Data Evaluation Report on the stability of penoxsulam in water

PMRA Submission Number {.....} EPA MRID Number 46433901

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. Storage stability of XDE-638, 5-hydroxy-XDE-638, XDE-638 sulfonic acid (BSA), XDE-638 sulfonamide, BSTCA, 2-amino-TP, XDE-638 TPSA, 5-OH-2-amino-TP in water. Unpublished study performed and submitted by Dow AgroSciences LLC, Indianapolis, IN. Laboratory Study ID: 010106.01. Experiment initiation August 24, 2001 and completion September 30, 2003 (p. 3). Final report issued October 20, 2004.

EXECUTIVE SUMMARY

A storage stability study was conducted by fortifying control water 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); 2-amino-TP (2-amino-5,8-dimethoxy-s-triazolo[1,5-c]pyrimidine); TPSA (5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid); and 5-OH-2-amino-TP (2-amino-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-5-ol), at 0.03 µg/mL, with subsequent analysis following 0, 130, 229, and 270-284 days of refrigerated storage (0, 130, 215, and 270 days for 5-OH-2-amino-TP).

Due to a fortification error involving the parent affecting the samples analyzed at 229 and 284 days of storage, the refrigerated storage stability study was repeated with penoxsulam only, using new storage intervals of 0, 101, 230, and 433 days. In addition, a frozen storage stability study was conducted with penoxsulam only using storage intervals of 0, 221, and 320 days. The fortification level for both experiments was 0.03 µg/mL.

Storage stability results indicate that penoxsulam decreased over the 433-day storage period, and that the transformation products 5-OH, sulfonamide, BSTCA, BSA, 2-amino-TP, TPSA, and 5-OH-2-amino-TP were stable for the duration of the 270 to 284-day storage interval. Corrected recoveries of penoxsulam from refrigerated samples were 109% at day 0, and decreased to 101% by 230 days and 93% by 433 days. Corrected recoveries of penoxsulam from frozen samples were 109% at day 0, 96% at 221 days, and decreased to 61% by 320 days. Corrected recoveries of 5-OH, sulfonamide, BSTCA, BSA, 2-amino-TP, TPSA and 5-OH-2-amino-TP ranged from 98-115%, 103-115%, 85-94%, 102-114%, 105-124%, 93-107%, and 105-116%, respectively, throughout the 270 to 284-day storage interval, with no pattern of decline.

Mean corrected recoveries from refrigerated samples.

Days posttreatment	Corrected recoveries							
	Penox-sulam	5-OH	Sulfona-mide	BSTCA	BSA	2-Amino-TP	TPSA	5-OH-2-amino-TP**
0	108%	100%	109%	85%	102%	107%	99%	105%
130	100%	115%	115%	94%	114%	124%	107%	110%
229	67%*	98%	103%	86%	104%	105%	93%	112%
284	69%*	100%	104%	91%	106%	119%	99%	116%

*Reported fortification error.

**Sampling intervals were 0, 130, 215, and 270 days.

Mean recovery of penoxsulam from refrigerated samples (restarted study).

Days posttreatment	Uncorrected	Corrected
0	113%	109%
101	109%	111%
230	101%	101%
433	105%	93%

Mean recovery of penoxsulam from frozen samples.

Days posttreatment	Uncorrected	Corrected
0	113%	109%
221	100%	96%
320	63%	61%

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

MATERIALS AND METHODS

A bulk control water sample (water quality parameters not reported) from Live Oak, California was obtained for use in the study (p. 15). Aliquots (25 g) 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); 2-amino-TP (2-amino-5,8-dimethoxy-s-triazolo[1,5-c]pyrimidine); TPSA (5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid); and 5-OH-2-amino-TP (2-amino-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-5-ol; Figure 1, pp. 49-51), at 0.03 µg/mL (pp. 16-18). Soil samples were fortified such that each sample was fortified with one analyte. Three fortified samples were prepared for each analyte for each designated sampling interval. Samples were removed from refrigerated storage (approximately 4°C) at 0, 130, 229, and 284 days (0, 130, 215, and 270 days for 5-OH-2-amino-TP) for analysis (Table 1, p. 28).

Due to a fortification error involving the parent affecting the samples analyzed at 229 and 284 days of storage, the refrigerated storage stability study was repeated with penoxsulam only, using new storage intervals of 0, 101, 230, and 433 days (p. 25; Table 1, p. 28). In addition, a frozen storage stability study was conducted with penoxsulam only, using storage intervals of 0, 221, and 320 days (pp. 16-17; Table 1, p. 28). The fortification level for both experiments was 0.03 µg/mL.

Aliquots of the samples were transferred to clean, glass GC vials and analyzed by HPLC with ion electrospray tandem mass spectrometry (LC/MS/MS; p. 18). Negative ion LC/MS/MS operating conditions were used for the analysis of 5-OH, BSTCA, 5-OH-2-amino-TP, TPSA, BSA, and sulfonamide analytes. Positive ion LC/MS/MS operating conditions were used for the

analysis of penoxsulam and 2-amino-TP analytes. The LOQ was 0.003 µg/mL for each analyte (p. 13).

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

Applicants Code Name	CAS Number	Chemical Name	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	
TPSA		5,8-Dimethoxy[1,2,4]triazolo-[1,5-c]pyrimidin-2-yl)sulfamic acid	$C_7H_9N_5O_5S$	275	
5-OH 2-amino-TP		2-Amino-8-methoxy[1,2,4-]triazolo[1,5-c]pyrimidin-5-ol	$C_6H_7N_5O_2$	181	

Data were obtained from Figure 1, pp. 49-51 of the study report.

Concurrent recoveries were determined on each day of analysis by fortifying two control samples with a mixture containing penoxsulam, 5-OH, BSA, BSTCA, XDE-638 sulfonamide, 2-amino-TP, TPSA, and 5-OH-2-amino-TP at 0.03 µg/g (p. 18).

RESULTS AND DISCUSSION

Storage stability results indicate that penoxsulam decreased over the 433-day storage period and that the transformation products 5-OH, sulfonamide, BSTCA, BSA, 2-amino-TP, TPSA, and 5-OH-2-amino-TP were stable for the duration of the 270 to 284-day storage interval (Tables 2-9 and 20, pp. 29-36 and 47; Figures 79-82, pp. 129-132). Corrected recoveries of penoxsulam from refrigerated samples were 109% at day 0, and decreased to 101% by 230 days and 93% by 433 days (Table 20, p. 47). Corrected recoveries of penoxsulam from samples stored frozen were 109% at day 0, 96% at 221 days, and decreased to 61% by 320 days (Table 18, p. 45). Corrected recoveries of 5-OH, sulfonamide, BSTCA, BSA, 2-amino-TP, TPSA and 5-OH-2-amino-TP ranged from 98-115%, 103-115%, 85-94%, 102-114%, 105-124%, 93-107%, and 105-116%, respectively, throughout the 270 to 284-day storage interval, with no pattern of decline.

Mean uncorrected recoveries from refrigerated samples.

Days posttreatment	Uncorrected recoveries							
	Penox-sulam	5-OH	Sulfona-mide	BSTCA	BSA	2-Amino-TP	TPSA	5-OH-2-amino-TP**
0	100%	98%	102%	74%	100%	104%	104%	97%
130	86%	109%	109%	78%	112%	111%	96%	101%
229	59%*	96%	105%	76%	101%	97%	85%	100%
284	61%*	90%	92%	70%	93%	99%	89%	88%

Data were obtained from Tables 2-9, pp. 29-36 of the study report.
* Reported fortification error.
** Sampling intervals were 0, 130, 215, and 270 days.

Mean corrected recoveries from refrigerated samples.

Days posttreatment	Corrected recoveries							
	Penox-sulam	5-OH	Sulfona-mide	BSTCA	BSA	2-Amino-TP	TPSA	5-OH-2-amino-TP**
0	108%	100%	109%	85%	102%	107%	99%	105%
130	100%	115%	115%	94%	114%	124%	107%	110%
229	67%*	98%	103%	86%	104%	105%	93%	112%
284	69%*	100%	104%	91%	106%	119%	99%	116%

Data were obtained from Tables 2-9, pp. 29-36 of the study report.
* Reported fortification error.
** Sampling intervals were 0, 130, 215, and 270 days.

Mean concurrent recoveries were 88 ± 4% for penoxsulam, 95 ± 4% for 5-OH, 95 ± 5% for sulfonamide, 84 ± 4% for BSTCA, 95 ± 5% for BSA, 91 ± 6% for 2-amino-TP, 94 ± 8% for TPSA, and 87 ± 7% for 5-OH-2-amino-TP (Tables 10-17, pp. 37-44).

Mean recovery of penoxsulam from refrigerated samples (restarted study).

Days posttreatment	Uncorrected	Corrected
0	113%	109%
101	109%	111%
230	101%	101%
433	105%	93%

Data were obtained from Table 20, p. 47 of the study report.
* The mean concurrent recovery was 104 ± 6% (Table 21, p. 48 of the study report).

Mean recovery of penoxsulam from frozen samples.

Days posttreatment	Uncorrected	Corrected
0	113%	109%
221	100%	96%
320	63%	61%

Data were obtained from Table 18, p. 45 of the study report.
* The mean concurrent recovery was 104% (from duplicate samples; Table 19, p. 46).

STUDY DEFICIENCIES

This study was not submitted to fulfill Subdivision N Guidelines.

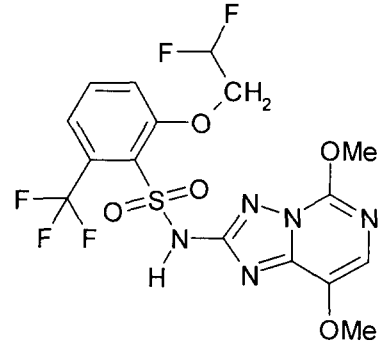
REVIEWER'S COMMENTS

1. Fortifications for the refrigerated stability study involving all analytes were made at three separate times: the 229- and 284-day storage samples were fortified on September 6, 2001; the 130-day samples were fortified on December 14, 2001; and the day 0 samples were fortified on April 23, 2002 (Table 1, p. 28). 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.

Attachment 1: Structures of Parent Compound and Transformation Products

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

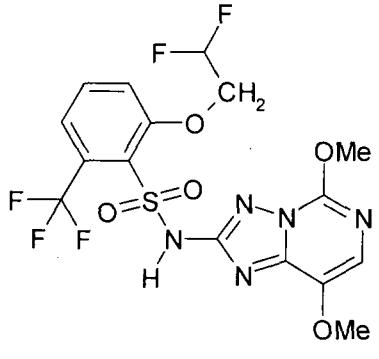
IUPAC Name:	3-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-sulfonamide. 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide. 6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide.
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

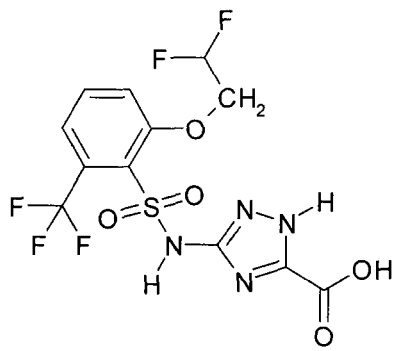
Penoxsulam [XDE-638; DE-638; TSN101649; SP1019 (SePRO)]

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.



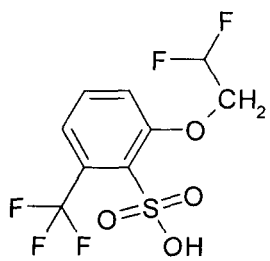
BSTCA [TSN103610; TSN101979]

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.



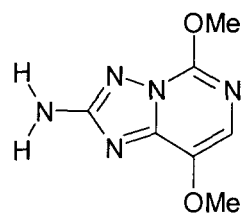
BSA [Penoxsulam sulfonic acid; TSN101980]

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.



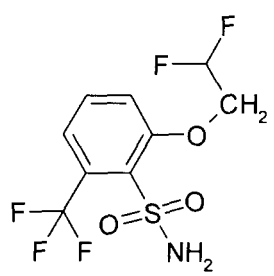
2-Amino-TP [TSN101824]

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.



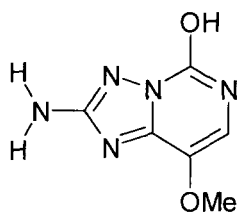
Sulfonamide [TSN102354]

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.



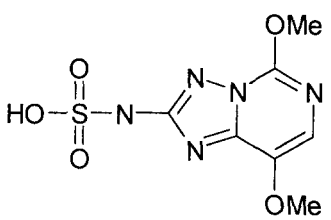
5-OH-2-Amino-TP [Analyte of XDE-638; TSN101837]

IUPAC Name: Not reported.
CAS Name: 2-Amino-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-5-ol.
CAS Number: Not reported.
SMILES String: n1c(nc2n1c(ncc2OC)O)N.



TPSA [Analyte of XDE-638; TSN102025]

IUPAC Name: Not reported.
CAS Name: (5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid.
CAS Number: Not reported.
SMILES String: n1c(nc2n1c(ncc2OC)OC)NS(=O)(=O)O.



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.