Data Evaluation Report on the stability of penoxsulam in soil

PMRA Submission Number {.....} EPA MRID Number 46433902

Data Requirement: PMRA Data Code:
EPA DP Barcode: D328374
OECD Data Point:
EPA Guideline: Non-Guideline

Test material:

Common name: Penoxsulam.

Chemical name:

IUPAC name:	3-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-sulfonamide. 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide. 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 No.:	219714-96-2.
Synonyms:	XDE-638; DE-638; TSN101649; SP1019 (SePRO).
Smiles string:	FC(c1cccc(c1S(=O)(=O)N(c1nn2c(n1)ccnc2))OCC(F)F)(F)F (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 6/27/06. n1c(nc2n1c(ncc2OC)OC)NS(=O)(=O)c3c(cccc3C(F)(F)F)OCC(F)F.

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Company Code
Active Code
Use Site Category
EPA PC Code: 119031

CITATION: Thomas, A.D. and D.A. Lindsay. 2004. Frozen storage stability of XDE-638, 5-hydroxy-XDE-638, XDE-638 sulfonic acid (BSA), XDE-638 sulfonamide, BSTCA, and 2-amino-TP in soil. Unpublished study performed and submitted by Dow AgroSciences LLC, Indianapolis, IN. Laboratory Study ID: 010096.01. Experiment initiation July 27, 2001 and completion September 16, 2003 (p. 3). Final report issued November 23, 2004.

EXECUTIVE SUMMARY

A storage stability study was conducted by fortifying control soil from California with penoxsulam (3-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide) and the transformation products 5-OH (6-(2,2-difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluene sulfonamide); BSTCA (3-[6-(2,2-difluoroethoxy)- α,α,α-trifluoro-o-toluenesulfonamido]-s-triazole-5-carboxylic acid); BSA (2-(2,2-difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid); XDE-638 sulfonamide (2-(2,2-difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide); and, 2-amino-TP (2-amino-5,8-dimethoxy-s-triazolo[1,5-c]pyrimidine), at 0.03 µg/g, with subsequent analysis following 0, 91, 182, 196, 327, 594, and 781 days of frozen storage.

Storage stability results indicate that penoxsulam and the transformation products 5-OH, sulfonamide, and BSA were stable for the duration of the storage interval, 781 days, and that the stability of BSTCA and 2-amino-TP was questionable. Corrected recoveries of penoxsulam, 5-OH, sulfonamide and BSA ranged from 80-97%, 70-84%, 90-102%, and 90-108%, respectively, throughout the storage interval. Corrected recoveries of 2-amino-TP were 53% at day 0, were 43-44% from 91-196 days, 52% at 327 days, and 40-43% from 594-781 days, indicating that recoveries were consistent, but low. Corrected recoveries of BSTCA ranged from 80-89% from 0 to 182 days, then decreased to 64-68% from 196-781 days. The study authors stated that the decreased recoveries of BSTCA after 182 days reflect the use of a new BSTCA recertified standard, and that results did no reflect a significant change during the use of the new standard.

Mean corrected recoveries of penoxsulam and its transformation products.

Days posttreatment	Corrected recoveries					
	Penoxsulam	5-OH	Sulfonamide	BSTCA	BSA	2-Amino-TP
0	84%	77%	99%	89%	98%	53%
91	81%	72%	95%	80%	92%	43%
182	85%	74%	97%	89%	90%	43%
196	80%	70%	90%	64%	105%	44%
327	97%	82%	97%	64%	108%	52%
594	93%	84%	99%	68%	98%	43%
781	97%	83%	102%	65%	100%	40%

Study Acceptability: This study is classified as acceptable. No significant deviations from good scientific practices were noted.

MATERIALS AND METHODS

A bulk control soil sample of a clay loam soil (sand: 32.8%, silt 33.2%, clay: 34%, pH 6.5, CEC 21.67 meq/100 g, organic matter 5.19%, bulk density 1.18 g/cm^3; Figure 1a, p. 43) from California was obtained for use in the study (p. 15). The soil was sieved, and 5-g samples were fortified separately with penoxsulam and the transformation products 5-OH (6-(2,2-

difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluene sulfonamide); BSTCA (3-[6-(2,2-difluoroethoxy)- α,α,α-trifluoro-o-toluenesulfonamido]-s-triazole-5-carboxylic acid); BSA (2-(2,2-difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid); XDE-638 sulfonamide (2-(2,2-difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide); and, 2-amino-TP (2-amino-5,8-dimethoxy-s-triazolo[1,5-c]pyrimidine; Figure 1, pp. 40-41) at 0.03 µg/g (pp. 16-17). Soil samples were fortified such that each sample contained only one analyte. Three fortified samples were prepared for each analyte for each designated sampling interval. Samples were removed from storage at 0, 91, 182, 196, 327, 594, and 781 days for analysis (Table 1, p. 27).

Samples were extracted by shaking with 25 mL of acetonitrile:1.0 N hydrochloric acid (90:10, v:v) for a minimum of 60 minutes (p. 18). Following a second extraction with 15 mL of the extraction solution for a minimum of 30 minutes, the extracts were combined and an aliquot of the extract was concentrated by evaporation using a Turbo Vap and diluted with 0.1 N hydrochloric acid. The extract was purified using a Waters MAX 96-well plate solid phase extraction plate. Penoxsulam and its transformation products were eluted from the SPE plate with methanol:acetonitrile (20:80, v:v). The eluate was concentrated to dryness, reconstituted with acetonitrile:methanol:water (5:5:90, v:v:v containing 0.1% acetic acid), and analyzed for penoxsulam and the transformation products 5-OH, BSTCA, BSA, sulfonamide, and 2-amino-TP by HPLC with positive-ion electrospray tandem mass spectrometry (LC/MS/MS). The LOQ was 0.003 µg/g for each analyte (p. 13).

Chemical names and CAS numbers for the transformation products of penoxsulam.

Applicants Code Name	CAS Number	Chemical Name (IUPAC)	Chemical Formula	Molecular Weight (g/mol)	Smiles String
5-OH-XDE-638		6-(2,2-Difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluene sulfonamide		469	
BSTCA		3-[6-(2,2-Difluoroethoxy)-α,α,α-trifluoro-o-toluenesulfonamido]-s-triazole-5-carboxylic acid		416	
BSA		2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid		306	
Sulfanomide		2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide		305	
2-amino-TP		2-Amino-5,8-dimethoxy-s-triazolo[1,5-c]pyrimidine		195	

Data were obtained from Figure 1, pp. 40-41 of the study report and MRID 46433901.

Concurrent recoveries were determined on each day of analysis by fortifying two control 5-g soil samples with a mixture containing penoxsulam, 5-OH, BSA, BSTCA, XDE-638 sulfonamide, and 2-amino-TP at 0.03 µg/g (p. 17).

RESULTS AND DISCUSSION

Storage stability results indicate that penoxsulam and the transformation products 5-OH, sulfonamide, and BSA were stable for the duration of the 781-day storage interval, and that the stability of BSTCA and 2-amino-TP was questionable (Tables 2-7, pp. 28-33; Figures 98-100, pp. 140-142). Corrected recoveries of penoxsulam were initially 84% and ranged from 80-97% from 91-781 days; corrected recoveries of 5-OH were initially 77% and ranged from 70-84% from 91-781 days; corrected recoveries of sulfonamide were initially 99% and ranged from 90-102% from 91-781 days; and corrected recoveries of BSA were initially 98% and ranged from 90-108% from 91-781 days. Corrected recoveries of 2-amino-TP were initially 53% at day 0, ranged from 43-44% from 91-196 days, 52% at 327 days, and ranged from 40-43% from 594-781 days, which indicates that recoveries were consistent but low. Corrected recoveries of BSTCA ranged from 80-89% from 0 to 182 days and then decreased to 64-68% from 196-781 days. The study authors stated that the decreased recoveries of BSTCA after 182 days reflect the use of a new BSTCA recertified standard, and that results did not reflect a significant change during the use of the new standard (p. 24).

Mean uncorrected recoveries of penoxsulam and its transformation products.

Days posttreatment	Uncorrected recoveries					
	Penoxsulam	5-OH	Sulfonamide	BSTCA*	BSA	2-Amino-TP
0	62%	61%	71%	67%	87%	42%
91	70%	60%	69%	65%	76%	33%
182	80%	63%	71%	69%	70%	29%
196	53%	62%	77%	50%	79%	35%
327	57%	62%	73%	54%	87%	37%
594	63%	67%	74%	46%	75%	33%
781	66%	71%	81%	44%	67%	29%

Data were obtained from Tables 2-7, pp. 28-33 of the study report.
*BSTCA recoveries are calculated from the average concentration at each sampling interval (registrant-calculated values for uncorrected recoveries were omitted).

Mean corrected recoveries of penoxsulam and its transformation products.

Days posttreatment	Corrected recoveries					
	Penoxsulam	5-OH	Sulfonamide	BSTCA	BSA	2-Amino-TP
0	84%	77%	99%	89%	98%	53%
91	81%	72%	95%	80%	92%	43%
182	85%	74%	97%	89%	90%	43%
196	80%	70%	90%	64%	105%	44%
327	97%	82%	97%	64%	108%	52%
594	93%	84%	99%	68%	98%	43%
781	97%	83%	102%	65%	100%	40%

Data were obtained from Tables 2-7, pp. 28-33 of the study report.

Mean concurrent recoveries were 73 ± 12% for penoxsulam, 83 ± 7% for 5-OH, 76 ± 5% for sulfonamide, 73 ± 5% for BSTCA, 78 ± 7% for BSA, and 75 ± 4% for 2-amino-TP (Tables 8-13, pp. 34-39).

STUDY DEFICIENCIES

This study was not submitted to fulfill Subdivision N Guidelines.

REVIEWER'S COMMENTS

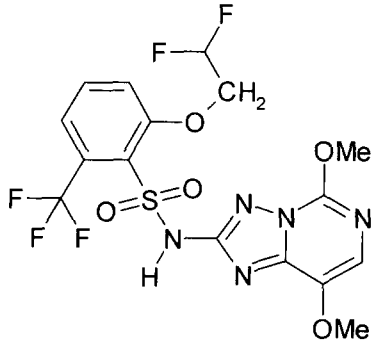
1. Fortifications for the stability study were made at three separate times: the 182-, 327-, and 781-day samples were fortified on July 27, 2001; the 91- and 196-day samples were fortified on October 25, 2001; and the day 0 and 594-day storage samples were fortified on January 24, 2002 (Table 1, p. 27). The reviewer notes that this practice of fortifying samples at different times is discouraged due to the variability that can be introduced when multiple fortifications are performed over time. All samples should have been fortified from the same stock solution at the same time, with different samples removed from storage at designated intervals.

2. Graphical representation of the stability of penoxsulam and its transformation products in frozen storage over time is presented in Figures 98-100 (pp. 140-142) of the study report. Recoveries were expressed as the percent of the day-0 recovery (day-0 recoveries were normalized to 100% recovery; values were reported in Tables 2-7, pp. 28-33).

Attachment 1: Structures of Parent Compound and Transformation Products

Penoxsulam [XDE-638; DE-638; TSN101649; SP1019 (SePRO)]

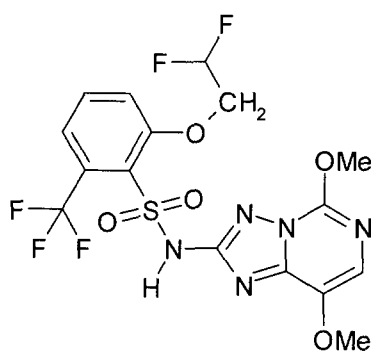
IUPAC Name:	3-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-sulfonamide. 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide. 6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide.
CAS Name:	2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide.
CAS Number:	219714-96-2.
SMILES String:	FC(c1cccc(c1S(=O)(=O)N(c1nn2c(n1)ccnc2))OCC(F)F)(F)F (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 6/27/06. n1c(nc2n1c(ncc2OC)OC)NS(=O)(=O)c3c(cccc3C(F)(F)F)OCC(F)F.



Identified Compounds

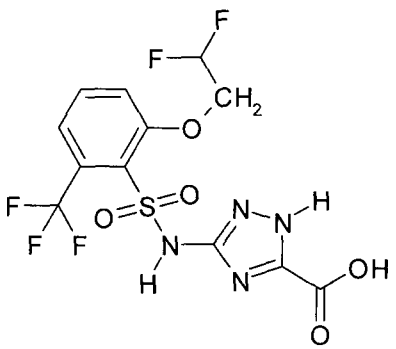
Penoxsulam [XDE-638; DE-638; TSN101649; SP1019 (SePRO)]

IUPAC Name:	3-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-sulfonamide. 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide. 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 Number:	219714-96-2.
SMILES String:	FC(c1cccc(c1S(=O)(=O)N(c1nn2c(n1)ccnc2))OCC(F)F)(F)F (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 6/27/06. n1c(nc2n1c(ncc2OC)OC)NS(=O)(=O)c3c(cccc3C(F)(F)F)OCC(F)F.



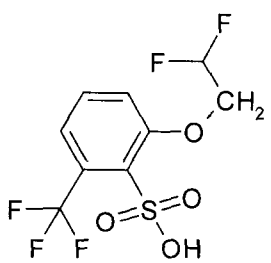
BSTCA [TSN103610; TSN101979]

IUPAC Name:	3-[6-(2,2-Difluoroethoxy)-α,α,α-trifluoro-o-toluenesulfonamido]-s-triazole-5-carboxylic acid.
CAS Name:	3-[[[2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylic acid.
CAS Number:	Not reported.
SMILES String:	n1c(nc(n1)C(O)=O)NS(=O)(=O)c2c(cccc2C(F)(F)F)OCC(F)F.



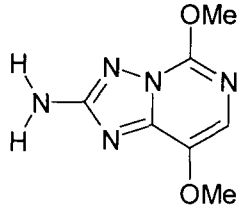
BSA [Penoxsulam sulfonic acid; TSN101980]

IUPAC Name:	6-(2,2-Difluoroethoxy)-α,α,α-trifluoro-o-toluenesulfonic acid.
CAS Name:	2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid.
CAS Number:	Not reported.
SMILES String:	S(=O)(=O)(c1c(cccc1C(F)(F)F)OCC(F)F)O.



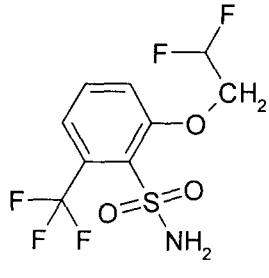
2-Amino-TP [TSN101824]

IUPAC Name: 2-Amino-5,8-dimethoxy-s-triazolo[1,5-c]pyrimidine.
CAS Name: 5,8-Dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-amine.
CAS Number: Not reported.
SMILES String: n1c(nc2n1c(ncc2OC)OC)N.



Sulfonamide [TSN102354]

IUPAC Name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide.
CAS Name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide.
CAS Number: Not reported.
SMILES String: NS(=O)(=O)c1c(cccc1C(F)(F)F)OCC(F)F.



5-OH-XDE-638 [5-Hydroxy-XDE-638; 5-OH-DE-638; TSN101756; 5-OH]

IUPAC Name:	6-(2,2-Difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide.
CAS Name:	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.
CAS Number:	Not reported.
SMILES String:	n1c(nc2n1c(ncc2OC)O)NS(=O)(=O)c3c(cccc3C(F)(F)F)OCC(F)F.