residues quantitated between the LOD and LOQ are italicized; the reported LOD and LOQ are 0.002 ppm a 1 0.01 ppm, respectively.

TABLE C.4. Summary f Residue Data from Crop Field Trials with Penoxsulam.

Commodity	Total Applic. Rate (lb ai/A); Formulation	PHI (days)	Analyte	Residue Levels (ppm) [1]					
				n	Min.	Max.	HAFT [2]	Mean	Std. Dev.
Rice, grain	0.088-0.093; suspension concentrate	47-97	Penoxsulam	32	ND	0.013	0.013	0.006	0.002
	0.09; G	64-101		32	ND	ND	<0.01	0.005	0
Rice, straw	0.088-0.093; suspension concentrate	47-97	Penoxsulam	32	ND	0.484	0.463	0.066	0.116
	0.09; G	64-101		32	ND	*0.008*	<0.01	0.005	0.001

[1] Nondetectable residues are rep rted as ND and residues quantitated between the LOQ and LOD are italicized. The study reviewer calculated the means a 1 standard deviations using ½ the LOQ for nondetectable residues and the actual residue value reported if >½ the LOQ.

[2] HAFT = Highest Average Fie Trial. Calculated by the study reviewer using the LOQ value for all nondetectable (ND) residues and for residues reporte between the LOQ and LOD.

D. CONCLUSION

The submitted rice field rial data reflect the use of penoxsulam as a single application of the suspension concentrate r G formulation to rice at 0.090 lb ai/A. Application of the suspension concentrate formulation vas made to rice at the 30-32 BBCH growth stage, and application of

the G formulation was made 40 days after seeding (21-23 BBCH), when the permanent flood was established. The residue decline data demonstrate that residues of penoxsulam decreased in immature rice forage with increasing sampling intervals. An acceptable method was used for quantitation of residues in/on rice commodities.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Template Version April 2003

Penoxsulam/XDE-638/PC Code 119031/Dow AgroSciences LLC
DACO 7.3/OPPTS 860.1380/OECD IIA 6.1.1 and IIIA 8.1.1
Storage Stability - Rice

Primary Evaluator	William Cutchin, Chemist HED/SIMB (7509C)	Date: 7/19/04	William Cutchin
Reviewer	Richard Loranger, Chemist HED/RAB2 (7509C)	7/22/04	Michael A Doherty for RAC
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874		

STUDY REPORT

45830717 Lindsay, D.; Miller, A.; Thomas, A. (2002) Frozen Storage Stability of XDE-638 in Rice (Raw Agricultural Commodities: Grain, Straw, Immature Forage) and its Processed Products (Bran, Hulls, Polished Rice)--Interim Report: Lab Project Number: 010100. Unpublished study prepared by Dow AgroSciences LLC. 78 p.

EXECUTIVE SUMMARY

Dow AgroSciences LLC has submitted the interim results of a 24-month storage stability study with penoxsulam. Untreated samples of homogenized rice grain, straw, immature forage, bran, hulls, and polished rice were fortified with penoxsulam at 0.10 ppm. The fortified samples were stored at -20 °C for up to 197 days (processed rice commodities) or 210 days (rice forage, grain, and straw). Under these conditions, residues of penoxsulam were relatively stable in rice grain, straw, immature forage, and processed rice commodities (bran, hulls, and polished rice).

Samples of rice matrices were analyzed for residues of penoxsulam using Dow AgroSciences Method GRM 01.25, an LC/MS/MS method. A complete description of the method is provided in the DER for MRID 45830714.

The interim storage stability data indicate that residues of penoxsulam are stable under frozen storage conditions in rice grain, straw, immature forage, bran, hulls, and polished rice for up to ~7 months. The petitioner stated that the full study will include storage intervals of up to 24 months for rice commodities.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA

Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported. An unsigned Quality Assurance statement was included, which noted that the data in the report are interim data and have not yet been audited.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

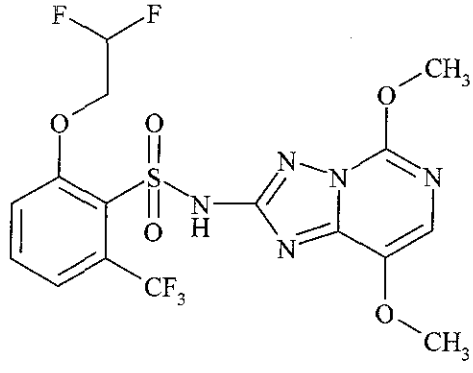
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value	Reference
Melting point/range	Not available	

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.			
Parameter	Value		Reference
pH	Not available		
Density	Not available		
Water solubility	pH	Solubility (mg/L)	MRID 45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	MRID 45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		MRID 45830720
Dissociation constant, pK_a	5.1		MRID 45830720
Octanol/water partition coefficient, $Log(K_{OW})$	pH	$Log(K_{OW})$	MRID 45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. EXPERIMENTAL DESIGN

B.1. Sample Preparation

Samples of untreated homogenized rice grain, straw, immature forage, bran, hulls, and polished rice were placed into polypropylene containers and fortified with penoxsulam at 0.10 ppm. Fortified samples were then stored frozen at -20 °C. The penoxsulam fortification standard was prepared in acetonitrile (ACN). Samples were fortified on a staggered schedule so that some samples were analyzed together and shared fresh fortification recoveries.

B.2. Analytical Methodology

Samples of fortified and unfortified rice matrices were analyzed for residues of penoxsulam using Dow AgroSciences Method GRM 01.25 following 0 and 210 days (RAC) or 0, 42, 83, and 197 days (processed commodities) of frozen storage. Fresh fortification samples of each rice matrix were analyzed for concurrent method recoveries. A complete description of the method is provided in the DER for MRID 45830714.

Briefly, homogenized samples of rice matrices were extracted with ACN:water (8:2; v:v) and centrifuged. An aliquot of the supernatant was diluted with water and purified by solid-phase extraction (SPE). Residues were eluted with ACN:formic acid (100:0.1, v:v), evaporated to dryness, and redissolved in ACN:methanol:water (15:15:70, v:v:v, each containing 0.1% acetic acid) for analysis by LC/MS/MS. The validated limit of quantitation (LOQ) was 0.01 ppm for all rice matrices. Although the petitioner made reference to "nondetectable" residues, no limit of detection was defined in the study. In the method submission (MRID 45830714), the LOD was defined as 0.002 ppm.

C. RESULTS AND DISCUSSION

The concurrent method validation data included in the study indicate that the LC/MS/MS method GRM 01.25 is adequate for the determination of residues of penoxsulam in/on rice grain, straw, immature forage, bran, hulls, and polished rice. Apparent residues were nondetectable (presumably <0.002 ppm) in all control (unfortified) samples (two samples each of rice grain, straw, and immature forage, and four samples each of bran, hulls, and polished rice).

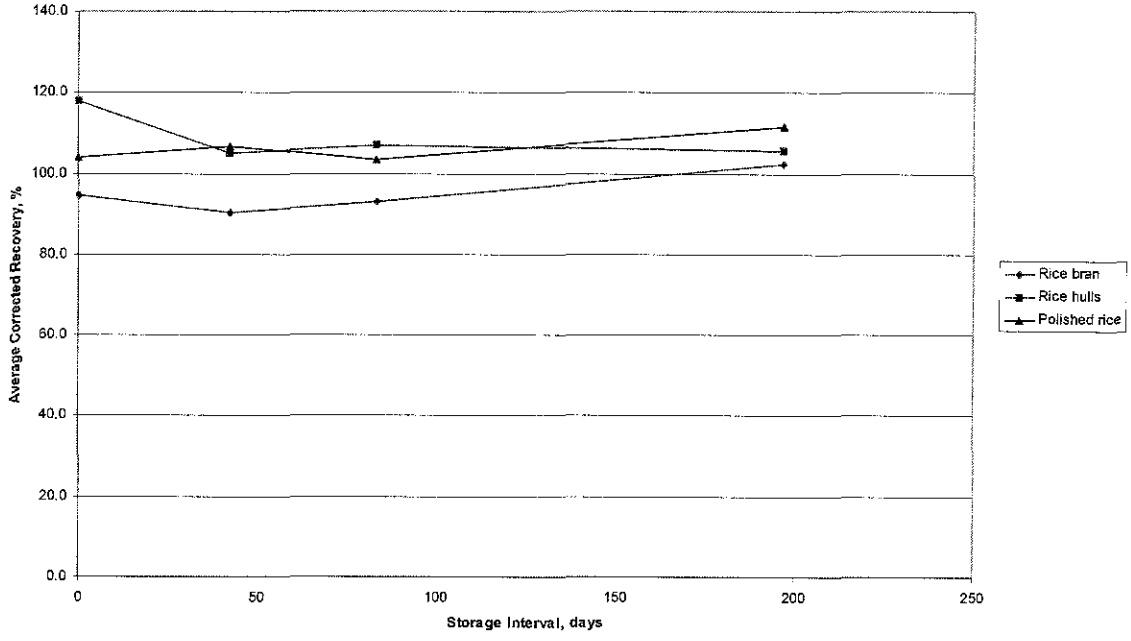
Residues of penoxsulam appear to be stable in rice grain, straw, and immature forage stored frozen for up to 210 days (6.9 months) and in processed rice commodities (bran, hulls, and polished rice) stored frozen for up to 197 days (6.5 months).

TABLE C.1. Summary of Concurrent Recoveries of Penoxsulam from Rice Matrices.

Matrix	Analyte	Spike level (ppm)	Storage Interval (days)	Sample size (n)	Recoveries (%)	Mean ± std dev
Rice grain	Penoxsulam	0.10	0	3	98, 100, 101	100 ± 1.5
			210	3	89, 96, 98	94 ± 4.7
Rice straw	Penoxsulam	0.10	0	3	100, 102, 104	102 ± 2.0
			210	3	92, 94, 97	94 ± 2.5
Rice forage	Penoxsulam	0.10	0	3	99, 102, 102	101 ± 1.7
			210	3	91, 97, 101	96 ± 5.0
Rice bran	Penoxsulam	0.10	0/42	3	83, 93, 132 [1]	88 ± 7.1
			83/197	3	95, 97, 100	97 ± 2.5
Rice hull	Penoxsulam	0.10	0/42	3	86, 88, 90	88 ± 2.0
			83/197	3	92, 95, 101	96 ± 4.6
Polished rice	Penoxsulam	0.10	0/42	3	90, 92, 94	92 ± 2.0
			83/197	3	97, 98, 101	99 ± 2.1

[1] This recovery value was not used in the mean and standard deviation calculation because it was considered by the petitioner to be an outlier.

FIGURE C.1. Graph of Residue Stability in Rice Processed Commodities.



Because only two time points were included in this interim report for rice grain, straw, and forage, a graph of residue stability was not created for these commodities.

TABLE C.2. Stability of Penoxsulam Residues in Rice Matrices Following Storage at 20 °C.				
Commodity	Spike level (ppm)	Storage interval (days)	Recovered residues (ppm)	Corrected % recovery [1]
Rice grain	0.10	0	0.088, 0.089, 0.092	88, 89, 92
		210	0.095, 0.097, 0.101	101, 103, 108
Rice straw	0.10	0	0.097, 0.099, 0.103	95, 97, 101
		210	0.113, 0.114, 0.115	120, 121, 122
Rice forage	0.10	0	0.098, 0.099, 0.104	97, 98, 103
		210	0.115, 0.116, 0.123	120, 121, 128
Rice bran	0.10	0	0.078, 0.078, 0.093	89, 89, 106
		42	0.073, 0.078, 0.085	83, 90, 98
		83	0.087, 0.091, 0.092	90, 94, 95
		197	0.097, 0.100, 0.101	100, 103, 104
Rice hull	0.10	0	0.101, 0.103, 0.108	114, 117, 123
		42	0.078, 0.100, 0.100	89, 113, 113
		83	0.101, 0.104, 0.104	105, 108, 108
		197	0.097, 0.100, 0.107	101, 104, 112
Polished rice	0.10	0	0.094, 0.094, 0.098	102, 103, 107
		42	0.096, 0.097, 0.100	105, 106, 109
		83	0.097, 0.100, 0.107	99, 102, 109
		197	0.107, 0.109, 0.113	109, 111, 115

[1] Corrected for average concurrent method recoveries.

D. CONCLUSIONS

The submitted interim storage stability study adequately demonstrates the stability of penoxsulam residues in rice matrices stored frozen for ~7 months. The data indicate that residues of penoxsulam are relatively stable under frozen storage conditions in rice grain, straw, and immature forage for up to 210 days and in processed rice commodities (bran, hulls, and polished rice) for up to 197 days. The petitioner stated that the full study will include storage intervals of up to 24 months for rice commodities.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Template Version April 2003

DRAFT – Confidential, Internal, and Deliberative Material
Penoxsulam/XDE-638/PC Code 119031/Dow AgroSciences LLC
DACO 7.2.4/OPPTS 860.1360/OECD IIIA 5.3.1
Multiresidue Analytical Methods

Primary Evaluator	William Cutchin, Chemist SIMB/HED	Date: 7/19/04
Reviewer	Richard Loranger, BSS RAB2/HED	7/22/04 for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874	

STUDY REPORT

45830716 Anderson, C.; West, S. (2002) Multiresidue Method Testing for XDE-638 According to PAM I, Appendix II, as Updated January, 1994: Lab Project Number: 47420: 021184. Unpublished study prepared by ABC Laboratories, Inc. and Dow AgroSciences, LLC. 50 p.

EXECUTIVE SUMMARY

Penoxsulam was analyzed according to the FDA Multi-Residue Method Test guidelines in PAM Vol. I, Appendix II (1/94). Testing using Protocols B and G was not required because penoxsulam is not an acid, phenol, or substituted urea. When tested, penoxsulam did demonstrate natural fluorescence; however, no peak above the baseline was observed using the HPLC/UV system described under Section 401 DL2, therefore, Protocol A testing was terminated. Testing using Protocol C indicated that further testing through Protocols D, E, and F was required; poor sensitivity observed during the testing indicated that Florisil column clean-up would be required for Protocol D. Penoxsulam could not be recovered using the Florisil column clean-up test in Protocols E and F, and testing under these protocols was terminated. Because the Florisil column clean-up steps in Protocol D are similar to those of Protocols E and F, testing under Protocol D was not conducted.

Penoxsulam is not adequately recovered using any of the multiresidue methods.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the multiresidue method data are classified as scientifically acceptable. These data has been forwarded to FDA for further evaluation.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would impact the validity of the study.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

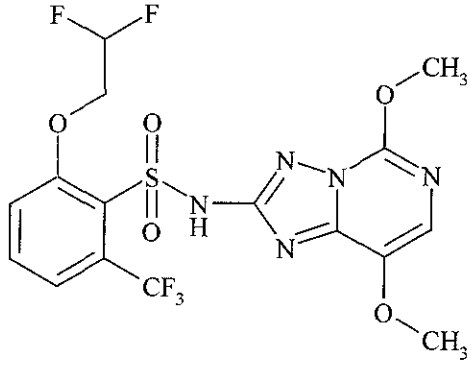
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value	Reference
Melting point/range	Not available	
pH	Not available	

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Density	Not available		
Water solubility	pH	Solubility (mg/L)	45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		45830720
Dissociation constant, pK_a	5.1		45830720
Octanol/water partition coefficient, $Log(K_{OW})$	pH	$Log(K_{OW})$	45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. MATERIALS AND METHODS

Penoxsulam was analyzed according to the FDA Multi-Residue Method Test guidelines in PAM Vol. I, Appendix II (1/94). Testing using Protocols B and G was not required because penoxsulam is not an acid or phenol, and is not a substituted urea. Penoxsulam was tested through Protocols A, C, E, and F. Protocol D testing required Florisil clean-up due to the lack of a selective detector for penoxsulam, and testing was not conducted because of poor Florisil clean-up recoveries in Protocols E and F.

C. RESULTS AND DISCUSSION

TABLE C.1. Results of Multiresidue Methods Testing with Penoxsulam.

PAM I Protocol	Results	Comments
A	Penoxsulam was found to be naturally fluorescent; however, no peak above the baseline was observed using the HPLC/UV system described under Section 401 DL2. Protocol A testing was terminated.	

TABLE C.1. Results of Multiresidue Methods Testing with Penoxsulam.

PAM I Protocol	Results	Comments
B		Not evaluated because penoxsulam is not an acid or phenol.
C	Penoxsulam did not chromatograph acceptably under Level I conditions using three columns, DB-1, DB-17, and DB-225, with electron capture detection (ECD) at 200 °C. Level II testing was performed using the DB-1 column with ECD and electrolytic conductivity detection in the halogen mode (ELCD-X) at 230 °C. Using ECD, two peaks were observed, one peak within the acceptable relative retention time limits and one peak outside the limits. Using ELCD-X, two peaks were observed, both within the limits but with low sensitivity.	
D		The results of Protocol C testing indicated that Florisil column clean-up would be required for Protocol D. Testing under Protocol D was not conducted because penoxsulam was not recovered from the similar Protocol E/F Florisil column clean-up steps.
E	No penoxsulam was observed to elute (0% recovery) through the Florisil clean-up steps 303/304 C1 or C2. Testing under Protocols E and F was terminated.	
F		
G		Not evaluated because penoxsulam is not a substituted urea compound.

D. CONCLUSION

The results of the study indicate that the FDA Multiresidue Testing protocols in PAM Vol. I are not applicable to penoxsulam.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Template Version April 2003

Primary Evaluator	William Cutchin, Chemist HED/SIMB (7509C)	Date: 7/19/04	William Cutchin
Reviewer	Richard Loranger, Chemist HED/RAB2 (7509C)	7/22/04	Michael A Doherty for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874		

STUDY REPORT

45830713 Smith, J.; Savides, M. (2002) Nature of Residue Study in the Lactating Goat Using (Carbon 14)-XDE-638: Lab Project Number: 000277: 012559. Unpublished study prepared by Dow AgroSciences LLC. 127 p.

Addendum to 45830713 Smith, J; Dow AgroSciences LLC and Plant Sciences Inc., 5/4/04 (Attachment).

EXECUTIVE SUMMARY

Dow AgroSciences LLC has submitted a study investigating the metabolism of [triazolopyrimidine-2-^{14}C]penoxsulam and [phenyl-U-^{14}C]penoxsulam in goats. Radiolabeled penoxsulam was administered orally to a single lactating goat for each label, at an average of 10.1 ppm (TP label) or 12.4 ppm (PH label) in the diet. The goats were dosed once per day for five consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice. The in-life phase of the study was conducted by Ricerca LLC (Painesville, OH), and the analytical phase of the study was conducted by Dow AgroSciences (Indianapolis, IN).

Total radioactive residues (TRR) were 0.002-0.008 ppm in milk, nondetectable in muscle and fat (<0.006 and <0.004 ppm, respectively), 0.038 ppm in kidney, and 0.071 ppm in liver from a single goat dosed orally with **[triazolopyrimidine-2-^{14}C]penoxsulam**, and were <0.001-0.007 ppm in milk, nondetectable in muscle and fat, 0.051 ppm in kidney, and 0.058 ppm in liver from a single goat dosed orally with **[phenyl-U-^{14}C]penoxsulam**. Because the TRR in milk, muscle, and fat were <0.01 ppm, only the kidney and liver samples (both labels) were extracted for metabolite characterization. The majority of the TRR (~94-108% TRR) was extracted from goat kidney using ACN/water and ACN/HCl, but only 42-50% TRR was extracted from liver using these solvents. Base hydrolysis of the nonextractable residues of liver released additional radioactivity (~36-37% TRR). These methods adequately extracted residues from goat matrices. Material balances, based on solvent extractions, were 97-122% for kidney and liver. The

petitioner has provided data to indicate that the samples did not degrade over the duration of the goat metabolism study.

Total residues amounting to 77-92% and 24-33% TRR were identified in kidney and liver, respectively. Parent penoxsulam was the only residue identified in kidney, at 77-92% TRR (0.029-0.047 ppm), and was the major residue identified in liver, at 24-31% TRR (0.017-0.018 ppm). The 5-OH XDE-638 metabolite was tentatively identified in PH-label liver as a minor residue (3% TRR, 0.002 ppm). An unknown was also characterized as a minor residue (<5% TRR, ≤0.002 ppm) in kidney (TP label) and liver (TP and PH labels). Base hydrolysis released a significant amount of radioactivity (36-37% TRR, 0.021-0.024 ppm) from liver samples; however, further partitioning was unsuccessful, and no further identification of the hydrolysates was performed.

The petitioner proposed that penoxsulam is primarily excreted and not significantly metabolized in goats. Because no significant differences were observed between the two labels, the sulfonanilide bridge in penoxsulam does not appear to be cleaved as a result of goat metabolism. The petitioner concluded that the low levels of residues observed in milk and tissues, combined with the rapid excretion of residues, demonstrated that penoxsulam would not be expected to bioconcentrate in ruminants.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the livestock metabolism data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

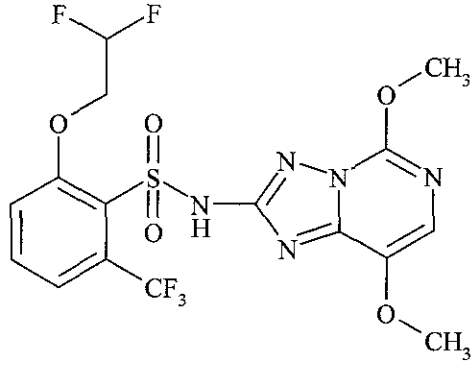
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Melting point/range	Not available		
pH	Not available		
Density	Not available		
Water solubility	pH	Solubility (mg/L)	MRID 45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	MRID 45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		MRID 45830720
Dissociation constant, pK_a	5.1		MRID 45830720

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.			
Parameter	Value		Reference
Octanol/water partition coefficient, Log(K_{OW})	pH	Log(K_{OW})	MRID 45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. EXPERIMENTAL DESIGN

B.1. Livestock

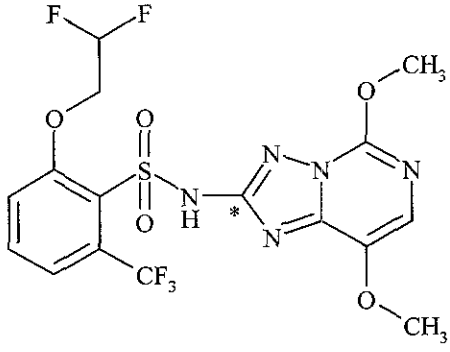
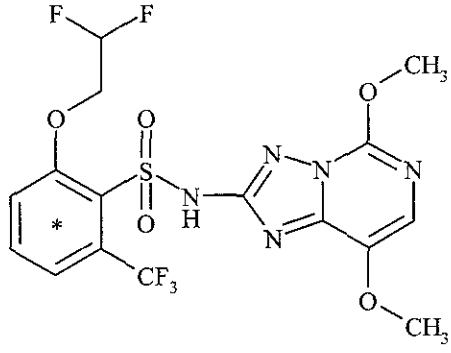
TABLE B.1.1. General Test Animal Information.					
Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Lactating goat (*Capra hircus*)	Not provided	1-2 years	38.80, 43.80	Appeared healthy throughout study	Stainless steel stanchions at Ricerca, LLC (Painesville, OH), at 16-27 °C, and 12 hour light/dark cycle.

TABLE B.1.2. Test Animal Dietary Regime.			
Diet	Water	Acclimation period	Predosing
Purina Rumilab® Diet (1.5 kg/day) and Purina Goat Chow® milking ration (200-250 g/milking)	Tap water, *ad libitum*	13 days; goats were free-ranged upon receipt, and caged for increasing periods of time. Goats were not caged for more than 5 straight days during the acclimation period.	None

TABLE B.1.3. Test Animal Dosing Regime.					
Treatment Type	Level of administered dose (mg/day)	Food consumption (g/day)	Residue intake in diet (ppm)	Vehicle	Timing/Duration
Oral	TP goat: 19.8	1922-2000	9.9-10.3 (10.1 average)	Gelatin capsule with cellulose, via bolus gun	Once per day after the morning milking for five consecutive days
	PH goat: 22	1648-1856	11.9-13.3 (12.4 average)		

B.2. Test Materials

TABLE B.2.1. Test Material Characteristics.

Chemical structure		
Radiolabel position	2-triazolopyrimidine labeled (TP)	Uniformly labeled on the phenyl ring (PH)
Lot No.	INV1456	INV1475
Purity	99%	98.4%
Specific activity	28.9 mCi/mmole; 18.02 µCi/mg (test substance)	24.6 mCi/mmole; 18.06 µCi/mg (test substance)
Code	N/A	N/A

The radiolabeled materials were diluted with nonlabeled penoxsulam and shipped to Ricerca, LLC.

B.3. Sampling Information

TABLE B.3.1. Sample Collection Information.

Milk collected	Urine, feces and cage wash collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Milk was collected twice daily. During the dosing period 743-899 (814 average) g/day/goat and 1086-1226 (1184 average) g/day/goat were collected (TP and PH label, respectively). During the acclimation period 645-1038 (813 average) g/day/goat and 822-1332 (996 average) g/day/goat were collected (TP and PH label, respectively).	Urine, feces, and cage washes collected daily	22 ± 2 hours	Kidney, liver, fat (composite of omental and perirenal), and muscle (composite of triceps, longissimus dorsi, and semimembranosus)

B.4. Identification/Characterization of Residues

B.4.1. Sample Preparation

Milk was collected twice daily, in the morning prior to dosing and in the afternoon; morning and afternoon milk samples were kept separate and frozen (<-15 C) if not radioassayed immediately

following collection. Tissue samples were chopped if necessary and were stored frozen (<-15 C) prior to homogenization for radioassay. Following radioassay, frozen samples of milk and homogenized tissues were shipped to Dow AgroSciences LLC, Regulatory Laboratories (Indianapolis, IN), where they were stored frozen (-20 °C) prior to residue characterization. Only the kidney and liver samples (both labels) were extracted for characterization of residues, because all milk, fat and muscle samples contained <0.01 ppm radioactivity.

Subsamples of liver and kidney were extracted with acetonitrile:water (50:50, v:v) at reflux for one hour, and the extract was isolated by centrifugation. The remaining nonextractable residues were extracted at reflux with acetonitrile:0.01 N HCl (90:10, v:v) for one hour; the extract was isolated by centrifugation. The acetonitrile/water extract was concentrated and diluted with 1% acetic acid for reverse phase C-18 solid phase extraction cleanup. Residues were eluted with acetonitrile (ACN), concentrated, and centrifuged for HPLC analysis. The ACN/HCl extract was not further characterized.

For liver, the solids remaining after extraction were subjected to base hydrolysis with 5 N NaOH; the conditions of hydrolysis were not described. The hydrolysate was partitioned with dichloromethane or dichloromethane:ACN (50:50, v:v), and the remaining aqueous phase was acidified with concentrated HCl and partitioned with dichloromethane.

B.4.2. Analytical Methodology

Total radioactive residues (TRR) in milk samples were determined by LSC, and TRR in kidney, liver, and muscle samples were determined by combustion/LSC. Fat samples were solubilized with 10% sodium hydroxide:methanol:triton (8:1:1, v:v:v) overnight at 60 °C prior to TRR determinations by LSC. The reported limit of detection for TRR determinations was 0.001-0.0013 ppm in milk and 0.004-0.007 ppm in tissues. Extracts and hydrolysates were radioassayed by LSC, and nonextractable residues were radioassayed by combustion/LSC.

ACN/water extracts of kidney and liver were analyzed by HPLC using a system equipped with a C-18 column, a UV detector, and a radiodetector; a gradient mobile phase of water and ACN, each containing 1.0% acetic acid, was used. Metabolites were identified by co-chromatography and/or retention time comparisons with those of unlabeled reference standards of penoxsulam and its 5-OH metabolite (5-OH XDE-638). Radioactivity was quantified by fraction collection/LSC.

LC/MS analyses were used to confirm the identification of penoxsulam in the ACN/water extract of liver (PH-label). Both the sample and reference standard were analyzed using the HPLC conditions described above with MS and MS/MS detection using electrospray ionization.

C. RESULTS AND DISCUSSION

Total radioactive residues (TRR) in goat milk and tissues are reported in Table C.2.1. TRR were 0.002-0.008 ppm in milk, nondetectable in muscle and fat (<0.006 and <0.004 ppm,

respectively), 0.038 ppm in kidney, and 0.071 ppm in liver from a single goat dosed orally with **[triazolopyrimidine-2-^{14}C]penoxsulam** at 10.1 ppm in the diet for 5 consecutive days. TRR were <0.001-0.007 ppm in milk, nondetectable in muscle and fat, 0.051 ppm in kidney, and 0.058 ppm in liver from a single goat dosed orally with **[phenyl-U-^{14}C]penoxsulam** at 12.4 ppm in the diet for 5 consecutive days. For both labels, radioactivity was highest in liver and lowest in muscle and fat; very low levels were observed in milk collected throughout the dosing period, and residues appeared to plateau in milk within the first day of dosing. The majority of the administered dose was excreted; urine, feces, and cage wash accounted for ~99-101% of the administered dose.

The distribution of radioactivity in goat commodities is reported in Tables C.2.2.1 (TP label) and C.2.2.2 (PH label). Because the TRR in milk, muscle, and fat were <0.01 ppm, only the kidney and liver samples (both labels) were extracted for metabolite characterization. The majority of the TRR (~94-108% TRR) was extracted from goat kidney using ACN/water and ACN/HCl, but only 42-50% TRR was extracted from liver using these solvents. Base hydrolysis of the nonextractable residues of liver released additional radioactivity (~36-37% TRR). These methods adequately extracted residues from goat matrices. Nonextractable residues accounted for 14-15% TRR (0.007-0.010 ppm) in goat kidney and were not reported for liver samples following base hydrolysis; however, material balances, based on solvent extractions, were 97-122% for kidney and liver.

The characterization and identification of radioactive residues is summarized in Tables C.2.3.1 (TP label) and C.2.3.2 (PH label). Total residues amounting to 77-92% and 24-33% TRR were identified in kidney and liver, respectively. Parent penoxsulam was the only residue identified in kidney, at 77-92% TRR (0.029-0.047 ppm), and was the major residue identified in liver, at 24-31% TRR (0.017-0.018 ppm). The 5-OH XDE-638 metabolite was tentatively identified in PH-label liver as a minor residue (3% TRR, 0.002 ppm). An unknown was also characterized as a minor residue (<5% TRR, ≤0.002 ppm) in kidney (TP label) and liver (TP and PH label).

For liver, base hydrolysis released a significant amount of radioactivity (36-37% TRR, 0.021-0.024 ppm). However, no radioactivity partitioned into dichloromethane or dichloromethane/ACN from the base hydrolysate, and no radioactive residues were liberated from the aqueous phase of the base hydrolysate when acidified and partitioned with dichloromethane. No further attempts were made to characterize the nonextractable residues.

C.1. Storage Stability

Total radioactive residues were determined for milk and tissue samples at the in-life facility prior to shipment to the analytical laboratory, within 21 days following sacrifice, and only kidney and liver samples were further analyzed. The study dates included in the submission indicated that initial extraction and analysis of samples was conducted within 135 days of sample collection, and final extraction or analysis of samples was conducted within 300 days of sample collection. Samples were kept frozen at either <-15 or 20 °C. Comparative analyses were conducted on Sample A extracts, those with sufficient radioactivity for further processing, at 135 (within the

recommended 4-6 month storage interval) and 300 days after sample collection. Results of the two analyses were similar. No additional storage stability data are required to support this study.

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temp. (°C)	Actual Storage Duration	Limit of Demonstrated Storage Stability
Goat, milk, muscle, and fat	<-15	<1 month	Samples stable up to 300 days
Goat, kidney	-20	Initial analysis: 135 days (4.4 months) Final analysis: 300 days (9.9 months)	
Goat, liver			

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Goat Milk, Tissue and Excreta.

Matrix	Collection Timing	TP label		PH label	
		ppm	% Administered Dose	ppm	% Administered Dose
Urine	Day 1	5.81	7.49	6.91	10.4
	Day 2	5.22	8.04	4.90	8.46
	Day 3	5.13	8.68	6.14	9.14
	Day 4	3.76	6.24	6.52	7.74
	Day 5	5.13	8.55	5.59	10.9
Feces	Day 1	4.29	6.92	5.36	7.78
	Day 2	7.79	13.4	6.10	8.72
	Day 3	8.23	12.7	8.62	11.6
	Day 4	7.96	12.5	9.04	12.0
	Day 5	9.21	15.4	6.47	11.3
Cage Washes	Day 1	0.554	0.15	0.930	0.25
	Day 2	2.42	0.62	0.541	0.12
	Day 3	0.756	0.13	1.70	0.09
	Day 4	0.428	0.14	0.794	0.21
	Day 5	0.301	0.19	0.414	0.29
Total Excreta	Study duration	--	101.15	--	99
Muscle	At termination	<0.006	0.00	<0.006	0.00
Fat	At termination	<0.004	0.00	<0.004	0.00
Kidney	At termination	0.038	0.00	0.051	0.01
Liver	At termination	0.071	0.06	0.058	0.04

TABLE C.2.1. Total Radioactive Residues (TRR) in Goat Milk, Tissue and Excreta.

Matrix	Collection Timing	TP label		PH label	
		ppm	% Administered Dose	ppm	% Administered Dose
Milk	Day 1, PM	0.008	0.001	0.007	0.002
	Day 1, AM	0.002	0.001	0.001	0.001
	Day 2, PM	0.006	0.002	0.005	0.002
	Day 2, AM	0.006	0.004	<0.001 (0.001)	0.001
	Day 3, PM	0.008	0.002	0.005	0.002
	Day 3, AM	0.002	0.001	0.001	0.001
	Day 4, PM	0.008	0.002	0.006	0.002
	Day 4, AM	0.003	0.002	0.002	0.001
	Day 5, PM	0.006	0.001	0.007	0.002
	Day 5, AM	0.004	0.003	0.002	0.002
Total	Study duration/termination	--	101.23	--	99.07

FIGURE C.2.1. Pharmacokinetics of Penoxsulam in Milk of Lactating Goat.

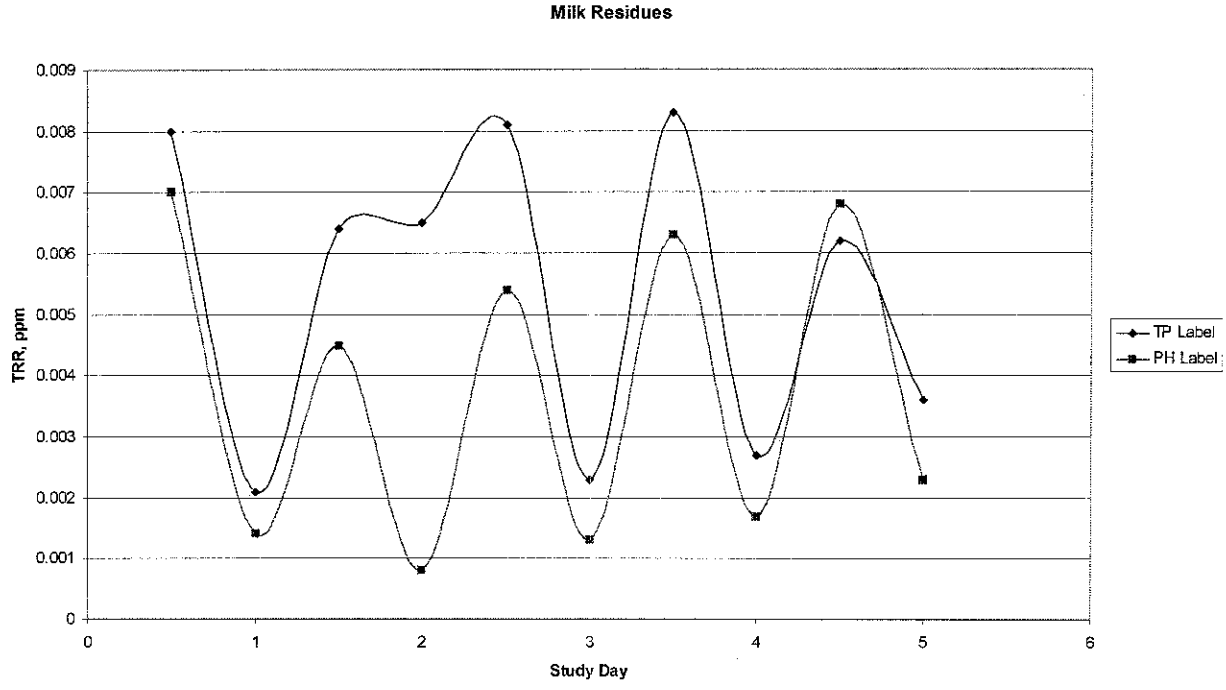


FIGURE C.2.1. Pharmacokinetics of Penoxsulam in Excreta of Lactating Goat.

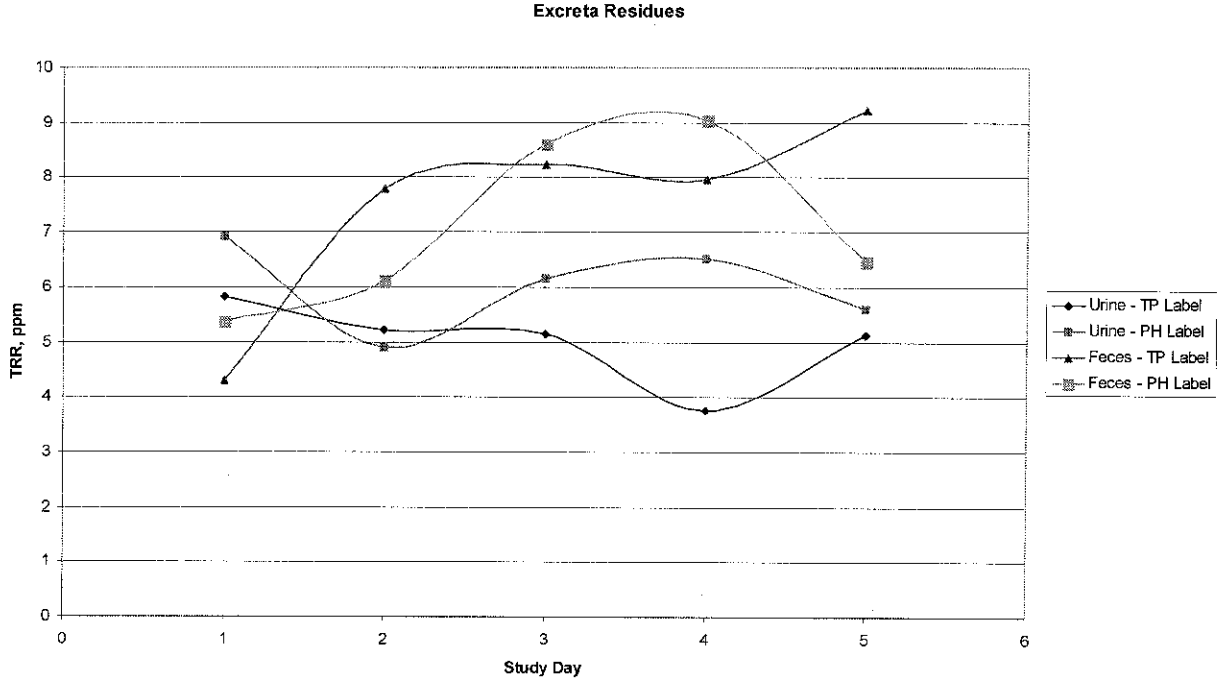


TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Livestock Matrices Following Dosing with [Triazolopyrimidine-2-^{14}C]Penoxsulam at 10.1 ppm in the Diet.[1]

Metabolite Fraction	Kidney		Liver	
	TRR = 0.038 ppm		TRR = 0.071 ppm	
	%TRR	ppm	%TRR	ppm
ACN/water extract	83.8	0.031	29.3	0.021
Penoxsulam	76.6	0.029	24.3	0.017
Unknown	4.3	0.002	2.4	0.002
ACN/HCl extract	10.6	0.004	12.2	0.009
Extracted solids			55.9	0.040
Base hydrolysate			35.8	0.026
Total extractable	94.4	0.035	77.3	0.056
Total identified	76.6	0.029	24.3	0.017
Total unidentified	14.9	0.006	50.4	0.036
Total bound residues (PES)	14.5	0.010	NR	NR
% Accountability	108.9		97.4 [2]	

[1] NR = Not reported. Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question. Ppm values for penoxsulam and the unknown were recalculated by the study reviewer because the values reported by the petitioner appeared to have been calculated incorrectly.
[2] Accountability for liver was calculated using extractable and nonextractable residues prior to base hydrolysis.

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Livestock Matrices Following Dosing with [Phenyl-U-^{14}C]Penoxsulam at 12.4 ppm in the Diet.[1]

Metabolite Fraction	Kidney		Liver	
	TRR = 0.051 ppm		TRR = 0.058 ppm	
	%TRR	ppm	%TRR	ppm
ACN/water extract	94.9	0.049	38.2	0.022
Penoxsulam	91.5	0.047	30.6	0.018
5-OH XDE-638	--	--	2.7	0.002
Unknown	--	--	2.3	0.001
ACN/HCl extract	13.1	0.007	11.4	0.007
Extracted solids			53.2	0.031
Base hydrolysate			36.5	0.021
Total extractable	108.0	0.056	86.1	0.050
Total identified	91.5	0.047	33.3	0.020
Total unidentified	13.1	0.007	50.2	0.029
Total bound residues (PES)	14.3	0.007	NR	NR
% Accountability	122.3		102.8 [2]	

[1] NR = Not reported. Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question. Ppm values for penoxsulam and the unknown were recalculated by the study reviewer because the values reported by the petitioner appeared to have been calculated incorrectly.
[2] Accountability for liver was calculated using extractable and nonextractable residues prior to base hydrolysis.

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Livestock Matrices Following Dosing with Triazolo-Pyrimidine-2- ^{14}C]Penoxsulam at 10.1 ppm in the Diet.

Compound	Kidney		Liver	
	TRR = 0.038 ppm		TRR = 0.071 ppm	
	% TRR	ppm	%TRR	ppm
Penoxsulam	76.6	0.029	24.3	0.017
Unknown	4.3	0.002	2.4	0.002
ACN/HCl extract	10.6	0.004	12.2	0.009
Base Hydrolysate	--	--	35.8	0.026
Total identified	76.6	0.029	24.3	0.017
Total characterized	14.9	0.006	50.4	0.036
Total extractable	94.4	0.035	77.3	0.056
Total bound	14.5	0.010	NR	NR

TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Livestock Matrices Following Dosing with [Phenyl-U- ^{14}C]Penoxsulam at 12.4 ppm in the Diet.

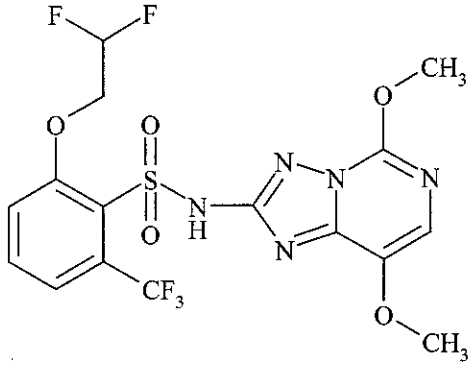
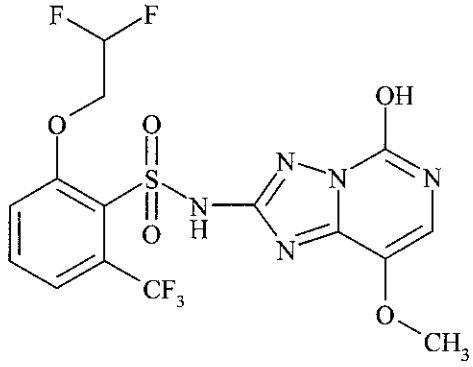
Compound	Kidney		Liver	
	TRR = 0.051 ppm		TRR = 0.058 ppm	
	% TRR	ppm	%TRR	ppm
Penoxsulam	91.5	0.047	30.6	0.018
5-OH XDE-638	--	--	2.7	0.002
Unknown	--	--	2.3	0.001
ACN/HCl extract	13.1	0.007	11.4	0.007
Base Hydrolysate	--	--	36.5	0.021
Total identified	91.5	0.047	33.3	0.020
Total characterized	13.1	0.007	50.2	0.029
Total extractable	108.0	0.056	86.1	0.050
Total bound	14.3	0.007	NR	NR

C.3. Proposed Metabolic Profile

FIGURE C.3.1. Proposed Metabolic Profile of Penoxsulam in Lactating Goat.

The petitioner did not propose a metabolic pathway for penoxsulam in goats.

TABLE C.3.1. Identification of Compounds from Metabolism Study.

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Penoxsulam; XDE-638	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]-pyrimidin-2-yl)-6-(trifluoromethyl)-benzenesulfonamide	
5-OH XDE-638	2-(2,2-difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo[1,2,4]triazolo[1,5-c]-pyrimidin-2-yl)-6-(trifluoromethyl) benzensulfonamide	

D. CONCLUSIONS

Total radioactive residues (TRR) were 0.002-0.008 ppm in milk, nondetectable in muscle and fat (<0.006 and <0.004 ppm, respectively), 0.038 ppm in kidney, and 0.071 ppm in liver from a single goat dosed orally with **[triazolopyrimidine-2-^{14}C]penoxsulam** at 10.1 ppm in the diet for 5 consecutive days. TRR were <0.001-0.007 ppm in milk, nondetectable in muscle and fat, 0.051 ppm in kidney, and 0.058 ppm in liver from a single goat dosed orally with **[phenyl-U-^{14}C]penoxsulam** at 12.4 ppm in the diet for 5 consecutive days. The majority of the administered dose was excreted; urine, feces, and cage wash accounted for ~99-101% of the administered dose.

The majority of the TRR (~94-108% TRR) was extracted from goat kidney using ACN/water and ACN/HCl, but only 42-50% TRR was extracted from liver using these solvents. Base hydrolysis of the nonextractable residues of liver released additional radioactivity (~36-37% TRR). The reported accountability, based on solvent extractions, ranged 97-122% for kidney and liver.

Total residues amounting to 77-92% and 24-33% TRR were identified in kidney and liver, respectively. Parent penoxsulam was the major residue identified in kidney and liver. The 5-OH XDE-638 metabolite was tentatively identified in PH-label liver as a minor residue. An unknown was also characterized as a minor residue in kidney (TP label) and liver (TP and PH labels). Base hydrolysis released a significant amount of radioactivity from liver samples, but residues could not be further characterized/identified.

The petitioner proposed that penoxsulam is primarily excreted and not significantly metabolized in goats. Because no significant differences were observed between the two labels, the sulfonanilide bridge in penoxsulam does not appear to be cleaved as a result of goat metabolism. The petitioner concluded that the low levels of residues observed in milk and tissues, combined with the rapid excretion of residues, demonstrated that penoxsulam would not be expected to bioconcentrate in ruminants.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Attachment: J. Smith, Dow AgroSciences,

Template Version April 2003

IN RESPONSE TO: Errico.Philip@epamail.epa.gov
SENT: Tuesday, May 04, 2004 2:20 PM

SUBJECT: Response to Additional Information Requested by Residue Chemistry for Penoxsulam

STUDY IDENTIFICATION: 45830713 Smith, J.; Savides, M. (2002)): Nature of Residue Study in the Lactating Goat Using (Carbon 14)-XDE-638: Lab Project Number: 000277: 012559.

REQUEST OF RESIDUE CHEMISTRY: "Total radioactive residues were determined for milk and tissue samples at the in-life facility prior to shipment to the analytical laboratory, within 21 days following sacrifice, and only kidney and liver samples were further analyzed. The study dates included in the submission indicated that initial extraction and analysis of samples was conducted within 135 days of sample collection, and final extraction or analysis of samples was conducted within 300 days of sample collection. No further extraction and analysis dates were provided, and the petitioner did not state which analyses were conducted on the "final" date. The petitioner must submit additional information pertaining to storage stability, including all extraction and analysis dates for each sample, and provide evidence that the identity of residues did not change during the period between collection and final analysis."

EPA Response:
RESPONSE OF PETITIONER:

Background: Samples collected from the lactating goat were milk, urine, feces, muscle, fat, liver and kidney. Only the liver and kidney tissues contained >0.01 ppm, and were subsequently analyzed.

The following tissue samples (135 days after collection for liver and 156 days for kidney) were initially extracted as summarized below:

Date	Sample	Extractions
15 Feb 01	Goat (TP label) liver	A, B, base hydrolysis and combustion
15 Feb 01	Goat (PH label) liver	A, B, base hydrolysis and combustion
8 Mar 01	Goat (TP label) kidney	A, B, base hydrolysis and combustion
8 Mar 01	Goat (PH label) kidney	A, B, base hydrolysis and combustion

Extract A-reflux with acetonitrile
Extract B-reflux with acetonitrile:0.01 N HCl (90:10)

Base hydrolysis- reflux of NER tissue with 5 N NaOH

Sample extracts A contained radioactivity in sufficient quantities for further processing. For both tissues, the sample extracts were processed by solid phase extraction (SPE) and concentration and analyzed by high performance liquid chromatography (HPLC) on March 13, 14 and 25, 2001. HPLC raw data results are summarized below:

Sample	Retention time (minutes)	Compound	% of HPLC (raw data)	% of TRR	ppm
Goat TP liver Extract A	35 31	penoxsulam 5-OH	87.4 9.1	32.8 3.4	0.009 0.001
Goat PH liver Extract A	35 32	penoxsulam Unknown	82.2 7.0	32.5 2.8	0.007 0.001
Goat TP kidney Extract A	35	penoxsulam	94.9	76.0	0.023
Goat PH kidney Extract A	35 31	penoxsulam 5-OH	93.3 3.5	78.4 2.9	0.034 0.001

Data presented in the report (300 days after collection) were for samples extracted and processed by SPE and concentrated on July 30 and 31, 2001. Analysis was performed on August 15 and 16, 2001. HPLC raw data results are summarized below:

Sample	Retention time (minutes)	Compound	% of HPLC (raw data)	% of TRR	ppm
Goat TP liver Extract A	35 32	penoxsulam unknown	82.9 8.1	24.3 2.4	0.005 0.001
Goat PH liver Extract A	35 32 31	penoxsulam Unknown 5-OH	80.2 5.1 7.1	30.6 2.3 2.7	0.007 <0.001 0.001
Goat TP kidney Extract A	35 32	penoxsulam Unknown	91.4 5.1	76.6 4.3	0.024 0.001
Goat PH kidney Extract A	35	penoxsulam	96.4	91.5	0.045

The Residue Chemistry Guidelines (OPPTS 860.1300 Nature of the Residue – Plants, Livestock, section (d)(7)) recommend that storage stability data should not normally be required for samples analyzed within 4 to 6 months of collection, provided evidence is given that attempts were made to limit degradation of residues by appropriate storage of matrices and extracts during the analytical portion of the study. Samples were stored at -20 °C (page 13, report 000277). Data presented shows that the distribution among residues is consistent between analyses performed on March 13, 14 and 25, 2001, compared to August 15 and 16, 2001. The major component of all analysis presented in the report was parent penoxsulam and all sample recoveries were between 84.7 and 100.2

% of applied (page 16, report 000277). This provides evidence that the identity of the residues did not change during the storage period.

Additional questions concerning the storage or any other aspect of this study may be directed to the study director:

Joelene Smith
Dow AgroSciences
(317) 337-3459
jksmith@dow.com

Primary Evaluator	William Cutchin, Chemist HED/SIMB (7509C)	Date: 7/19/04 William Cutchin
Reviewer	Richard Loranger, Chemist HED/RAB2 (7509C)	7/22/04 Michael A Doherty for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874	

STUDY REPORT

45830720 Graper, L. (2002) A Confined Rotational Crop Study With (Carbon 14) XDE-638 Using Three Different Crops: Lab Project Number: 000266. Unpublished study prepared by Dow AgroSciences LLC and Research For Hire. 134 p.

Addendum to 45830720 Graper, L.; Dow AgroSciences LLC and Plant Sciences Inc., 5/4/04 (Attachment).

EXECUTIVE SUMMARY

Dow AgroSciences LLC has submitted a confined rotational crop study with [triazolopyrimidine-2-^{14}C]penoxsulam and uniformly ring-labeled [phenyl-U-^{14}C]penoxsulam. The radiolabeled test substances were applied directly to sandy loam soil in pots maintained outdoors at 0.045-0.046 lb ai/A (low treatment rate) or 0.090-0.093 lb ai/A (high treatment rate), and rotational kale, potato, and wheat were planted directly into that soil 90 days after treatment (DAT). The in-life phase of the study was conducted by Research for Hire (Porterville, CA), and the analytical phase was conducted by Dow AgroSciences (Indianapolis, IN).

Total radioactive residues (TRR) accumulated at ≥0.01 ppm in certain rotated crops planted 90 days following a single soil application of [triazolopyrimidine-2-^{14}C]penoxsulam (TP) at 0.045 and 0.093 lb ai/A, or [phenyl-U-^{14}C]penoxsulam (PH) at 0.046 and 0.090 lb ai/A. At the low treatment rate, TRR were >0.01 ppm in potato foliage (0.024 ppm from the TP plot and 0.047 ppm from the PH plot), wheat hay (0.021 ppm, PH plot only), and wheat straw (0.011 ppm, TP plot; 0.024 ppm, PH plot). At the higher treatment rate, TRR were >0.01 ppm in kale (0.014 ppm, TP plot only), potato foliage (0.038 ppm, TP plot; 0.062 ppm, PH plot), wheat hay (0.022 ppm, TP plot; 0.032 ppm, PH plot), and wheat straw (0.030 ppm, TP plot; 0.028 ppm, PH plot). TRR were <0.01 ppm in the following matrices: potato tuber (≤0.003 ppm), wheat forage (≤0.007 ppm), and wheat grain (<0.005 ppm) from both labels at both treatment rates; TP-treated kale (0.003 ppm) at the low treatment rate and PH-treated kale (≤0.008 ppm) at both treatment

rates; and TP-treated wheat hay (0.009 ppm) at the low treatment rate. TRR were generally higher in PH-treated commodities than in TP-treated commodities.

Only crop samples with TRR ≥0.008 ppm were extracted. Solvent extraction released 62-97% TRR from rotational crop matrices. The majority of the extractable residues remained in the aqueous phase after partitioning with dichloromethane, and only the organic phase of potato foliage was subjected to further partitioning. Nonextractable residues in rotational crop commodities ranged 4-31% TRR (<0.001-0.009 ppm). The extraction procedures released sufficient residues from rotational crop matrices; material balances were 84-107%. Samples were analyzed within 5 months of harvest. All samples were stored frozen. No further storage stability data are required to support this study.

Only the extracts of PH-treated potato foliage were analyzed by HPLC for metabolite identification. In all other samples, because the aqueous extracts contained <0.03 ppm and the organic extracts contained <0.01 ppm, no further characterization was attempted. Total identified residues were 8.4% and 38.9% TRR in PH-label potato foliage at the low and high treatment rates, respectively. The 5-OH metabolite was identified at 8.4-13.9% TRR (0.004-0.009 ppm), and a single unknown was characterized at approximately the same level (8.9-11.8% TRR, 0.004-0.007 ppm) in both the low and high treatment rate potato foliage. In addition, the 3-[[[2-(2,2-difluoroethoxy)-6-(trifluoromethyl) phenyl]sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylic acid (BSTCA) metabolite was identified in potato foliage from the high treatment rate, at 25.0% TRR (0.015 ppm). Three unknowns were also characterized, each present at ≤18.0% TRR (≤0.011 ppm). Residues were characterized/identified in potato foliage by HPLC analysis, and, because no confirmatory method was used, the identifications are considered tentative. However, because no parent was detected and no single component was present at >0.015 ppm in potato foliage, RAB2 concludes that these methods successfully identified the predominant residues in rotational crop matrices.

The petitioner proposed that the penoxsulam is metabolized in rotated potato foliage to 5-OH XDE-638 and BSTCA, and that both 5-OH XDE-638 and BSTCA are then metabolized to unknowns and nonextractable residues.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the confined rotational crop residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would impact the validity of the study.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

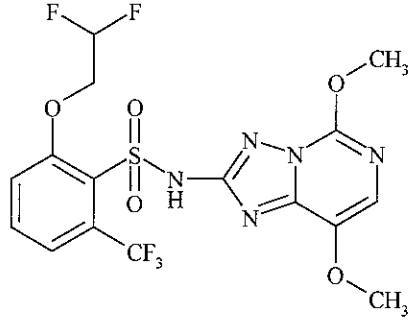
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value	Reference
Melting point/range	Not available	
pH	Not available	
Density	Not available	

TABLE A.2. Physicochemical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Water solubility	pH	Solubility (mg/L)	45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		45830720
Dissociation constant, pK_a	5.1		45830720
Octanol/water partition coefficient, $Log(K_{OW})$	pH	$Log(K_{OW})$	45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. EXPERIMENTAL DESIGN

B.1. Test Site and Crop Information

TABLE B.1.1. Test Site Information.

Testing Environment and location	Soil characteristics						
	Type	% Sand	% Silt	% Clay	%OM	pH	CEC (meq/100 g)
Plastic-lined boxes in outdoor plots at Research For Hire (Porterville, CA)	Sandy loam	74	20	6	0.7	7.2	6.9

The monthly minimum and maximum temperatures and precipitation were provided for the study period (not available electronically). Historical weather data were not provided; however, no unusual circumstances were noted. During the period between application of the test substance and planting of the rotational crops, the soil received 0.75 inches/A of water weekly. Irrigation of the rotated plants was conducted by hand as needed.

TABLE B.1.2. Crop Information.

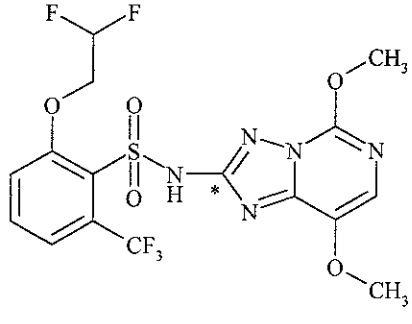
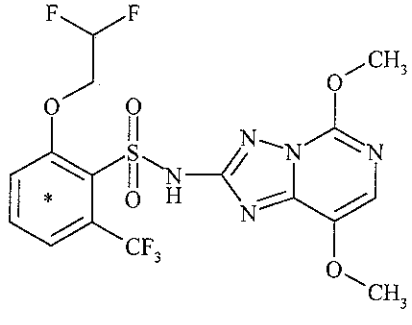
Crop; crop group	Variety	Plantback intervals (days)	Growth stage at harvest [1]	Harvested RAC	Harvesting procedure
Kale; Vegetable, *brassica*, leafy, group 5	Dwarf Blue Curled	90	Mature, 148-201 DAP	Leaves	Harvest methods were not specified.
Potato; Vegetable, root and tuber, group 1	White	90	Mature, 208 DAP	Tops (foliage)	
			Mature, 215 DAP	Tubers	
Wheat; Grain, cereal, group 15, and Grain, cereal, forage, fodder, and straw, group 16	Yecora Rojo	90	Immature, 97 DAP	Forage	Harvest method was not specified.
			Immature, 162 DAP	Hay	Hay was dried in a greenhouse for 11 days prior to collection.
			Mature, 204 DAP	Straw and grain	Grain was separated from the chaff, and the chaff was added to the straw sample.

[1] DAP = Days after planting.

We note that Swiss chard was grown with kale as an alternative leafy vegetable but was not allowed to mature once kale was chosen (77 days following planting) as the leafy vegetable to be grown to maturity. Phytotoxicity was observed in treated kale and potatoes (and Swiss chard) within two to three months of planting; however, six months after planting, treated kale and potatoes were growing and maturing normally.

B.2. Test Materials

TABLE B.2.1. Test Material Characteristics.

Chemical structure		
Radiolabel position	2-triazolopyrimidine labeled (TP)	Uniformly labeled on the phenyl ring (PH)
Lot No.	INV1456	INV1475
Purity	99%	98.4%
Specific activity	28.9 mCi/mmole; 40,700 dpm/µg (test substance)	24.6 mCi/mmole; 40,900 dpm/µg (test substance)
Code	N/A	N/A

The radiolabeled materials were dissolved in ACN and diluted with nonlabeled penoxsulam prior to shipment to Research For Hire.

B.3. Study Use Pattern

TABLE B.3.1. Use Pattern Information.	
Chemical name	[triazolopyrimidine-2-^{14}C]penoxsulam and [phenyl-U-^{14}C]penoxsulam
Application method	Each test substance was dissolved in ACN and diluted to volume with ACN for direct application to the soil surface using a backpack pressurized sprayer.
Application rate	A low-dose treatment was made to three boxes for each radiolabel, and a high-dose treatment was made to three other boxes for each radiolabel. TP-label: 0.045 lb ai/A (50.9 g ai/ha); 0.093 lb ai/A (104.1 g ai/ha) PH-label: 0.046 lb ai/A (51.1 g ai/ha); 0.090 lb ai/A (101.3 g ai/ha)
Number of applications	One
Timing of applications	90 days prior to the first planting rotation
PHI	N/A; application to bare soil

B.4. Identification/Characterization of Residues

B.4.1. Sample Preparation

Potato tuber samples were washed with water and gentle rubbing to remove adhering soil. Wheat grain was separated from the chaff, and the chaff was added to the straw sample. Except for wheat grain, all rotated crop samples were cut into smaller pieces prior to milling in the presence of dry ice or liquid nitrogen. Because of low TRR levels (<0.010 ppm) in potato tubers and wheat forage and grain from both labels at both treatment levels, and in kale from both labels at the low treatment level, only wheat hay and straw and potato foliage from both labels at both treatment levels, and kale from both labels at the higher treatment level were extracted.

In general, samples were extracted (3x) with acetonitrile:water (80:20, v:v) and vacuum filtered. The combined filtrates were concentrated and partitioned (3x) with dichloromethane, and the dichloromethane phases were combined.

The combined dichloromethane phases of PH-treated potato foliage (both treatment levels) were concentrated and partitioned between hexane and acetonitrile (ACN). The resulting ACN phase was concentrated, diluted with ACN and water, and filtered for HPLC analysis. A subsample of the aqueous phase of PH-treated potato foliage (high treatment level) remaining following dichloromethane partitioning was also concentrated to near dryness, diluted with water, and filtered for HPLC analysis.

B.4.2. Analytical Methodology

Total radioactive residues (TRR) in replicate (3-9) milled samples were determined by combustion/LSC. The combustion/LSC limit of quantitation (LOQ) was reported as 0.002 ppm

for wheat forage, kale, and potato tubers, and 0.005 ppm for wheat hay, straw, and grain, and potato foliage; the limit of detection (LOD) was reported as 0.001 ppm for all plant matrices. Radioactivity in the extracts was determined by LSC, and nonextractable radioactivity was determined by combustion/LSC.

Only the ACN and aqueous phases of the extracts of PH-treated potato foliage were analyzed by HPLC. In all other samples, because the aqueous extracts contained <0.03 ppm and the organic extracts contained <0.01 ppm, no further characterization was attempted. HPLC analyses were performed using a system equipped with a C-18 column, UV detector (254 nm), flow-through radioactivity detector, and fraction collector. A gradient mobile phase of water and ACN, each with 0.1% acetic acid, was used. Reference standards of unlabeled penoxsulam; 2-(2,2-difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl) benzenesulfonamide (5-OH XDE-638); 3-[[[2-(2,2-difluoroethoxy)-6-(trifluoromethyl) phenyl]sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylic acid (BSTCA); BSTCA, triethylammonium salt; and 2-(2,2-difluoroethoxy)-N-1H-1,2,4-triazol-3-yl-6-(trifluoromethyl)benzenesulfonamide (BST) were used. No confirmatory methods were used; therefore, all identifications were considered to be tentative. Fraction collection/LSC was used for quantitation of metabolites.

C. RESULTS AND DISCUSSION

TRR in rotational crops are reported in Table C.2.1. TRR accumulated at ≥0.01 ppm in certain rotated crops planted 90 days following a single soil application of [triazolopyrimidine-2-^{14}C]penoxsulam (TP) at 0.045 or 0.093 lb ai/A, or [phenyl-U-^{14}C]penoxsulam (PH) at 0.046 or 0.090 lb ai/A. At the low treatment rate, TRR were >0.01 ppm in potato foliage (0.024 ppm from the TP plot and 0.047 ppm from the PH plot), wheat hay (0.021 ppm, PH plot only), and wheat straw (0.011 ppm, TP plot; 0.024 ppm, PH plot). At the higher treatment rate, TRR were >0.01 ppm in kale (0.014 ppm, TP plot only), potato foliage (0.038 ppm, TP plot; 0.062 ppm, PH plot), wheat hay (0.022 ppm, TP plot; 0.032 ppm, PH plot), and wheat straw (0.030 ppm, TP plot; 0.028 ppm, PH plot). TRR were <0.01 ppm in the following matrices: potato tuber (≤0.003 ppm), wheat forage (≤0.007 ppm), and wheat grain (<0.005 ppm) from both labels at both treatment rates; TP-treated kale (0.003 ppm) at the low treatment rate and PH-treated kale (≤0.008 ppm) at both treatment rates; and TP-treated wheat hay (0.009 ppm) at the low treatment rate. TRR were generally higher in PH-treated commodities than in TP-treated commodities.

Only crops with TRR ≥0.008 ppm were subjected to extraction procedures. The distribution of radioactivity in the rotated crops, kale (high treatment rate only), potato foliage, and wheat hay and straw, is presented in Tables C.2.2.1 through C.2.2.4. Solvent extraction (ACN/water) released 62-97% TRR from rotational crop matrices. The majority of the extractable residues remained in the aqueous phase after partitioning with dichloromethane, and only the organic phase of potato foliage was subjected to further partitioning. Nonextractable residues in rotational crop commodities ranged 4-31% TRR (<0.001-0.009 ppm). These procedures extracted sufficient residues from rotational crop matrices.

Only the extracts of PH-treated potato foliage were analyzed by HPLC for metabolite identification; the characterization and identification of residues in PH-label potato foliage is summarized in Table C.2.3.1. Total identified residues were 8.4% and 38.9% TRR in PH-label potato foliage at the low and high treatment rates, respectively. The 5-OH metabolite was identified at 8.4-13.9% TRR (0.004-0.009 ppm), and a single unknown was characterized at approximately the same level (8.9-11.8% TRR, 0.004-0.007 ppm) in both the low and high treatment rate potato foliage. In addition, the BSTCA metabolite was identified in potato foliage from the high treatment rate, at 25.0% TRR (0.015 ppm). Three unknowns were also characterized, each present at ≤18.0% TRR (≤0.011 ppm).

Residues were characterized/identified in potato foliage by HPLC analysis, and, because no confirmatory method was used, the identifications are considered tentative. However, because no parent was detected and no single component was present at >0.015 ppm in potato foliage, RAB2 concludes that these methods successfully identified the predominant residues in rotational crop matrices. No storage stability data were submitted in conjunction with the confined rotational crop study. Samples for this confined rotational crop study were analyzed within 5 months of harvest. As samples were analyzed within an acceptable time frame, no further storage stability data are necessary.

We note that data concerning the radioactivity and characterization/identification of metabolites in treated soil were included with this submission; however, these data are not presented herein.

C.1. Storage Stability

Samples of rotated crops were stored frozen (-20 °C) at the field site within 2 hours of collection, except for wheat hay samples, which were dried in the greenhouse for 11 days after collection, and potato tuber samples, which were placed on "blue" ice for immediate shipment to the analytical laboratory. Samples of kale, potato foliage, and wheat hay and straw were extracted within 34-173 days (<6 months) of harvest; samples of potato tubers and wheat forage and grain were not extracted, but TRR determinations were conducted within 1 month of harvest. Actual analysis dates were not provided for potato foliage extracts (the only rotational crop matrix analyzed by HPLC). Samples for this confined rotational crop study were analyzed within 5 months of harvest. As samples were analyzed within an acceptable time frame, no further storage stability data are necessary.

TABLE C.1. Summary of Storage Conditions.

Matrix	Plantback interval	Storage Temp.	Actual Storage Duration	Limit of Demonstrated Storage Stability
Kale	90 days	Frozen; storage temperature at laboratory not specified	36-89 days (harvest to extraction)	Within 4-6 month guideline
Potato, foliage			127 days (harvest to final extraction)	
Potato, tubers			16 days (harvest to combustion/LSC)	
Wheat, forage			23 days (harvest to combustion/LSC)	
Wheat, hay			173 days (harvest to final extraction)	
Wheat, straw			34 days (harvest to extraction)	
Wheat grain			28 days (harvest to combustion/LSC)	

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Rotated Crop Matrices.

Matrix	Plantback interval (days)	TP-label (ppm)[1]		PH-label (ppm)[1]	
		Low Treatment: 0.045 lb ai/A	High Treatment: 0.093 lb ai/A	Low Treatment: 0.046 lb ai/A	High Treatment: 0.090 lb ai/A
Kale	90	0.003	0.014	0.005	0.008
Potato, foliage	90	0.024	0.038	0.047	0.062
Potato, tuber	90	<LOQ	0.003	<LOQ	0.003
Wheat, forage	90	<LOQ	0.005	0.004	0.007
Wheat, hay	90	0.009	0.022	0.021	0.032
Wheat, straw	90	0.011	0.030	0.024	0.028
Wheat, grain	90	<LOD	<LOQ	<LOD	<LOQ

[1] The LOQ was 0.002 ppm for wheat forage, kale, and potato tubers, and 0.005 ppm for wheat hay, straw, and grain, and potato foliage; the LOD was 0.001 ppm for all plant matrices.

TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Rotational Crop Matrices Planted 90 Days Following Application of [Triazolopyrimidine-2-^{14}C]Penoxsulam to the Soil at 0.045 lb ai/A.

Metabolite Fraction	Potato Foliage		Wheat Hay		Wheat Straw	
	TRR = 0.024 ppm		TRR = 0.009 ppm		TRR = 0.011 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN/water extract	70.1	0.017	73.3	0.006	62.7	0.007
Aqueous phase	47.3	0.011	53.4	0.005	53.1	0.006
Dichloromethane phase	17.0	0.004	26.2	0.002	13.0	0.001
Total extractable	64.3	0.015	79.6	0.007	66.1	0.007
Total identified	0	0	0	0	0	0
Total unidentified	64.3	0.015	79.6	0.007	66.1	0.007
Total bound residues	21.0	0.005	27.5	0.002	25.6	0.003
% Accountability	85.3		107.1		91.7	

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Rotational Crop Matrices Planted 90 Days Following Application of [Phenyl-U-^{14}C]Penoxsulam to the Soil at 0.046 lb ai/A.[1]

Metabolite Fraction[2]	Potato Foliage		Wheat Hay		Wheat Straw	
	TRR = 0.047 ppm		TRR = 0.021 ppm		TRR = 0.024 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN/water extract	79.8	0.037	88.1	0.019	90.8	0.022
Aqueous phase	60.8	0.029	65.1	0.014	69.2	0.017
Dichloromethane phase	19.5	0.009	12.7	0.003	14.6	0.004
Hexane phase	0.5	<0.001				
ACN phase	19.7	0.009				
5-OH XDE-638	8.4	0.004				
Unknown Rt=27-28 min	8.9	0.004				
Total extractable	81.0	0.038	77.8	0.017	83.8	0.021
Total identified	8.4	0.004	0	0	0	0
Total unidentified	70.2	0.033	77.8	0.017	83.8	0.021
Total bound residues	13.4	0.006	23.6	0.005	11.5	0.003
% Accountability	94.4		101.4		95.3	

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] The 5-OH XDE-638 metabolite was tentatively identified by HPLC.

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Rotational Crop Matrices Planted 90 Days Following Application of [Triazolopyrimidine-2-^{14}C]Penoxsulam to the Soil at 0.093 lb ai/A.

Metabolite Fraction	Kale		Potato Foliage		Wheat Hay		Wheat Straw	
	TRR = 0.014 ppm		TRR = 0.038 ppm		TRR = 0.022 ppm		TRR = 0.030 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN/water extract	96.5	0.013	74.6	0.028	81.1	0.018	61.6	0.018
Aqueous phase	54.1	0.007	53.5	0.020	51.5	0.011	51.2	0.015
Dichloromethane phase	31.5	0.004	16.9	0.006	23.0	0.005	13.6	0.004
Total extractable	85.6	0.011	70.4	0.026	74.5	0.016	64.8	0.019
Total identified	0	0	0	0	0	0	0	0
Total unidentified	85.6	0.011	70.4	0.026	74.5	0.016	64.8	0.019
Total bound residues	13.4	0.002	22.1	0.008	27.8	0.006	31.2	0.009
% Accountability	99.0		92.5		102.3		96.0	

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Rotational Crop Matrices Planted 90 Days Following Application of [Phenyl-U-^{14}C]Penoxsulam to the Soil at 0.090 lb ai/A.[1]

Metabolite Fraction[2]	Kale		Potato Foliage		Wheat Hay		Wheat Straw	
	TRR = 0.008 ppm		TRR = 0.062 ppm		TRR = 0.032 ppm		TRR = 0.028 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN/water extract	80.9	0.007	95.6	0.060	93.8	0.030	86.2	0.024
Aqueous phase	63.0	0.005	68.1	0.042	76.7	0.025	69.3	0.019
BSTCA			25.0	0.015				
Unknown Rt=7 min			18.0	0.011				
Unknown Rt=20 min			16.5	0.010				
Unknown Rt=27-28 min			11.1	0.007				
Dichloromethane phase	16.5	0.001	27.1	0.017	16.6	0.005	17.6	0.005
Hexane phase			0.6	<0.001				
ACN phase			25.3	0.016				
5-OH XDE-638			13.9	0.009				
Unknown Rt=27-28 min			11.8	0.007				
Total extractable	79.5	0.006	94.0	0.058	93.3	0.030	86.9	0.024
Total identified	0	0	38.9	0.024	0	0	0	0
Total unidentified	79.5	0.006	58.0	0.035	93.3	0.030	86.9	0.024
Total bound residues	4.1	<0.001	6.8	0.004	7.8	0.003	15.7	0.004
% Accountability	83.6		100.8		101.1		102.6	

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] The 5-OH XDE-638 and BSTCA metabolites were tentatively identified by HPLC.

TABLE C.2.3.1 Summary of Characterization and Identification of Radioactive Residues in Rotational Crop Matrices Planted 90 Days Following Application of [Phenyl-U-^{14}C]Penoxsulam to the Soil at 0.046 lb ai/A (Low Treatment) or at 0.090 lb ai/A (High Treatment).

Compound	Potato Foliage; Low Treatment		Potato Foliage; High Treatment	
	TRR = 0.047 ppm		TRR = 0.062 ppm	
	% TRR	ppm	% TRR	ppm
5-OH XDE-638	8.4	0.004	13.9	0.009
BSTCA	--	--	25.0	0.015
Unknown Rt=7 min	--	--	18.0	0.011
Unknown Rt=20 min	--	--	16.5	0.010
Unknown Rt=27-28 min	8.9	0.004	22.9	0.014
Aqueous phase	60.8	0.029	--	--
Hexane phase	0.5	<0.001	0.6	<0.001
Total identified	8.4	0.004	38.9	0.024
Total characterized	70.2	0.033	58.0	0.035
Total extractable	81.0	0.038	94.0	0.058
Total bound	13.4	0.006	6.8	0.004

C.3. Proposed Metabolic Profile

FIGURE C.3.1. Proposed Metabolic Profile of Penoxsulam in Rotational Potato Foliage.

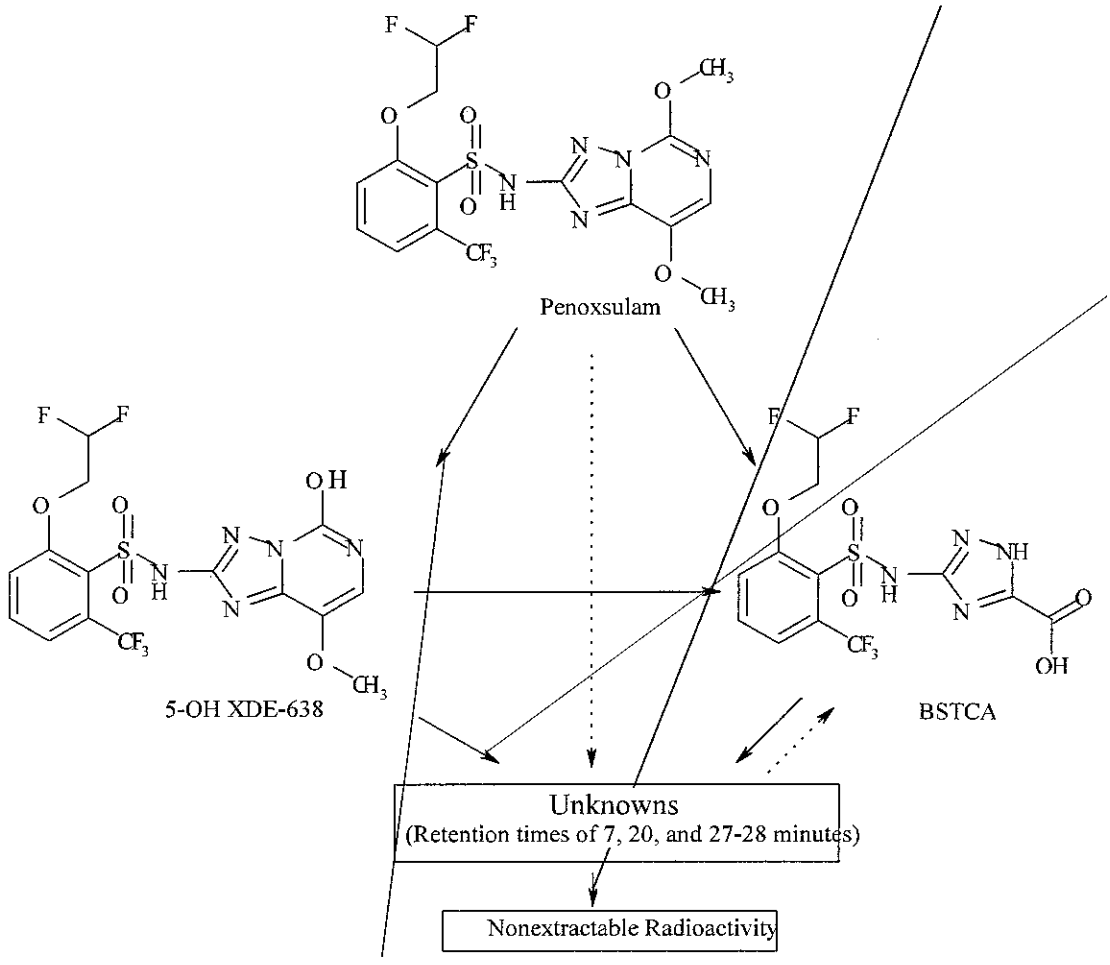
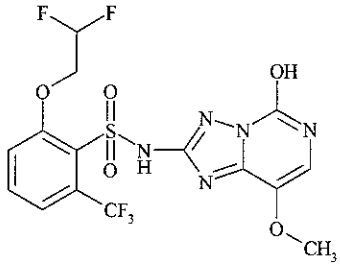
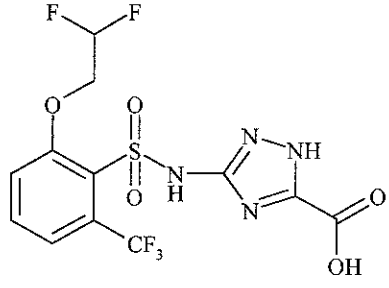

Penoxsulam
5-OH XDE-638
BSTCA
Unknowns
(Retention times of 7, 20, and 27-28 minutes)
Nonextractable Radioactivity

TABLE C.3.1. Identification of Compounds from the Confined Rotational Crop Study.		
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
5-OH XDE-638	2-(2,2-difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl) benzenesulfonamide	
BSTCA	3-[[[2-(2,2-difluoroethoxy)-6-(trifluoromethyl) phenyl]sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylic acid	

D. CONCLUSIONS

TRR accumulated at ≥0.01 ppm in certain rotated crops planted 90 days following a single soil application of [triazolopyrimidine-2-^{14}C]penoxsulam at 0.045 and 0.093 lb ai/A, or [phenyl-U-^{14}C]penoxsulam at 0.046 and 0.090 lb ai/A. At the low treatment rate, TRR were 0.024-0.047 ppm in potato foliage (both labels), 0.021 ppm in PH-treated wheat hay, and 0.011-0.024 ppm in wheat straw (both labels). At the higher treatment rate, TRR were 0.014 ppm in TP-treated kale, 0.038-0.062 ppm in potato foliage (both labels), 0.022-0.032 ppm in wheat hay (both labels), and 0.028-0.030 ppm in wheat straw (both labels). TRR were <0.01 ppm in potato tuber, wheat forage, and wheat grain from both labels at both treatment rates, in TP-treated kale at the low treatment rate, in PH-treated kale at both treatment rates, and in TP-treated wheat hay at the low treatment rate. TRR were generally higher in PH-treated commodities than in TP-treated commodities.

Only the extracts of PH-treated potato foliage were analyzed by HPLC for metabolite identification. Total identified residues were 8.4% and 38.9% TRR in PH-treated potato foliage at the low and high treatment rates, respectively, and the parent, penoxsulam, was not detected in either sample. The 5-OH XDE-638 and BSTCA metabolites (≤0.015 ppm each) were tentatively identified in potato foliage.

Based on data from the confined rotational crop study, no quantifiable residues of penoxsulam or 5-OH XDE-638 are expected to be present in the raw agricultural commodities of small grains, leafy vegetables, and root crops planted 90 days following treatment with penoxsulam at 0.045 or

0.090 lb ai/A. The data also indicate that residues of BSTCA could be present at ≥0.01 ppm in the foliage of root crops planted 90 days following treatment at 0.090 lb ai/A.

The petitioner proposed that the penoxsulam is metabolized in rotated potato foliage to 5-OH XDE-638 and BSTCA, and that both 5-OH XDE-638 and BSTCA are then metabolized to unknowns and nonextractable residues.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Attachment: L. Graper, Dow AgroSciences, 5/4/04

Template Version April 2003

IN RESPONSE TO: Errico.Philip@epamail.epa.gov
SENT: Tuesday, May 04, 2004 2:20 PM

SUBJECT: Response to Additional Information Requested by Residue Chemistry for Penoxsulam

STUDY IDENTIFICATION: 45830720 Graper, L. (2002) A Confined Rotational Crop Study With (Carbon-14) XDE-638 Using Three Different Crops: Lab Project Number: 000266.

REQUEST OF RESIDUE CHEMISTRY: Residue Chemistry commented that actual analysis dates were not provided for potato foliage extracts (the only rotational crop matrix analyzed by HPLC) and requested that the petitioner submit the actual analysis dates for potato foliage extracts to allow RAB2 to determine whether storage stability data are required to support the confined rotational crop studies.

RESPONSE OF PETITIONER: The requested dates have been added to an excerpt of Table 3 (page 46, report 000266) shown below and are indicated in **bold**.

Event	Date	Days after Treatment (DAT)	Days after Planting (DAP)	Days after Harvest/ Sampling (DAH)
Mature Potato Foliage Harvest	14-May-01	298	208	0
Milling Completed	30-May-01	N/A	N/A	16
Combustion Analysis	01-Jun-01	N/A	N/A	18
Initial Extraction	19-Jun-01	N/A	N/A	36
Final Extraction	18-Sep-01	N/A	N/A	127
Initial HPLC Analysis	**6-Sep-01**	**N/A**	**N/A**	**115**
Final HPLC Analysis	**10-Oct-01**	**N/A**	**N/A**	**149**

The additional dates refer to the HPLC analyses for the potato foliage found in Figures 12, 13 and 14 which are located on pages 76, 77 and 78, respectively, in the final report.

These analysis dates demonstrate that the HPLC analyses were done within approximately 4 to 5 months of harvest of the potato foliage.

The Residue Chemistry Guidelines (OPPTS 860.1300 Nature of the Residue – Plants, Livestock, section (d)(7)) recommend that storage stability data should not normally be required for samples analyzed within 4 to 6 months of collection, provided evidence is given that attempts were made to limit degradation of residues by appropriate storage of matrices and extracts during the analytical portion of the study. Since the 4 to 5 month analysis intervals for potato foliage fall within the recommended 4 to 6 month period and the final report (section 3.7.4, page 28, report 000266) indicates that samples were stored in the freezer, it is the opinion of the petitioner that the supplied data adequately address any concerns of storage stability for residues in this study.

Additional questions concerning the storage or any other aspect of this study may be directed to the study director:

L. Kurt Graper
Dow AgroSciences
317-337-3668
lkgraper@dow.com

Primary Evaluator	William Cutchin, Chemist HED/SIMB (7509C)	Date: 7/19/04
Reviewer	Richard Loranger, Chemist HED/RAB2 (7509C)	7/22/04 for RAL
Contractor	Dynamac Corporation 20440 Century Blvd., Suite 100 Germantown, MD 20874	

STUDY REPORT

45830712 Yoder, R.; Embrey, S. (2001) Nature of Residue of XDE-638 in Rice Following Post-Emergent, Foliar Application: Lab Project Number: 990028. Unpublished study prepared by Dow AgroSciences LLC and Plant Sciences Inc. 116 p.

Addendum to 45830712 Yoder, R; Dow AgroSciences LLC and Plant Sciences Inc., 5/4/04 (Attachment).

EXECUTIVE SUMMARY

Dow AgroSciences LLC has submitted a study investigating the metabolism of [triazolopyrimidine-2-^{14}C]penoxsulam and [phenyl-U-^{14}C]penoxsulam in rice. Each radiolabeled test substance was formulated as a suspension concentrate formulation and applied as a foliar broadcast spray to rice plants at the 5- to 6-leaf growth stage at ~0.089 lb ai/A (~100 g ai/ha). Rice plants were grown in galvanized steel tubs maintained in outdoor screenhouses; water levels in the rice plots were maintained at 2.5-5 inches depending on the growth stage of the rice crop. Approximately 4 weeks prior to mature harvest, a plot dry-back period was initiated, with no further irrigation until harvest. Immature rice shoots were harvested at posttreatment intervals (PTIs) of 0, 3, 7, 14, and 30 days, and mature rice straw and grain were harvested 134 days posttreatment. The in-life phase was conducted by Plant Sciences (Manteca, CA), and the analytical phase of the study was conducted by Dow AgroSciences, Global Environmental Chemistry Laboratory (Indianapolis, IN).

The total radioactive residues (TRR) were 0.021 and 0.003 ppm in mature rice straw and grain, respectively, following treatment with **[triazolopyrimidine-2-^{14}C]penoxsulam** (TP) at 0.083 lb ai/A. TRR were 5.17 ppm in immature rice shoots collected on the day of treatment and declined with each subsequent sampling interval to 0.048 ppm at the 30-day PTI.

In rice matrices harvested at maturity following treatment with **[phenyl-U-^{14}C]penoxsulam** (PH) at 0.095 lb ai/A, TRR were 0.023 and 0.004 ppm in mature rice straw and grain, respectively.

TRR were 3.99 ppm in i mature rice shoots collected on the day of treatment and declined with each subsequent samplir ; interval to 0.056 ppm at the 30-day PTI.

The majority of the TRR (~63-160% TRR) was extracted from rice matrices (immature shoots, and mature rice straw an grain) using acetonitrile/water. Nonextractable residues were <10% TRR or <0.05 ppm in all samples of immature shoots (0.7-24.7% TRR, 0.012-0.051 ppm) and mature straw (19.6-40.5' TRR, 0.005-0.008 ppm); material balances ranged 87-110% for rice shoots and straw. Nonex ractable residues in mature rice grain samples were not determined due to very low levels of radi activity. Residues were characterized/identified by HPLC analysis with confirmatory analys s by TLC. These methods successfully identified the predominant residues in rice matrices. Samples were analyzed within 2 months of harvest. All samples were stored frozen. No furthe storage stability data are required to support this study.

In general, identification of residues was most successful in immature rice shoots and mature straw and was less succe sful in rice grain due to very low levels of radioactivity. No significant differences were observe l between the two labels. Total identified residues ranged ~46-102% TRR in immature shoots 35-38% TRR in straw, and 9-11% TRR in grain. Parent penoxsulam was the major componer identified in immature rice shoots (both labels) harvested at 0-, 3-, 7-, and 14-day PTIs, ranging from 94.4-99.9% TRR (3.831-5.161 ppm) at the 0-day PTI to 53.5-62.0% TRR (0.197-0.22' ppm) at the 14-day PTI. Penoxsulam remained the major component identified in PH-label 30 day PTI immature shoots, at 41.3% TRR (0.023 ppm), but was present in TP-label 30-day PTI i mature shoots at lower levels (12.3% TRR, 0.006 ppm). Penoxsulam was also identified as a r inor component in mature rice straw and grain (both labels), at 4.2-8.9% TRR (<0.001-0.00 ppm). The metabolite 5-OH XDE-638 was identified as the major component in 30-day PT immature rice shoots and mature rice straw (both labels) at 16.2-33.5% TRR (0.009-0.016 ppm) nd 29.5-30.4% TRR (0.007-0.009 ppm), respectively. The 5-OH XDE-638 metabolite wa also identified as a minor component in immature rice shoots harvested at 0-, 3-, 7-, and 14-day I TIs (both labels), at 1.8-14.2% TRR (0.043-0.209 ppm), and in mature rice grain, at 2.2-3.3% T R (<0.001 ppm). In addition, two unknowns, present individually at levels of ~1-23% TRR, ere characterized by HPLC in rice matrices as being more polar than penoxsulam and 5-OH X DE-638. Because of the low levels of the unknowns in mature straw samples, no attempts we made to further identify these residues; however, the petitioner stated that one of the unknown was likely comprised of conjugates of less polar metabolites.

Residues of penoxsulam were highest in earlier sampled immature shoot samples. The metabolite patterns in su sequent immature shoot samples indicated that residues of the parent declined, and levels of th 5-OH metabolite increased with increasing posttreatment intervals.

The petitioner proposed at penoxsulam primarily degrades to its 5-OH metabolite and at least two minor unknown met bolites in rice matrices; little translocation of penoxsulam residues or its metabolites was obse ed into the grain.

STUDY/WAIVER AC EPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the rice metabolism data are classified as scientifically acceptable

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D288152.

COMPLIANCE

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Penoxsulam (company code XDE-638; PC Code 119031) is an herbicide intended for the control of *Echinochloa* grasses, broadleaf weeds, and sedge weeds in both water-injected (transplanted paddy) and postemergence (direct-seeded) rice. A single postemergence application of penoxsulam is to be made to rice from the one-leaf growth stage (7-12 days after seeding) to 60 days prior to rice harvest. The application is to be made by aerial or ground equipment once per growing season at a maximum rate of 0.045 lb ai/A (50 g ai/ha). Penoxsulam is to be formulated as a granular (for water-seeded rice) or suspension concentrate (for direct-seeded rice) formulation.

TABLE A.1. Penoxsulam Nomenclature.

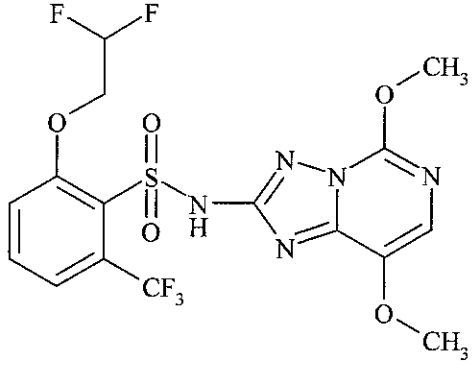
Compound	
Common name (proposed)	Penoxsulam
Company experimental name	XDE-638
IUPAC name	6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide
CAS name	2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS #	219714-96-2
End-use product/EP	GF-443 SC SF (File Symbol 62719-LNN); GF-947 Granule SF (File Symbol 62719-LNG); GF-947 Granule CA (File Symbol 62719-LNR).

TABLE A.2. Physicoch mical Properties of Technical Grade Penoxsulam.

Parameter	Value		Reference
Melting point/range	Not available		
pH	Not available		
Density	Not available		
Water solubility	pH	Solubility (mg/L)	MRID 45830720
	(unbuffered)	4.91	
	5	5.66	
	7	408	
	9	1460	
Solvent solubility	Solvent	Solubility (g/L)	MRID 45830720
	DMSO	78.4	
	NMP	40.3	
	DMF	39.8	
	acetone	20.3	
	acetonitrile	15.3	
	ethyl acetate	3.23	
	methanol	1.48	
	octanol	0.035	
	xylene	0.017	
	heptane	<1 µg/mL	
Vapor pressure	7.16×10^{-16} mm Hg at 25 °C		MRID 45830720
Dissociation constant, pK_a	5.1		MRID 45830720
Octanol/water partition coefficit, $Log(K_{OW})$	pH	$Log(K_{OW})$	MRID 45830720
	(unbuffered)	-0.354	
	5	1.137	
	7	-0.602	
	9	-1.418	

B. EXPERIMENT L DESIGN

B.1. Test Site and Cr p Information

TABLE B.1.1. Test Site I formation.

Testing Environment	Soil characteristics			
	Type	%OM	pH	CEC (meq/100 g)
Galvanized steel tanks lined wit plastic sheeting located in outdoor screenhouses at Plant Sciences (Watsonville, CA)	Not applicable to this study (no soil treatment)			

The daily minimum and aximum temperatures and relative humidity were provided for the study period. Historical eather data were not provided. The petitioner did not note any unusual weather circumstances. est plots were irrigated by hand to maintain 2.5-5 inches of water in the test containers up to 4 we eks prior to harvest. Rice plots were fertilized during the study period as necessary, and a coppe -containing algicide was applied to the water in the test containers pre- and post-application. Nc maintenance pesticides were applied during the in-life phase.

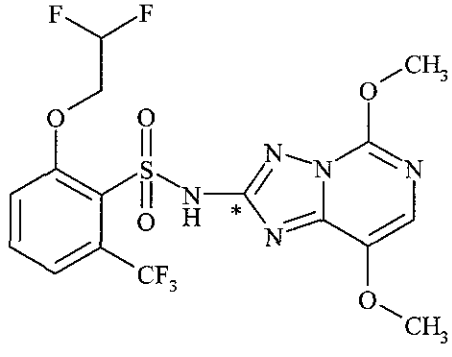
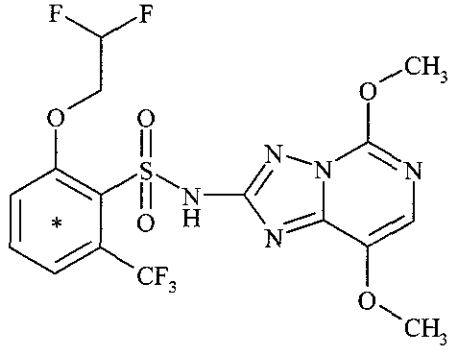
TABLE B.1.2. Crop Information.

Crop; crop group	Variety	Growth stage at application	Growth stage at harvest	Harvested RAC	Harvesting procedure
Rice; Grain, cereal group 15, and Grain, cereal, forage, fodder, and straw, group 16	M-202, japonica type	5- to 6-leaf growth stage	Immature at 0, 3, 7, 14, and 30 days posttreatment	Immature rice shoots	Immature shoots were cut by hand slightly above the highest water level
			Mature at 134 days posttreatment	Mature grain and straw.	Mature panicles were cut by hand from the straw, and the remaining straw was cut 14-15 cm above soil level. The panicle samples were dried (15-48 hours) on screened racks. Unhulled grain was hand stripped from the chaff, and the chaff was added to the straw sample.

Water levels in the rice plots were maintained at 2.5-5 inches depending on the growth stage of the rice crop. Approximately 4 weeks prior to mature harvest, a plot dry-back period was initiated, with no further irrigation until harvest.

B.2. Test Materials

TABLE B.2.1. *Test Material Characteristics.*

Chemical structure		
Radiolabel position	2-triazolopyrimidine labeled (TP)	Uniformly labeled on the phenyl ring (PH)
Lot No.	INV1456	INV1475
Radiochemical Purity	99%	98.2%
Specific activity	28.9 mCi/mmole (prior to isotopic dilution); 9.4 mCi/mmole (spray solution)	24.6 mCi/mmole (prior to isotopic dilution); 6.7 mCi/mmole (spray solution)
Code	N/A	N/A

The radiolabeled materials were diluted with nonlabeled penoxsulam and formulated as a 10% suspension concentrate; formulated test substances were shipped to Plant Sciences.

B.3. Study Use Patte n

TABLE B.3.1. Use Patte n Information.	
Chemical name	[tria olopyrimidine-2-^{14}C]penoxsulam and [phenyl-U-^{14}C]penoxsulam
Application method	Eac test substance was formulated as a suspension concentrate (using formulation blank) and then dilu d with water. Foliar broadcast application was made using a spray bottle.
Application rate	TP- bel: 0.083 lb ai/A (93 g ai/ha) PH- bel: 0.095 lb ai/A (107 g ai/ha)
Number of applications	One
Timing of applications	5- tc 5-leaf growth stage of the rice crop
PHI	Imr ture plants collected at 0, 3, 7, 14, and 30 days posttreatment; mature crop commodities coll ted at 134 days posttreatment.

The petitioner conducted tests prior to study initiation to determine the highest rate of test substance that could be a plied to rice without phytotoxic effects. Rice plants were treated at rates of 75, 100 (=0.089 ai/A), 150, 250, and 500 g ai/ha. Phytotoxic effects were seen in plants treated at rates of 50 g ai/ha and higher.

B.4. Identification/C aracterization of Residues

B.4.1. Sample Prepara ion

A sample of unhulled gra n was separated into hulls and brown (hulled) rice using a hand-operated rice-husking ma hine. Samples of immature plants, and mature unhulled grain, straw (plus chaff), brown rice, nd hulls were then frozen at the field site. Immature plant and mature rice grain samples were g ound in the presence of liquid nitrogen, and mature straw was milled in the presence of dry ice w hin one day prior to extraction.

Samples of immature sho ts and mature grain and straw were extracted (three times) with acetonitrile:water (80:20, v:v) followed by vacuum filtration. Due to small sample sizes, for the 0- and 3-DAT immature lants, the entire sample was ground with the extraction solvent and the TRR were determined fo the extractable and nonextractable fractions. The combined extracts of immature samples were p rtitioned 2 or 3 times with hexane to remove pigmented co-extractives; any additi nal hexane was evaporated from the remaining aqueous phase, and the extract was filtered for H LC analysis. The combined extracts of mature samples were not subjected to partitioning ith hexane, but were concentrated and filtered prior to HPLC analysis.

Nonextractable residues om mature rice straw (both labels) were subjected to acid hydrolysis (1 N HCl at reflux for 4 h urs) for further characterization. The hydrolysate was vacuum filtered, and the remainin pellet was extracted again with 1 N HCl with shaking for 30 minutes followed by vacuum filtr ion. The radioactivity in the combined hydrolysates was determined by LSC.

B.4.2. Analytical Methodology

Total radioactive residues (TRR) in replicate (3 or 5) immature and mature rice samples, except for the 0- and 3-day immature samples, were determined by combustion/LSC. Because of small sample sizes, TRR in the 0- and 3-day immature samples were determined by summing the extractable and nonextractable radioactivity. Extracts were radioassayed by LSC, and nonextractable residues were radioassayed by combustion/LSC. The reported limit of quantitation (LOQ) was 40 dpm (background) for rice matrices.

Extracts of rice matrices were analyzed by HPLC using a system equipped with a C-18 column and a UV detector (254 nm); radioactivity was quantified using fraction collection and LSC. A gradient mobile phase of water and acetonitrile, each containing 1% acetic acid, was used. Reference standards of unlabeled penoxsulam, 5-OH XDE-638, and TSN101806 [2-(2,2-difluoroethoxy)-N-1H-1,2,4-triazol-3-yl-6-(trifluoromethyl)benzenesulfonamide] were used.

Identification of penoxsulam and 5-OH XDE-638 was confirmed by TLC co-chromatography of a sample extract (sample not specified) with reference standards. TLC analyses were conducted on phosphorescent silica gel plates using a solvent system of toluene:isopropanol:acetic acid (70:20:10, v:v:v). Radioactivity was scanned using a radiographic imaging system and non-labeled standards were visualized by UV light.

C. RESULTS AND DISCUSSION

Total radioactive residues (TRR) in rice matrices are reported in Table C.2.1. The total radioactive residues were 0.021 and 0.003 ppm in mature rice straw and grain, respectively, harvested 134 days following a single postemergence application of **[triazolopyrimidine-2-^{14}C]penoxsulam** to rice plants at the 5- to 6-leaf growth stage at 0.083 lb ai/A. TRR were 5.17 ppm in immature rice shoots collected on the day of treatment and declined with each subsequent sampling interval to 0.048 ppm at the 30-day PTI.

In mature rice matrices harvested 134 days following a single postemergence application of **[phenyl-U-^{14}C]penoxsulam** to rice plants at the 5- to 6-leaf growth stage at 0.095 lb ai/A, TRR were 0.023 and 0.004 ppm in mature rice straw and grain, respectively. TRR were 3.99 ppm in immature rice shoots collected on the day of treatment and declined with each subsequent sampling interval to 0.056 ppm at the 30-day PTI.

The majority of the TRR (~63-160% TRR) was extracted from rice matrices using acetonitrile/water. Nonextractable residues were <10% TRR or <0.05 ppm in all samples of immature shoots (0.7-24.7% TRR, 0.012-0.051 ppm) and mature straw (19.6-40.5% TRR, 0.005-0.008 ppm). Nonextractable residues in mature rice grain samples were not determined due to very low levels of radioactivity. Attempts to release additional radioactivity from immature shoot samples (14- and 30-day PTI) and mature straw samples using acid hydrolysis were unsuccessful; only ~1% TRR was released from 14-day PTI immature shoots, 4-8% TRR was released from 30-day PTI immature shoots, and <0.001 ppm was released from mature straw

samples. Due to the low radioactivity in the acid hydrolysates, further analyses were not conducted. Difficulties were also encountered in analyzing the post-hydrolysis nonextractable residues. Because of the difficulties, the acid hydrolysate results are not included in the distribution or summary ables below. Residues were characterized/identified by HPLC analysis with confirmatory analy s by TLC. These methods successfully identified the predominant residues in rice matrices Samples were stored frozen at -20 °C. Samples for this nature of the residue study were analy ed within 2 months of harvest. The petitioner has provided adequate supporting data and chro natograms. As samples were analyzed within an acceptable time frame, no further storage stabili y data are necessary.

The distribution of radio ctivity in rice matrices is presented in Tables C.2.2.1 (triazolo-pyrimidine-label rice) an C.2.2.2 (phenyl-label rice); characterization and identification of residues are summarized n Tables C.2.3.1 (triazolo-pyrimidine-label rice) and C.2.2.2 (phenyl-label rice). In general, ic ntification of residues was most successful in immature rice shoots and mature straw and was les successful in rice grain due to very low levels of radioactivity. No significant differences w re observed between the two labels.

Parent penoxsulam was t e major component identified in immature rice shoots (both labels) harvested at 0-, 3-, 7-, an 14-day PTIs, ranging from 94.4-99.9% TRR (3.831-5.161 ppm) at the 0-day PTI to 53.5-62.0% TRR (0.197-0.227 ppm) at the 14-day PTI. Penoxsulam remained the major component identif ed in PH-label 30-day PTI immature shoots, at 41.3% TRR (0.023 ppm), but was present in TP-label 30-day PTI immature shoots at lower levels (12.3% TRR, 0.006 ppm). Penoxsulan was also identified as a minor component in mature rice straw and grain (both labels), at 4.2 8.9% TRR (<0.001-0.003 ppm). The metabolite 5-OH XDE-638 was identified as the major c nponent in 30-day PTI immature rice shoots and mature rice straw (both labels) at 16.2-33.5 % TRR (0.009-0.016 ppm) and 29.5-30.4% TRR (0.007-0.009 ppm), respectively. The 5-OH DE-638 metabolite was also identified as a minor component in immature rice shoots har ested at 0-, 3-, 7-, and 14-day PTIs (both labels), at 1.8-14.2% TRR (0.043-0.209 ppm), and i mature rice grain, at 2.2-3.3% TRR (<0.001 ppm). In addition, two unknowns, present indivi lually at levels of ~1-23% TRR, were characterized by HPLC in rice matrices as being more p lar than penoxsulam and 5-OH XDE-638. Because of the low levels of the unknowns in mature raw samples, no attempts were made to further identify these residues; however, the petitioner s ted that one of the unknowns was likely comprised of conjugates of less polar metabolites.

Residues of penoxsulam were highest in earlier sampled immature shoot samples. The metabolite patterns in sul sequent immature shoot samples indicated that residues of the parent declined and levels of the 5-OH metabolite increased with increasing posttreatment intervals. Leaf samples from imma ure rice shoots (both labels) were surface washed with a dilute soap solution to determine sur ace residues. Surface radioactivity from immature shoot leaves decreased from 0.005-0.0 .5 µg/cm^2 in 0-DAT immature shoot samples to below the LOQ (<0.001) by the 30-day sa npling interval. Very little translocation of radioactivity into the grain fraction of the plant was bserved.

C.1. Storage Stability

All samples were extracted within 6-55 days of harvest and subjected to acid hydrolysis within 21-27 days of harvest. Samples were stored frozen at -20 °C. All samples were analyzed within 2 months of harvest. The petitioner conducted a repeat extraction and analysis of 14-day PTI immature rice shoots several weeks after the initial extraction and analysis and similar metabolite profiles were observed.

TABLE C.1. Summary of Storage Conditions.

Matrix (RAC or Extract)	Storage Temp. (°C)	Actual Study Duration	Limit of Demonstrated Storage Stability
Immature rice shoots	-20	6-14 days to extraction	Within 4-6 month guideline
Mature rice straw		19 days to extraction	
Mature rice grain		55 days to extraction	

The storage stability data provided by the petitioner are sufficient to fulfill data requirements for this study.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Rice Matrices.

Matrix	Timing and Applic. No.	PHI (days)	TP-label	PH-label
			ppm	ppm
Immature rice shoots	1	0	5.17	3.99
		3	1.83	2.34
		7	1.02	0.838
		14	0.424	0.318
		30	0.048	0.056
Mature rice straw	1	134	0.021	0.023
Mature rice grain	1	134	0.003	0.004
- Brown (hulled) rice	1	134	0.002	0.003
- Rice hulls	1	134	0.003	0.004

TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Rice Matrices Following a Single Postemergence Application of [Triazolo-pyrimidine-2-^{14}C]Penoxsulam at 0.083 lb ai/A. [1]

Metabolite Fraction	Immature Rice Shoots (0-day)		Immature Rice Shoots (3-day)		Immature Rice Shoots (7-day)		Immature Rice Shoots (14-day)		Immature Rice Shoots (30-day)		Mature Rice Straw		Mature Rice Grain	
	TRR = 5.17 ppm		TRR = 1.83 ppm		TRR = 1.02 ppm		TRR = 0.424 ppm		TRR = 0.048 ppm		TRR = 0.021 ppm		TRR = 0.003 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN/water extract	99.3	5.13	97.8	1.79	98.9	1.01	90.8	0.386	62.5	0.030	66.9	0.014	67.6	0.002
Penoxsulam	99.9	5.161	84.5	1.556	66.2	0.675	53.5	0.227	12.3	0.006	8.9	0.003	6.4	<0.001
5-OH XDE-638	1.8	0.095	7.0	0.129	8.0	0.081	10.2	0.043	33.5	0.016	29.5	0.009	2.2	<0.001
Unknown Rt 6 mins	--	--	0.6	0.011	2.5	0.026	4.0	0.017	9.2	0.004	10.9	0.003	4.1	<0.001
Unknown Rt 15 mins	0.8	0.044	--	--	--	--	2.9	0.012	6.8	0.003	12.1	0.003	1.1	<0.001
Total extractable	99.3	5.13	97.8	1.79	98.9	1.01	90.8	0.386	62.5	0.030	66.9	0.014	67.6	0.002
Total identified	101.7	5.26	91.5	1.685	74.2	0.756	63.7	0.270	45.8	0.022	38.4	0.012	8.6	<0.001
Total unidentified	0.8	0.044	0.6	0.011	2.5	0.026	6.9	0.029	16.0	0.007	23.0	0.006	5.2	<0.001
Total bound residues	0.7	0.034	2.2	0.041	5.0	0.051	9.2	0.039	24.7	0.012	40.5	0.008	NA [3]	NA
% Accountability	100 [2]		100 [2]		103.9		100.1		87.2		107.4		67.6	

[1] Duplicate samples (except 0-, 3-, and 7-day immature shoot and mature grain samples) were extracted and analyzed by HPLC; values for the sample with the highest level of extracted/characterized residues are reported.

[2] Accountabilities for the 0- and 3-day immature shoot samples were 100% because the TRR was calculated by summing the extractable and nonextractable radioactivity.

[3] NA = Not analyzed.

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TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Rice Matrices Following a Single Postemergence Application of [Phenyl-U-^{14}C]Penoxsulam at 0.095 lb ai/A. [1]

Metabolite Fraction	Immature Rice Shoots (0-day)		Immature Rice Shoots (3-day)		Immature Rice Shoots (7-day)		Immature Rice Shoots (14-day)		Immature Rice Shoots (30-day)		Mature Rice Straw		Mature Rice Grain	
	TRR = 3.99 ppm		TRR = 2.34 ppm		TRR = 0.838 ppm		TRR = 0.318 ppm		TRR = 0.056 ppm		TRR = 0.023 ppm		TRR = 0.004 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN/water extract	98.9	3.94	98.1	2.30	100.7	0.84	94.1	0.299	78.7	0.044	90.1	0.021	159.6	0.006
Penoxsulam	94.4	3.831	81.1	1.978	74.6	0.625	62.0	0.197	41.3	0.023	4.2	0.001	7.2	<0.001
5-OH XDE-638	2.9	0.118	8.6	0.209	10.5	0.088	14.2	0.045	16.2	0.009	30.4	0.007	3.3	<0.001
Unknown Rt 6 mins	--	--	--	--	0.6	0.005	1.6	0.005	8.0	0.004	21.9	0.005	14.7	0.001
Unknown Rt 15 mins	0.6	0.026	4.1	0.099	4.9	0.041	8.0	0.025	8.7	0.005	23.2	0.005	2.4	<0.001
Total extractable	98.9	3.94	98.1	2.30	100.7	0.84	94.1	0.299	78.7	0.044	90.1	0.021	159.6	0.006
Total identified	97.3	3.949	89.7	2.187	85.1	0.713	76.2	0.242	57.5	0.032	34.6	0.008	10.5	<0.001
Total unidentified	0.6	0.026	4.1	0.099	5.5	0.046	9.6	0.030	16.7	0.009	45.1	0.010	17.1	0.001
Total bound residues	1.1	0.045	1.9	0.045	3.7	0.031	5.8	0.019	21.9	0.012	19.6	0.005	NA [3]	NA
% Accountability	100 [2]		100 [2]		104.4		99.9		100.6		109.7		159.6	

[1] Duplicate samples (except 0-, 3-, and 7-day immature shoot and mature grain samples) were extracted and analyzed by HPLC; values for the sample with the highest level of extracted/characterized residues are reported.
[2] Accountabilities for the 0- and 3-day immature shoot samples were 100% because the TRR was calculated by the summation of the extractable and nonextractable radioactivity.
[3] NA = Not analyzed.

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TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Rice Matrices Following a Single Postemergence Application of [Triazolo-pyrimidine-2-^{14}C]Penoxsulam at 0.083 lb ai/A.

Compound	Immature Rice Shoots (0-day)		Immature Rice Shoots (3-day)		Immature Rice Shoots (7-day)		Immature Rice Shoots (14-day)		Immature Rice Shoots (30-day)		Mature Rice Straw		Mature Rice Grain	
	TRR = 5.17 ppm		TRR = 1.83 ppm		TRR = 1.02 ppm		TRR = 0.424 ppm		TRR = 0.048 ppm		TRR = 0.021 ppm		TRR = 0.003 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Penoxsulam	99.9	5.16	84.9	1.56	66.2	0.675	53.3	0.227	12.3	0.006	8.9	0.003	6.4	<0.001
5-OH XDE-638	1.8	0.095	7.0	0.129	8.0	0.081	10.2	0.043	33.5	0.016	29.5	0.009	2.2	<0.001
Unknown Rt 6 mins.	--	--	0.6	0.011	2.5	0.026	4.0	0.017	9.2	0.004	10.9	0.003	4.1	<0.001
Unknown Rt 15 mins.	0.8	0.044	--	--	--	--	2.9	0.012	6.8	0.003	12.1	0.003	1.1	<0.001
Total identified	101.7	5.26	91.5	1.69	74.2	0.756	63.7	0.270	45.8	0.022	38.4	0.012	8.6	<0.001
Total characterized	0.8	0.044	0.6	0.011	2.5	0.026	6.9	0.029	16.0	0.007	23.0	0.006	5.2	<0.001
Total extractable	99.3	5.13	97.8	1.79	98.9	1.01	90.8	0.386	62.5	0.030	66.9	0.014	67.6	0.002
Total bound	0.7	0.034	2.2	0.041	5.0	0.051	9.2	0.039	24.7	0.012	40.5	0.008	NA	NA

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TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Rice Matrices Following a Single Postemergence Application of [Phenyl-U-^{14}C]Penoxsulam at 0.095 lb ai/A.

Compound	Immature Rice Shoots (0-day)		Immature Rice Shoots (3-day)		Immature Rice Shoots (7-day)		Immature Rice Shoots (14-day)		Immature Rice Shoots (30-day)		Mature Rice Straw		Mature Rice Grain	
	TRR = 3.99 ppm		TRR = 2.34 ppm		TRR = 0.838 ppm		TRR = 0.318 ppm		TRR = 0.056 ppm		TRR = 0.023 ppm		TRR = 0.004 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Penoxsulam	94.4	3.83	81.1	1.98	74.6	0.625	62.0	0.197	41.3	0.023	4.2	0.001	7.2	<0.001
5-OH XDE-638	2.9	0.118	8.6	0.209	10.5	0.088	14.2	0.045	16.2	0.009	30.4	0.007	3.3	<0.001
Unknown Rt 6 mins.	--	--	--	--	0.6	0.005	1.6	0.005	8.0	0.004	21.9	0.005	14.7	0.001
Unknown Rt 15 mins.	0.6	0.026	4.1	0.099	4.9	0.041	8.0	0.025	8.7	0.005	23.2	0.005	2.4	<0.001
Total identified	97.3	3.95	89.7	2.19	85.1	0.713	76.2	0.242	57.5	0.032	34.6	0.008	10.5	<0.001
Total characterized	0.6	0.026	4.1	0.099	5.5	0.046	9.6	0.030	16.7	0.009	45.1	0.010	17.1	0.001
Total extractable	98.9	3.94	98.1	2.30	100.7	0.84	94.1	0.299	78.7	0.044	90.1	0.021	159.6	0.006
Total bound	1.1	0.045	1.9	0.045	3.7	0.031	5.8	0.019	21.9	0.012	19.6	0.005	NA	NA

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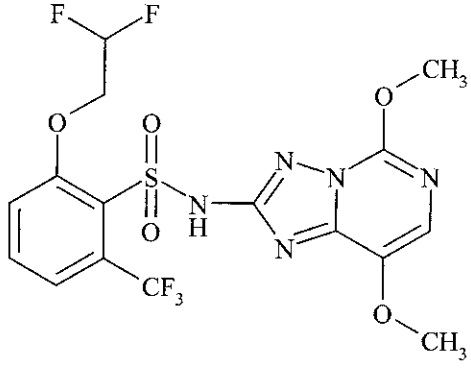
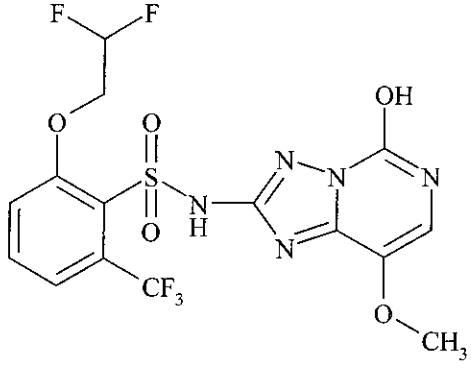
C.3. Proposed Metal olic Profile

FIGURE C.3.1. P posed Metabolic Profile of Penoxsulam in Rice.

The petitioner did not pr pose a metabolic pathway for penoxsulam residues in rice.

TABLE C.3.1. Identifica on of Compounds from Metabolism Study.

Common name/code Figure C.3.1 ID No.	Chemi l name	Chemical structure
Penoxsulam; XDE-638	benzen sulfonamide, 2-(2,2-difluor ethoxy)-N-(5,8-dimeth xy[1,2,4]triazolo[1,5-c]-pyrimi n-2-yl)-6-(trifluoromethyl)-	
5-OH XDE-638	2-(2,2-methox fluoroethoxy)-N-(5,6-dihydro-8--5-oxo[1,2,4]triazolo[1,5-c]-pyrimi n-2-yl)-6-(trifluoromethyl) benzen ulfonamide	

D. CONCLUSION

The total radioactive resi ues were 0.021 and 0.003 ppm in mature rice straw and grain, respectively, harvested 1 4 days following a single postemergence application of **[triazolopyrimidine-2-^{14}C]penoxsulam** to rice plants at the 5- to 6-leaf growth stage at 0.083 lb ai/A. TRR were 5.17 ppm in immature rice shoots collected on the day of treatment and declined with each subsequent sampling interval, to 0.048 ppm at the 30-day PTI.

In mature rice matrices harvested 134 days following a single postemergence application of **[phenyl-U-^{14}C]penoxsulam** to rice plants at the 5- to 6-leaf growth stage at 0.095 lb ai/A, TRR were 0.023 and 0.004 ppm in mature rice straw and grain, respectively. TRR were 3.99 ppm in

immature rice shoots collected on the day of treatment and declined with each subsequent sampling interval, to 0.056 ppm at the 30-day PTI.

Total identified residues ranged ~46-102% TRR in immature shoots, 35-38% TRR in straw, and 9-11% TRR in grain. Parent penoxsulam was the major component identified in immature rice shoots (both labels) harvested at 0-, 3-, 7-, and 14-day PTIs. Penoxsulam remained the major component identified in PH-label 30-day PTI immature shoots, but was present in TP-label 30-day PTI immature shoots at lower levels. Penoxsulam was also identified as a minor component in mature rice straw and grain (both labels). The metabolite 5-OH XDE-638 was identified as the major component in 30-day PTI immature rice shoots and mature rice straw (both labels). The 5-OH metabolite was identified as a minor component in immature rice shoots harvested at 0-, 3-, 7-, and 14-day PTIs (both labels). In addition, two unknowns, present individually at levels of ~1-23% TRR, were characterized by HPLC in rice matrices as being more polar than penoxsulam and 5-OH XDE-638. Because of the low levels of the unknowns in mature straw samples, no attempts were made to further identify these residues.

The petitioner proposed that penoxsulam primarily degrades to its 5-OH metabolite and at least two minor unknown metabolites in rice matrices; little translocation of penoxsulam residues or its metabolites was observed into the grain.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: R. Loranger (7/9/04)
Petition Number(s): 3F06542
DP Barcode(s): D288152
PC Code: 119031

Template Version April 2003

Attachment: R. Yoder, Dow AgroSciences, 5/4/04

IN RESPONSE TO Errico.Philip@epamail.epa.gov
SENT: Tuesday, M y 04, 2004 2:20 PM

SUBJECT: Respon e to Additional Information Requested by Residue Chemistry for Penoxsulam

STUDY IDENTIFI ATION: 45830712 Yoder, R.; Embrey, S. (2001) Nature of Residue of XDE-638 in Rice Following Post-Emergent, Foliar Application: Lab Project Number: 990028.

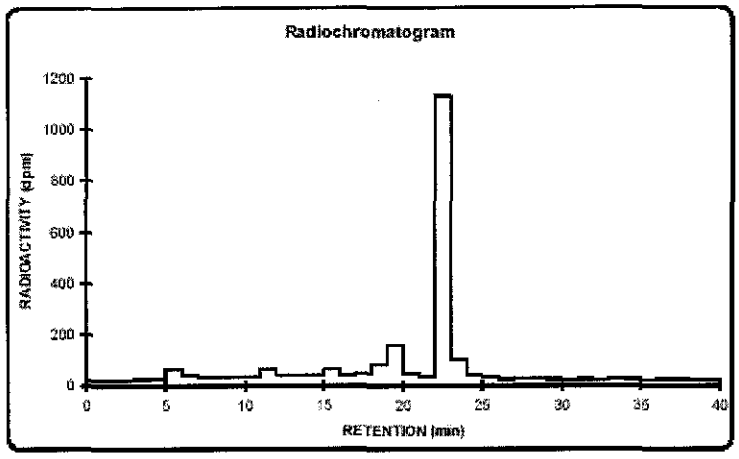
REQUEST OF RES DUE CHEMISTRY: Residue Chemistry commented that the petitioner indicated hat storage stability analyses had been conducted to support the study, but did not pr vide any supporting data or chromatograms. In addition, the dates of analysis were not provided for any sample, so it could not be determined how long samples were stored prior to analysis.

RESPONSE OF PE ITIONER: The requested dates have been included below.

Sample	Date Harvest	Shipped	Extract	HPLC
0 DAT	06/08/99	06/09/99	06/22/99	06/29/99
3 DAT	06/11/99	06/16/99	06/23/99	06/29/99
7 DAT	06/15/99	06/16/99	06/25/99	06/30/99
14 DAT	06/22/99	06/23/99	06/28/99	07/01/99
2nd extrac			07/17/99	08/03/99
30 DAT	07/08/99	07/14/99	07/16/99	07/30/99
Straw	10/20/99	11/01/99	11/08/99	11/23/99
Rice	10/20/99	11/01/99	12/14/99	12/21/99

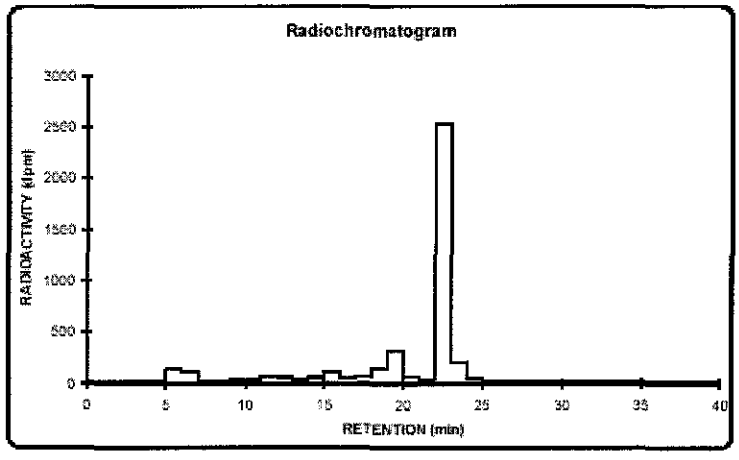
The Residue Chemi ry Guidelines (OPPTS 860.1300 Nature of the Residue – Plants, Livestock, section ((7)) recommend that storage stability data should not normally be required for samples analyzed within 4 to 6 months of collection, provided evidence is given that attempts were made to limit degradation of residues by appropriate storage of matrices and extract during the analytical portion of the study. All samples were analyzed within 2 m nths of harvest; most samples were analyzed within one month. All samples were stored n a freezer when not undergoing analysis. As samples were analyzed within the ecommended 4-6 month time frame, no storage stability data were necessary.

Chromatograms for he TP-labeled samples of the 14 DAT extracts are posted below to show there were no ifferences between samples during a brief frozen storage period.



Day 14 TP-labeled sample extracted on 7/17/99

Retention Time (min)	% of HPLC	% of TRR	ppm	Compound
6.0	3.7%	2.7%	0.012	
12.0	4.1%	3.0%	0.013	
16.0	4.0%	2.9%	0.012	
20.0	14.3%	10.6%	0.045	5-OH
23.0	72.2%	53.1%	0.225	penoxsulam



Day 14 TP-labeled sample extracted on 6/28/99

Retention Time (min)	% of HPLC	% of TRR	ppm	Compound
6.0	5.5%	4.0%	0.017	
12.0	3.4%	2.5%	0.010	
16.0	3.9%	2.9%	0.012	
20.0	14.0%	10.2%	0.043	5-OH
23.0	73.1%	53.5%	0.227	penoxsulam

Additional questions concerning the storage or any other aspect of this study may be directed to the study director:

Robin Yoder
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(317) 337-3471
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Flumioxazin/129034/Valent USA/59639
OPPTS 860.1380
Storage Stability -Almonds

Primary Evaluator	William Cutchin, Chemist SIMB/HED (7509C)	Date: 7/19/04
Peer Reviewer	William Drew, Chemist RAB2/HED (7509C)	
Approved by	Richard Loranger Branch Senior Scientist RAB2/HED (7509C)	for RAL 7/22/04

STUDY REPORTS:

MRID No. 45375505 T. Schreier (2001) Magnitude of the Residue of Flumioxazin on Almonds: Lab Project Number: 20116. Unpublished study prepared by Valent U.S.A. Corp. 368 pages.

EXECUTIVE SUMMARY:

Samples of whole almond nutmeats and hulls were fortified with flumioxazin (100%) at a level of 0.05 ppm and stored at -20°C for a duration of 186 days. Samples of almond nutmeats were also fortified with 1-hydroxy-trans-1,2-cyclohexanedicarboxylic acid (1-OH-HPA; 96.7%) at a level of 0.1 ppm and stored at -20°C for a duration of 263 days. Under these conditions, residues of the parent and the metabolite essentially did not change in almond nutmeats and hulls.

The analytical method used to analyze samples for flumioxazin in/on the almond matrices of almond nutmeat and almond hulls is adequate for data collection purposes. In the method, RM-30A-1, flumioxazin is extracted from almond nutmeat and hulls using acetone:water, partitioned into dichloromethane then between hexane and acetonitrile, and cleaned up by column chromatography. Gas chromatographic analysis is performed using a nitrogen-phosphorus specific detector. The limit of quantitation (LOQ) and limit of detection (LOD) of the residue method for flumioxazin in/on almond nutmeat and almond hulls were 0.01 ppm and 0.005 ppm, respectively.

The analytical method used to analyze samples for 1-OH-HPA during this study is adequate for data collection purposes. In the method, based on RM-30M4, the metabolite 1-OH-HPA is extracted from almond hulls using acid hydrolysis followed by liquid/liquid partition into ethyl acetate. The 1-OH-HPA is methylated, partitioned into hexane, and cleaned up by column chromatography. The residues of 1-OH-HPA are analyzed as its dimethyl ester, 1-OH-HPA-DME-1 (a.k.a. 1-HPA-DME, HPADME) using gas chromatography and a mass selective detector. The LOQ and LOD of the residue method for 1-OH-HPA in/on almond hulls were 0.1 ppm and 0.05 ppm, respectively.

The data indicate that residues of fluazinam are stable at -20°C for a duration of 186 days in almond nutmeats and hulls. The data also indicate that residues of 1-OH-HPA are stable at -20°C for a duration of 263 days in almond hulls.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP Barcode D301247]

COMPLIANCE:

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported for this study.

A. BACKGROUND INFORMATION

Flumioxazin is a new N-phenylphthalimide herbicide proposed for preemergence application for the selective control of susceptible broadleaf weeds. While flumioxizin was applied as Valor™ WDG (EPA Reg. No. 59639-99) during the almond field trials, it is formulated for use on almonds as Chateau™ WDG (EPA Reg. No. 59639-RRO), both formulations are water dispersible granules comprised of 51% ai.

TABLE A.1. Test Compound Nomenclature

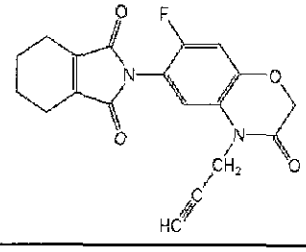
Compound	Chemical Structure
	
Common name	Flumioxazin
Company experimental name	S-53482
IUPAC name	*N*-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2*H*-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboxamide
CAS name	2-[7-fluoro-3,4-dihydro-3-oxo-4-(2-propynyl)-2*H*-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione
CAS #	103361-09-7
End-use product/EP	Chateau™ WDG

TABLE A.2. Physicochemical Properties	
Parameter	Value
Melting point/range (°C)	202-204
pH	7.29 @ 25°C
Density	1.51 g/mL @ 20°C
Water solubility (25°C)	1.79 mg/L
Solvent solubility (mg/L at __°C)	NA
Vapour pressure	2.41 x 10^{-6} mm Hg
Dissociation constant (pK_a)	NA
Octanol/water partition coefficient Log(K_{OW})	2.55 @ 20°C
UV/visible absorption spectrum	NA

B. EXPERIMENTAL DESIGN

B.1. Sample Handling and Preparation

The stability of flumioxazin in/on almond nutmeat and almond hulls, and 1-OH-HPA in almond hulls, was determined by the storage and periodic analysis of laboratory spiked samples. For the evaluation, aliquots of each matrix were weighed into plastic storage bags. Each aliquot was fortified with a freshly prepared solution of flumioxazin (0.5 or 1.0 mL, depending on sample size, at 1.0 µg/mL) or 1-OH-HPA (0.25 mL at 10.0 µg/mL) in acetone. The acetone was allowed to evaporate before sealing the bags. Three aliquots of each matrix/analyte combination were immediately extracted and analyzed to establish initial (Day 0) recovery; the remaining bags were placed in a freezer (nominally -20°C) and stored for the duration of the study. At periodic intervals duplicate samples were removed from storage and analyzed along with an untreated control and a freshly fortified sample.

B.2. Analytical Methodology

The analytical method used to analyze samples for flumioxazin in/on the almond matrices of almond nutmeat and almond hulls was RM-30A-1. The method has undergone both a successful ILV trial and has been successfully validated down to an LOQ of 0.01 ppm by the Agency (PP#s 7F4841 and 0F6171, DP Barcodes: D259493 and D268181, D. Dotson, 3/12/2001). Flumioxazin is extracted from almond nutmeat and hulls using acetone:water. The residues of flumioxazin are partitioned into dichloromethane, partitioned between hexane and acetonitrile, and subjected to a Florisil column chromatography cleanup. Gas chromatographic analysis is performed using a nitrogen-phosphorus specific detector and a DB-5 or DB-17 column. The LOQ and LOD of the residue method for flumioxazin in/on both almond nutmeat and almond hulls were 0.01 ppm and 0.005 ppm, respectively.

The analytical method used to analyze samples for 1-OH-HPA during this study was based on RM-30M4. The method has been determined to be adequate for data collection of 1-OH-HPA from peanuts and soybeans down to an *LOQ and LOD of 0.02 ppm and 0.01*, respectively (PP#s 7F4841 and 0F6171, DP Barcodes: D259493 and D268181, D. Dotson, 3/12/2001). The metabolite 1-OH-HPA is extracted from almond hulls using acid hydrolysis. A diatomaceous earth partition column in the original method was replaced with the more common liquid/liquid partition. Both the diatomaceous earth column and the liquid/liquid partition allow the 1-OH-HPA to be partitioned into ethyl acetate. The 1-OH-HPA is methylated with dimethyl sulfate, partitioned between water and hexane, and cleaned up using Florisil column chromatography. The residues of 1-OH-HPA are analyzed as its dimethyl ester, 1-OH-HPA-DME-1 (a.k.a. 1-HPA-DME, HPADME). Gas chromatographic analysis is performed using a mass selective detector and an RTX-200 column. The LOQ and LOD of the residue method for 1-OH-HPA in/on almond hulls were 0.1 ppm and 0.05 ppm, respectively.

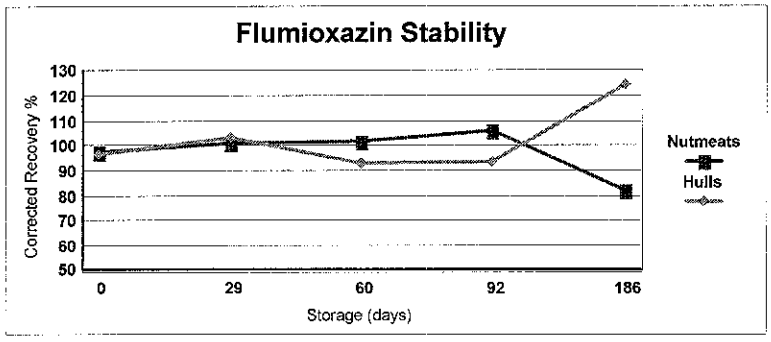
C. RESULTS AND DISCUSSION

The analytical methods used to determine the residues of flumioxazin and 1-OH-HPA on almond nutmeats and hulls are adequate for data collection. The data indicate that residues of fluazinam are stable at -20°C for a duration of 186 days in almond nutmeats and hulls. The data also indicate that residues of 1-OH-HPA are stable at -20°C for a duration of 263 days in almond hulls.

TABLE C.1. Summary of Concurrent Recoveries of Flumioxazin from Almond Matrices.

Matrix	Spike level (mg/kg)	Storage Interval (days)	Fresh Fortified Recovery (%)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)	Avg Corrected Recovery (%)
Flumioxazin							
nutmeat	0.05	0	101	2	98,99	99 ± 1.0	98
		29	115	2	117,116	116 ± 0.5	101
		60	95	2	94,100	97 ± 3.0	102
		92	119	2	123,130	127 ± 3.5	106
		186	99	2	83,79	81 ± 2.0	81
hulls	0.05	0	94	2	91,91	91	97
		29	103	2	100,112	106 ± 6.0	103
		60	95	2	89,88	89 ± 0.5	93
		92	101	2	93,96	127 ± 3.5	94
		186	78	2	92,102	81 ± 2.0	124
1-OH-HPA							
hulls	0.1	0	89	2	90,88	98 ± 1.0	100
		27	94	2	94,97	96 ± 1.5	102
		55	80	2	77,81	79 ± 2.0	99
		131	76	2	77,80	79 ± 1.5	103
		263	70	2	72,70	71 ± 1.0	101

FIGURE C.1. Graphs of Flumioxazin and 1-OH-HPA Storage Stability Study



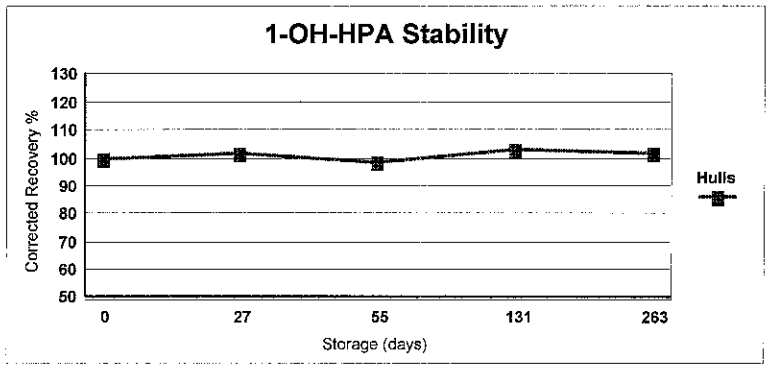


TABLE C.2. Stability of Flumioxazin Residues in Almonds Following Storage at -20°C.				
Commodity	Spike level (mg/kg)	Storage interval (days)	Recovered residues (mg/kg)	Corrected % recovery*
Flumioxazin				
nutmeat	0.05	186	0.052	98
hulls	0.05	186	0.048	101
1-OH-HPA				
hulls	0.1	263	0.041	101

* Corrected for concurrent-recoveries for all data

D. CONCLUSION

The study indicates that residues of flumioxazin are stable at -20°C for a duration of 186 days in almond nutmeats and hulls. The study also indicates that residues of 1-OH-HPA are stable at -20°C for a duration of 263 days in almond hulls. The data are sufficient to satisfy the Agency's requirement for storage stability data for almond commodities.

E. REFERENCES

PP#s 7F4841 and 0F6171. Tolerance Petitions for the Use of Flumioxazin on Peanuts, Soybeans, and Sugarcane. Evaluation of Residue Chemistry and Analytical Methodology. DP Barcodes: D259493 and D268181, D. Dotson, 3/12/2001.

F. DOCUMENT TRACKING

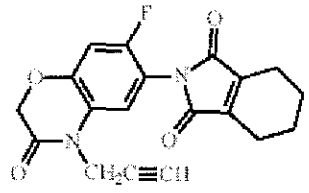
RDI: W. Drew (7/13/04), R. Loranger (7/19/04)
Petition Number(s): 1F6296
DP Barcode(s): D284045
PC Code: 129034

Template Version September 2003

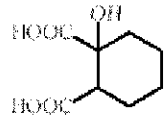
Attachment Structures of Flumioxazin and Metabolites

Attachment Structures of Flumioxazin and Metabolites

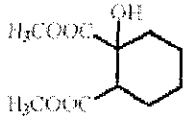
Flumioxazin



1-OH-HPA



1-OH-HPA-DME-1
Methylated Product of 1-OH-HPA



Flumioxazin/59639-RRO/129034/Valent USA/59639
DACO 7.4.1/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3
Crop Field Trial - Almond

Primary Evaluator	William Cutchin, Chemist SIMB/HED (7509C)	Date: 7/19/04
Peer Reviewer	William Drew, Chemist RAB2/HED (7509C)	
Approved by	Richard Loranger Branch Senior Scientist RAB2/HED (7509C)	7/22/04

STUDY REPORTS:

MRID No. 45375505 T. Schreier (2001) Magnitude of the Residue of Flumioxazin on Almonds: Lab Project Number: 20116. Unpublished study prepared by Valent U.S.A. Corp. 368 pages.

EXECUTIVE SUMMARY:

The registrant has submitted field trial data for flumioxazin on almonds. Five field trials trials were conducted encompassing Regions 10 (CA) during the 1999 growing season. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 and Directive 98-02; Section 9. At four of the locations, flumioxazin, formulated as Valor™ WDG, was twice broadcast to the soil at 0.375 lb ai/A (0.42 kg ai/ha) at a 60-day retreatment interval for a total seasonal application rate of 0.75 lb ai/A (0.84 kg ai/ha). At the fifth location, flumioxazin, formulated as Valor™ WDG, was twice broadcast to the soil at 0.75 lb ai/A (0.84 kg ai/ha) at a 60-day retreatment interval for a total seasonal application rate of 1.5 lb ai/A (1.68 kg ai/ha). An adjuvant was added to the spray mixture for all applications, but not always identified. Almonds were harvested at 60-61 day PHI.

The analytical method used to analyze samples for flumioxazin in/on the almond matrices of almond nutmeat and almond hulls is adequate for data collection purposes. In the method, RM-30A-1, flumioxazin is extracted from almond nutmeat and hulls using acetone:water, partitioned into dichloromethane then between hexane and acetonitrile, and cleaned up by column chromatography. Gas chromatographic analysis is performed using a nitrogen-phosphorus specific detector. The limit of quantitation (LOQ) and limit of detection (LOD) of the residue method for flumioxazin in/on almond nutmeat and almond hulls were 0.01 ppm and 0.005 ppm, respectively.

The analytical method used to analyze samples for 1-hydroxy-trans-1,2-cyclohexanedicarboxylic acid (1-OH-HPA) during this study is adequate for data collection purposes. In the method, based on RM-30M4, the metabolite 1-OH-HPA is extracted from almond hulls using acid hydrolysis followed by liquid/liquid partition into ethyl acetate. The 1-OH-HPA is methylated, partitioned into hexane, and cleaned up by column chromatography.

The residues of 1-OH-H A are analyzed as its dimethyl ester, 1-OH-HPA-DME-1 (a.k.a. 1-HPA-DME, HPADME) sing gas chromatography and a mass selective detector. The LOQ and LOD of the residue meth od for 1-OH-HPA in/on almond hulls were 0.1 ppm and 0.05 ppm, respectively.

The results from ese trials show that maximum flumioxazin residues are 0.007 ppm on almond nutmeats for bot total application rates, 0.75 lb ai/A and 1.5 lb ai/A, and 60-day PHI. The results also show tha maximum flumioxazin residues on almond hulls are 0.066 ppm for the 0.75 lb ai/A total applica ion rate, and 0.617 ppm for the 1.5 lb ai/A total application rate, both with 60-day PHIs. No re idues of 1-OH-HPA were found above the 0.05 ppm LOQ on almond hulls for either applicatic 1 rate. A residue decline study was not conducted.

STUDY/WAIVER ACC EPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditi ns and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chem stry Summary Document [DP Barcode D301247].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statement were provided. With the exception of the following items, this study was performed in compli nce with EPA GLP FIFRAStandards [40 CFR Part 160]: weather and miscellaneous field infor ation (e.g. field history, irrigation and cultural practices, and plot description) included in t is report was not collected following GLP standards; storage temperature data for Tria B were not collected in accordance with GLPs; scales used to weigh field samples for Trial B nd Trial C were not maintained in accordance with GLPs; and, some entries in the Field Noteb ok for Trial E were not initialed and dated at the time of entry. The deviations from regulator requirements do not adversely impact the validity of the study.

A. BACKGROUNI INFORMATION

Flumioxazin is a 1 ew N-phenylphthalimide herbicide proposed for preemergence application for the selecti e control of susceptible broadleaf weeds.

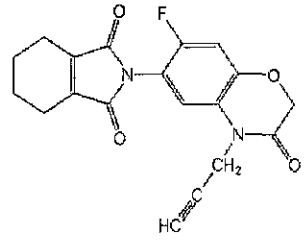
TABLE A.1. Test Compound Nomenclature	
Compound	Chemical Structure 
Common name	Flumioxazin
Company experimental name	S-53482
IUPAC name	*N*-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2*H*-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboxamide
CAS name	2-[7-fluoro-3,4-dihydro-3-oxo-4-(2-propynyl)-2*H*-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione
CAS #	103361-09-7
End-use product/EP	Chateau™ WDG

TABLE A.2. Physicochemical Properties	
Parameter	Value
Melting point/range (°C)	202-204
pH	7.29 @ 25°C
Density	1.51 g/mL @ 20°C
Water solubility (25°C)	1.79 mg/L
Solvent solubility (mg/L at __°C)	NA
Vapour pressure	2.41 x 10^{-6} mm Hg
Dissociation constant (pK_a)	NA
Octanol/water partition coefficient Log(K_{ow})	2.55 @ 20°C
UV/visible absorption spectrum	NA

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

TABLE B.1.1 Trial Site Conditions			
Trial Identification (City, State/Year)	Soil Type	Meteorological data	
		Overall monthly rainfall range	Overall T°C range
Chico, CA 1999 V-20116-A	Vina sandy loam	12 in (sprinkler irrigation)	NR

Hughson, CA 1999 V-20116-B	Hanford	4-6 in (flood irrigation)	reported as within historical norms
Kerman, CA 1999 V-20116-C	Hanford sandy loam	4-8 in (flood irrigation)	reported as cooler than average
Madera, CA 1999 V-20116-D	Tugunga	2-12 in (microsprinkler irrigation)	reported as below normal
Terra Bella, CA 1999 V-20116-E	Hanford fine sandy loam	8-10 in (microsprinkler irrigation)	reported as below normal

NR= not reported

The reported temperatur s are below the average historical values for the residue study period. The actual rainfall avera e was within the historical rainfall average. Irrigation was used to supplement as needed.

TABLE B.1.2. Study Use P ttern.

Location (City, State/Year)	EP [1]	Application					Tank Mix Adjuvants
		Method/Timing	Vol, GPA[2]	Rate, g a.i./A	RTI, [3] days	Total Rate, g a.i./A (lb a.i./A) (kg ai/ha)	
Chico, CA 1999	Valor WDG Herbicide	b oadcast to soil/ nut d velopment	18	169.6	60	341.5 (0.753) (0.845)	crop oil conc.
		b oadcast to soil/ nut n aturation prior to h ll split	18	171.9			
	Valor WDG Herbicide	b oadcast to soil/ nut d velopment	18	339.3	60	682.2 (1.5) (1.69)	crop oil conc
		b oadcast to soil/ nut n aturation prior to h ll split	18	342.9			
Hughson, CA 1999	Valor WDG Herbicide	b oadcast to soil/ g en nut	25	172.0	60	343.7 (0.758) (0.85)	identity of adjuvant not indicated
		b oadcast to soil/ b ginning hull split	25	171.7			
Kerman, CA 1999	Valor WDG Herbicide	b oadcast to soil/ nuts tc 1 ½ ", trees leafed	20	168.7	60	338.3 (0.746) (0.84)	Agridex
		b oadcast to soil/ b ore hull split, trees m ture	20	169.6			
Madera, CA 1999	Valor WDG Herbicide	b oadcast to soil/ fr its 1 ½ - 2 ½ "	20	171.5	60	340.7 (0.751) (0.84)	identity of adjuvant not indicated
		b oadcast to soil/ fr ts 1 ½ - 2 ½ "	20	169.2			

TABLE B.1.2. Study Use Pattern.

Location (City, State/Year)	EP [1]	Application					Tank Mix Adjuvants
		Method/Timing	Vol, GPA[2]	Rate, g a.i./A	RTI, [3] days	Total Rate, g a.i./A (lb a.i./A) (kg ai/ha)	
Terra Bella, CA 1999	Valor WDG Herbicide	broadcast to soil/ fruit maturation	20	170.2	60	339.8 (0.749) (0.84)	RMA crop oil
		broadcast to soil/	24	169.6			

[1]EP = End-use Product
[2] Gallons per acre
[3] Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations

NAFTA Growing Region	Almond	
	Submitted	Requested US
1		
1A		
2		
3		
4		
5		
5A		
5B		
6		
7		
7A		
8		
9		
10	5	5
11		
12		
13		

14		
15		
16		
17		
18		
19		
20		
21		
Total	5	5

B.2. Sample Handlin ; and Preparation

Almonds were cc lected at normal mature harvest from the untreated control plots and from the five treated plot (in duplicate). All almond nutmeat and hull samples harvested for this study were shipped froze ı and stored at -20°C until analysis.

B.3. Analytical Meth dology

The analytical me hod used to analyze samples for flumioxazin in/on the almond matrices of almond nutmeat and a nond hulls was RM-30A-1. The method has undergone both a successful ILV trial and l as been successfully validated down to an LOQ of 0.01 ppm by the Agency (PP#s 7F4841 ar l 0F6171, DP Barcodes: D259493 and D268181, D. Dotson, 3/12/2001). Flumioxazir is extracted from almond nutmeat and hulls using acetone:water. The residues of flumioxazin a e partitioned into dichloromethane, partitioned between hexane and acetonitrile, and subjecte to a Florisil column chromatography cleanup. Gas chromatographic analysis is performed usi g a nitrogen-phosphorus specific detector and a DB-5 or DB-17 column. The LOQ and L)D of the residue method for flumioxazin in/on both almond nutmeat and almond hulls were 0.)1 ppm and 0.005 ppm, respectively.

The analytical me hod used to analyze samples for 1-OH-HPA during this study was based on RM-30M4. Th method has been determined to be adequate for data collection of 1-OH-HPA from peanuts a d soybeans down to an LOQ and LOD of 0.02 ppm and 0.01, respectively (PP#s 7F484 and 0F6171, DP Barcodes: D259493 and D268181, D. Dotson, 3/12/2001). The metabol te 1-OH-HPA is extracted from almond hulls using acid hydrolysis. A diatomaceous earth partit on column in the original method was replaced with the more common liquid/liquid partition. Bc h the diatomaceous earth column and the liquid/liquid partition allow the 1-OH-HPA to be part tioned into ethyl acetate. The 1-OH-HPA is methylated with dimethyl sulfate, partitioned betwe n water and hexane, and cleaned up using Florisil column chromatography. The re: dues of 1-OH-HPA are analyzed as its dimethyl ester, 1-OH-HPA-DME-1 (a.k.a. 1-HPA-D fE, HPADME). Gas chromatographic analysis is performed using a mass selective detector a d an RTX-200 column. The LOQ and LOD of the residue method for

1-OH-HPA in/on almond hulls were 0.1 ppm and 0.05 ppm, respectively.

C. RESULTS AND DISCUSSION

The storage stability study (45375505ss.der.wpd, W. Cutchin) supports the storage durations/conditions of samples in the crop field trials. The analytical methods for flumioxazin and 1-OH-HPA are adequate for data collection for this study. Flumioxazin fortification of control samples of almond nutmeats and hulls were conducted at 0.01 to 1.0 ppm and 1-OH-HPA fortification of control samples of almond hulls were conducted at 0.01 to 0.5 ppm. Concurrent recoveries ranges from 71 to114 (avg 91 ± 10%). The LOQ and LOD of the residue method for flumioxazin in/on both almond nutmeat and almond hulls were 0.01 ppm and 0.005 ppm, respectively. The petitioner provided adequate sample chromatograms of control samples of various crop matrices that show no interfering peaks. Although no calibration curves were presented, adequate sample chromatograms of standard solutions were provided to indicate that the analytical method provided a linear response. The LOQ and LOD of the residue method for 1-OH-HPA in/on almond hulls were 0.1 ppm and 0.05 ppm, respectively.

The number and geographic location of the submitted studies were adequate. The results from these trials show that maximum flumioxazin residues are 0.007 ppm on almond nutmeats for both total application rates, 0.75 lb ai/A and 1.5 lb ai/A, and 60-day PHI. The results also show that maximum flumioxazin residues on almond hulls are 0.066 ppm for the 0.75 lb ai/A total application rate, and 0.617 ppm for the 1.5 lb ai/A total application rate, both with 60-day PHIs. No residues of 1-OH-HPA were found above the 0.05 ppm LOQ on almond hulls for either application rate. A residue decline study was not conducted.

TABLE C.1. Summary of Concurrent Recoveries of Flumioxazin and from Almond Matrices.

Matrix	Spike level (mg/kg)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
Flumioxazin				
nutmeat	0.01 0.5	5 5	94,106,90,89,105 101,110,106,98,114	97 ± 7.3 106 ± 5.8
hulls	0.01 0.5 1.0	5 5 1	90,71,75,77,83 83,84,86,88,96 83	79 ± 6.7 87 ± 4.6 83
1-OH-HPA				
hulls	0.01 0.5	5 5	90,93,81,86,86 98,96,90,84,93	87 ± 4.1 92 ± 4.9

TABLE C.2. Summary of Storage Conditions

Matrix	Storage Temp. (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Flumioxazin			
nutmeat	-20	152-185	186
hulls	-20	152-185	186

	1-OH-HPA		
hulls	-20	235-254	263

TABLE C.3. Residue D ta from Crop Field Trials with Flumioxazin.

Trial ID (City, State/Year)	Region	Crop/ Variety	Commodity or Matrix	Total Rate, g a.i./A (lb a.i./A) (kg ai/ha)	PHI (days)	Flumioxazin (ppm)	1- OH-HPA (ppm)
Chico, CA 1999	X	Carmel	nutmeat	341.5 (0.753) (0.845)	60	0.005,<0.005 <0.005,<0.005	NA
			hulls			0.013,0.014 0.029,0.032	<0.05,<0.05 <0.05,<0.05
Hughson, CA 1999	X	Carmel	nutmeat	682.2 (1.5) (1.69)	60	0.006,0.007	NA
			hulls			0.487,0.617	<0.05,<0.05
Kerman, CA 1999	X	Carmel	nutmeat	343.7 (0.758) (0.85)	60	<0.005,<0.005	NA
			hulls			<0.005,<0.005	<0.05,<0.05
Madera, CA 1999	X	N n-Pareil	nutmeat	340.7 (0.751) (0.84)	60	<0.005,<0.005	NA
			hulls			0.037,0.041	<0.05,<0.05
Terra Bella, CA 1999	X	Carmel	nutmeat	339.8 (0.749) (0.84)	61	0.006,0.007	NA
			hulls			0.062,0.066	<0.05,<0.05

TABLE C.4. Summary f Residue Data from Crop Field Trials with Flumioxazin.

Commodity	Total Applic Rate, g a.i./A (lb a.i./A) (kg ai/ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Flumioxazin									
nutmeat	340 (0.75) (0.84)	60-61	10	<0.005	0.007	0.0065	0.0025	0.0036	0.0017
hulls			10	<0.005	0.041	0.039	0.0305	0.0299	0.0213
nutmeat	682 (1.5) (1.69)	60	2	0.006	0.007	0.0065	0.0065	0.0065	0.0005
hulls			2	0.487	0.617	0.552	0.552	0.552	0.065
1-OH-HPA									
hulls	340 (0.75) (0.84)	60-61	2	<0.005	<0.005	<0.005	<0.005	<0.005	0
	682 (1.5) (1.69)	60	2	<0.005	<0.005	<0.005	<0.005	<0.005	0

* HAFT = Highest Average Fiel Trial.

D. CONCLUSION

The submitted studies are adequate to determine the residues of flumioxazin on almond nutmeats and hulls as a result of the of the use pattern.

E. REFERENCES

PP#s 7F4841 and 0F6171. Tolerance Petitions for the Use of Flumioxazin on Peanuts, Soybeans, and Sugarcane. Evaluation of Residue Chemistry and Analytical Methodology. DP Barcodes: D259493 and D268181, D. Dotson, 3/12/2001

F. DOCUMENT TRACKING

RDI: W. Drew (7/13/04), R. Loranger (7/19/04)
Petition Number(s): 1F6296
DP Barcode(s): 284045
PC Code: 129034

Template Version September 2003

13544

R100658

Chemical:

PC Code:
HED File Code 11000 Chemistry Reviews
Memo Date: 07/19/2004
File ID: 00000000
Accession Number: 412-04-0235

HED Records Reference Center
08/06/2004