(10-27-03)

Data Evaluation Report on the hydrolysis of penoxsulam

PMRA Submission Number {.....} EPA MRID Number 45830721

Data Requirement: PMRA Data Code:
EPA DP Barcode: D288160
OECD Data Point:
EPA Guideline: 161-1

Test material:
Common name: Penoxsulam.
Chemical names:
IUPAC: 6-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy-s-triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluoro-o-toluenesulfonamide,
3-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide
CAS : 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
SMILES string: n1c(nc2n1c(ncc2OC)OC)NS(=O)(=O)c3c(cccc3C(F)(F)F)OCC(F)F

Primary Reviewer: Lisa Koterwas
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Company Code:
Active Code:
Use Site Category:
EPA PC Code: 119031

CITATION: Simon, K., and J. K. Smith. 2001. Hydrolysis of XDE-638 in buffered and natural water as a function of pH. Unpublished study performed, sponsored, and submitted by Global Environmental Chemistry Laboratory-Indianapolis Lab, Dow AgroSciences LLC, 9330 Zionsville Road, Indianapolis, Indiana 46268-1054. Study No.: 000134. Experiment initiated March 2, 2000, and completed June 27, 2000 (p.3). Final report issued August 9, 2001.

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EXECUTIVE SUMMARY

The hydrolysis of [triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]- labeled 3-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide (penoxsulam; XDE-638) were studied at 25°C for 30 days at pH 5 (acetate), pH 7 (piperazineethanesulfonic acid), pH 9 (borate), and natural water (pH 8.0; from White River, Indiana) at a nominal application rate of 1 mg/L. This study was performed in accordance with US EPA Pesticide Assessment Guidelines Subdivision N §161-1 and in compliance with US EPA GLP Standards. Sterile glass vials were filled to capacity (ca. 10 mL) with treated sterile buffer (pH 5, 7 or 9) or natural water to minimize headspace (p.14). A single sample of each label was collected at 0, 1, 3, 7, 9, 15, 21 and 30 days. Sterility and pH were checked at each sampling interval (buffer solutions only). Aliquots were analyzed for total radioactivity using LSC and for [^{14}C]penoxsulam by reverse-phase HPLC. [^{14}C]Compounds were identified by comparison with unlabeled reference standards.

Test conditions were maintained throughout the experiment.

Overall radiolabeled material (both labels) averaged 100.2 ± 1.9% (range 97.0-104.0%), 99.6 ± 2.3% (range 95.5-104.8%), 99.0 ± 2.3% (range 94.7-102.2%), and 99.7 ± 1.4% (range 95.4-100.7%) of the applied in the pH 5, pH 7, pH 9 and natural water, respectively. There was no indication of a pattern of decline.

[Triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam were stable at 25°C in pH 5, pH 7 and pH 9 buffer solutions. Penoxsulam concentrations were slightly variable, however there was no indication of a pattern of decline at any pH level for either label. At pH 5 (both labels), penoxsulam ranged from 97.0-104.0% of the applied. At pH 7 (both labels), penoxsulam ranged from 95.5-104.8%. At pH 9 (both labels), penoxsulam ranged from 92.5-102.1%. In natural water (both labels), penoxsulam ranged from 93.6-100.7% of the applied. No transformation products were reported. The reviewer calculated the residual radioactive fraction from the difference between the total recovery and the parent as percent of the applied. The residual radioactivity (both labels) was ≤3.7% of the applied for all buffer solutions and the natural water. Volatiles were not collected.

No transformation pathway was reported, however penoxsulam was stable in all experimental aqueous solutions at 25°C.

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RESULTS SYNOPSIS:

25°C	[^{14}C]penoxsulam		
	Half life	Transformation products	Residual Radioactivity
pH 5 pH 7 pH 9 Natural water	Stable.	None identified.	≤ 3.7% of the applied radioactivity

Study Acceptability: This study is classified as acceptable and can be used to satisfy the USEPA Pesticide Assessment Guidelines, Subdivision N §161-1.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was designed in accordance with US EPA Pesticide Assessment Guidelines, Subdivision N §161-1; Official Journal of the European Communities Method C.7; OECD, Method 111 guideline (PMRA-DACO 8.2.3.2; Trade Memorandum T-1-255, Section 6.2.A.2; and JMAFF (p.9). No significant deviations from Subdivision N Guidelines §161-1 were noted.

COMPLIANCE: This study was conducted in compliance with USEPA GLP Standards 40 CFR Part 160 (1989; pp.3, 9). Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided (pp.2-5). A Certificate of Authenticity was not provided.

A. MATERIALS:

1. Test Material [Triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]- labeled penoxsulam (p.11).

Chemical Structure: See DER Attachment 2.

Description: None reported.

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Purity:

[^{14}C-TP]-label: Radiochemical purity: 100% (p.11).
Inventory No. INV1456.
Analytical purity: Not reported.
Specific activity: 28.9 mCi/mmole.
Location of the radiolabel: 3-Carbon in the triazolopyrimidine (TP) ring.

[^{14}C-Ph]-label: Radiochemical purity: 98.1%
Inventory No. INV1475.
Analytical purity: Not reported.
Specific activity: 24.6 mCi/mmole.
Location of the radiolabel: Uniformly on the phenyl (Ph) ring.

Storage conditions of test chemicals: Not reported.

Physico-chemical properties of penoxsulam.

Parameter	Values	Comments
Molecular Weight	483.37 amu	
Molecular Formula	Not reported.	
Water solubility (ppm):	44 6	At pH 3.17; At pH 1.25.
Density	Not reported.	
Vapor pressure:	1.87×10^{-16} 7.16×10^{-16}	At 20°C; At 25°C.
UV absorption	Not reported.	
pK_a	4.37	
K_{ow}/log K_{ow}	Not reported.	
Melting point	Not reported.	
Log K_{oc}	Not reported.	
Stability of compound at room temperature	Not reported.	

Data obtained from pp.12, 45 of the study report.

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2. Buffer Solution: The following buffer solutions were prepared using purified water (Millipore):

Table 1a: Description of buffer solutions.

pH	Type and final molarity of buffer	Composition
5	0.05M sodium acetate trihydrate	0.05M sodium acetate trihydrate buffer adjusted with glacial acetic acid.
7	0.05M 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid	0.05M 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid buffer adjusted with 1.0N sodium hydroxide.
9	0.05M sodium borate	0.05M sodium borate buffer adjusted with concentrated hydrochloric acid.

Data obtained from p.12 of the study report.

2b. Natural Water: The following sample of natural water was collected and analyzed prior to study initiation:

Table 1b: Description of natural water.

Parameter		Details
Location of collection		White River, Indianapolis, Indiana.
Storage:		Natural water was stored in an incubator at 25°C prior to use.
Temperature		Incubated at 25°C prior to use.
pH		8.0
Alkalinity (mg/L $CaCO_3$):		284
Hardness (mg/L $CaCO_3$):		393
Conductivity (mS/cm):		2.06
Total Suspended Solids (mg/L):		24
Dissolved Oxygen (mg/L):		7.5
Microbial Plate Count (CFU/mL):	Actinomycetes	91
	Fungi	3
	Bacteria	1030
Other Details		Natural water was not sterilized prior to use.

Data obtained from pp.12, 13; and Table 1, p.21 of the study report.

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B. EXPERIMENTAL CONDITIONS

1. Preliminary Studies: A preliminary study was conducted to evaluate [triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]- labeled 3-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide (penoxsulam; XDE-638) at 50°C for 120 hours (5 days) in pH 4 (acetate), pH 7 (piperazineethanesulfonic acid), pH 9 (borate), and natural water (pH 8.0) at a nominal application rate of 1 mg/L (pH 4 and pH 9 buffers), and 10 mg/L (natural water and pH 7 buffer; p.14). [^{14}C-TP]Penoxsulam was applied at application rates of 0.70 mg/L, 9.08 mg/L, 0.79 mg/L, and 9.96 mg/L in the pH 4, pH 7, pH 9, and natural water, respectively. [^{14}C-Ph]Penoxsulam was applied at application rates of 0.63 mg/L, 10.23 mg/L, 0.71 mg/L, and 11.17 mg/L in the pH 4, pH 7, pH 9, and natural water, respectively (Table 4, p.24). This study was performed under the same conditions described in the definitive study. Sterile glass vials were filled to capacity (ca. 10 mL) with treated sterile buffer (pH 4, 7 or 9) or natural water to minimize headspace (p.14). A single sample of each label was collected at 0, 2, 4, 24 and 120 hours. Sterility and pH were checked at each sampling interval (buffer solutions only; p.15; Table 5, p.25). Aliquots (8 µL or 200 µL) were analyzed for total radioactivity using LSC and for [^{14}C]penoxsulam by reverse-phase HPLC. [^{14}C] Compounds were identified by comparison with unlabeled reference standards.

Sterility was maintained in the aqueous buffer solutions throughout the study and the pH ranged from 4.10-4.30 for the pH 4 buffer, 6.90-7.10 for the pH 7 buffer, and 8.90-9.00 for the pH 9 buffer (Table 5, p.25).

Overall radiolabeled material (both labels) averaged 99.2 ± 8.0% (range 89.9-113.5%), 100.6 ± 5.0% (range 90.4-106.3%), 105.1 ± 3.7% (range 100.0-108.6%), and 97.4 ± 3.8% (range 91.6-102.4%) of the applied in the pH 4, pH 7, pH 9, and natural water, respectively (Table 7, pp.28, 29; see Attachment 1).

[^{14}C]Penoxsulam (both labels) was stable in all buffer solutions and natural water over 120 hours (p.17). At pH 4, penoxsulam ranged from 89.5-113.5% of the applied. At pH 7, penoxsulam ranged from 90.4-106.3%. At pH 9, penoxsulam ranged from 100.0-10.8.6%. In natural water, penoxsulam ranged from 91.6-102.4% (Table 7, pp.28, 29). Radioactive residues were ≤1.4% of the applied. Volatiles were not collected.

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2. Experimental conditions

Table 2: Experimental parameters

Parameters		Details
Duration of the study		30 days (both labels).
Test concentrations	Nominal (mg/L):	1
	Measured (mg/L):	pH 5: 0.89. pH 7: 0.91-0.94. pH 9: 0.96-1.02. Natural water: 0.89-0.96.
No. of replications		Single samples from each radiolabel were collected at each sampling interval.
Preparation of test medium	Volume used/treatment	Not reported.
	Method of sterilization	All buffered solutions (prior to dosing), glassware, and disposable laboratory equipment (pipette tips, etc.) were autoclaved. The sample preparation were reported as sterile.
	Co-solvent	Acetonitrile, unspecified volume.
Test apparatus (type/material/volume)		Pre-labeled amber glass vials (ca. 10-mL capacity) were filled with ca. 10 mL of the [^{14}C-TP]penoxsulam and [^{14}C-Ph]penoxsulam bulk solutions.
Details of traps for volatile, if any		Volatiles were not trapped.
If no traps were used, is the test system closed/open?		Not reported.
Is there any indication of the test material adsorbing to the walls of the test apparatus?		Not indicated.
Experimental conditions Temperature (°C): Lighting: pH Ranges:		 25°C. Dark. pH 5- 5.02 to 5.09, pH 7- 6.92 to 7.03, pH 9- 8.90 to 9.02.
Other details, if any		The sampling log for the study was provided in Table 3, p.23. All experiments were performed at the same time.

Details obtained from pp.11, 13-15; Table 4, p.24; and Table 6, pp.26-27 of the study report.

3. Supplementary Experiments: No supplementary experiments were reported.

4. Sampling:

Table 3: Sampling details.

Criteria	Details
Sampling intervals	0, 1, 3, 7, 9, 15, 21, and 30 days (both labels).
Sampling method	A single vial from each radiolabel was collected at each sampling interval.
Sampling methods for the volatile compounds, if any	Volatiles were not measured.
Sampling intervals/times for: pH measurement: Sterility check:	 pH was measured at each sampling interval. Sterility was determined at each sampling interval.
Sample storage before analysis	Not reported.
Other observation, if any:	Sterility was measured at each sampling interval by collecting an aliquot (500 µL) of each sample, transferring to approximately 10 mL of soy broth solution, and incubating for 3 to 5 days at 25°C. The turbidity of the solutions was the measure of sterility. The pH and sterility were not measured for natural water samples.

Details obtained from pp.13, 15 of the study report.

C. ANALYTICAL METHODS

Extraction/clean up/concentration methods, if used: Aqueous samples were measured as collected without manipulation.

Volatile residue determination: Volatiles were not trapped in the definitive study.

Total ^{14}C measurement: Total ^{14}C was determined from an aliquot (200-µL) of each sample using LSC (p.15).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of the parent: Penoxsulam was identified and quantified using a reverse-phase HPLC under the following conditions (Appendix A, p.44): YMC ODS-AQ column (250 x 4.6 mm; 5 µ), gradient mobile phase consisting of (A) water with 1% acetic acid and (B) acetonitrile with 1% acetic acid [percent A:B (v:v) 0 minutes, 70:30, 40 minutes, 30:70, 40.01 minutes, 5:95, 45 minutes, 5:95, and 45.01 minutes, 70:30], UV detection (254 nm), flow rate, 1.0 mL/minute, UV (254 nm) and radioflow detection. Penoxsulam was identified by cochromatography with a non-radiolabeled reference standard (TSN 101649; 100% analytical

purity; p.12; Figures 7-10, pp.39-42). The typical retention time for the parent was 22.6 minutes with the described HPLC system (p.44). HPLC column recoveries were 90-110%.

Identification and quantification of transformation products: Identification and quantification of transformation products was not necessary because penoxsulam was stable in all buffers and natural water.

Detection limits (LOD, LOQ) for the parent: Not reported.

Detection limits (LOD, LOQ) for the transformation products: Not reported.

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: The pH 5 buffer solutions ranged from pH 5.02-5.09. The pH 7 buffer ranged from pH 6.92-7.03. The pH 9 buffer ranged from pH 8.90-9.02 (Table 6, pp.26-27). The aqueous buffer solutions remained sterile throughout all experiments.

B. MASS BALANCE: Overall radiolabeled material (both labels) averaged 100.2 ± 1.9% (range 97.0-104.0%), 99.6 ± 2.3% (range 95.5-104.8%), 99.0 ± 2.3% (range 94.7-102.2%), and 99.7 ± 1.4% (range 95.4-100.7%) of the applied in the pH 5, pH 7, pH 9 and natural water, respectively (Table 8, pp.30-31). There was no indication of a pattern of decline.

Table 4a. Hydrolysis of [triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam, expressed as percentage of the applied radioactivity (mean ± s.d., n = 1) at pH 5 and 25°C.

Compound		Sampling times (days)							
		0	1	3	7	9	15	21	30
XDE-638 (Penoxsulam)[1]	Triazolopyrimidine	100.0	101.2	100.1	100.2	100.7	98.1	97.0	104.0
	Phenyl	100.0	101.5	100.7	100.6	98.6	98.2	97.1	103.2
Other		Metabolites were not measured.							
Residual Radioactivity[2]	Triazolopyrimidine	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0
	Phenyl	0.0	0.0	0.0	0.0	1.3	0.0	0.0	0.0
Volatiles		Volatiles were not measured.							
Total % recovery	Triazolopyrimidine	100.0	101.2	101.2	100.2	100.7	98.1	97.0	104.0
	Phenyl	100.0	101.5	100.7	100.6	100.2	98.2	97.1	103.2

Data obtained from Table 8, p.30 of the study report.

1 The percent of applied radioactivity for the parent was calculated based on the % of parent in the chromatogram and the total % recovery.

2 The residual radioactivity was calculated as the difference between the total % recovery and the parent.

Table 4b. Hydrolysis of [triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam, expressed as percentage of the applied radioactivity (mean ± s.d., n = 1), at pH 7 and 25°C.

Compound		Sampling times (days)							
		0	1	3	7	9	15	21	30
XDE-638 (Penoxsulam)[1]	Triazolopyrimidine	100.0	99.4	98.7	98.7	100.0	98.4	95.5	103.2
	Phenyl	100.0	97.6	100.4	98.0	97.1	96.5	96.1	104.8
Other		Metabolites were not measured.							
Residual Radioactivity[2]	Triazolopyrimidine	0.0	0.9	1.4	0.0	0.0	0.0	0.0	0.0
	Phenyl	0.0	2.8	0.0	1.1	2.5	1.0	0.0	0.0
Volatiles		Volatiles were not measured.							
Total % recovery	Triazolopyrimidine	100.0	100.3	100.1	98.7	100.0	98.4	95.5	103.2
	Phenyl	100.0	100.4	100.4	99.1	99.6	97.5	96.1	104.8

Data obtained from Table 8, p.30 of the study report.

1 The percent of applied radioactivity for the parent was calculated based on the % of parent in the chromatogram and the total % recovery.

2 The residual radioactivity was calculated as the difference between the total % recovery and the parent.

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Table 4c. Hydrolysis of [triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam, expressed as percentage of the applied radioactivity (mean ± s.d., n = 1), at pH 9 and 25°C.

Compound		Sampling times (days)							
		0	1	3	7	9	15	21	30
XDE-638 (Penoxsulam)[1]	Triazolopyrimidine	99.0	100.0	99.8	100.0	99.3	92.7	96.7	102.1
	Phenyl	100.0	100.3	97.9	100.4	98.4	95.1	92.5	100.6
Other		Metabolites were not measured.							
Residual Radioactivity[2]	Triazolopyrimidine	1.0	0.0	0.0	0.0	0.0	2.0	0.0	0.0
	Phenyl	0.0	0.0	1.1	0.0	0.9	0.0	3.1	1.6
Volatiles		Volatiles were not measured.							
Total % recovery	Triazolopyrimidine	100.0	100.0	99.8	100.0	99.3	94.7	96.7	102.1
	Phenyl	100.0	100.3	99.0	100.4	99.3	95.1	95.6	102.2

Data obtained from Table 8, p.31 of the study report.

1 The percent of applied radioactivity for the parent was calculated based on the % of parent in the chromatogram and the total % recovery.

2 The residual radioactivity was calculated as the difference between the total % recovery and the parent.

Table 4d. Hydrolysis of [triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam, expressed as percentage of the applied radioactivity (mean ± s.d., n = 1), in natural water at 25°C.

Compound		Sampling times (days)							
		0	1	3	7	9	15	21	30
XDE-638 (Penoxsulam)[1]	Triazolopyrimidine	98.8	100.6	100.3	98.4	100.0	100.2	96.9	100.7
	Phenyl	96.3	99.8	100.0	100.6	100.0	99.2	93.6	99.3
Other		Metabolites were not measured.							
Residual Radioactivity[2]	Triazolopyrimidine	1.2	0.0	0.0	2.2	0.0	0.0	0.0	0.0
	Phenyl	3.7	0.0	0.0	0.0	0.9	0.0	1.8	0.9
Volatiles		Volatiles were not measured.							
Total % recovery	Triazolopyrimidine	100.0	100.6	100.3	100.6	100.0	100.2	96.9	100.7
	Phenyl	100.0	99.8	100.0	100.6	100.0	99.2	95.4	100.2

Data obtained from Table 8, p.31 of the study report.

1 The percent of applied radioactivity for the parent was calculated based on the % of parent in the chromatogram and the total % recovery .

2 The residual radioactivity was calculated as the difference between the total % recovery and the parent.

C. TRANSFORMATION OF PARENT COMPOUND: [Triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam were stable at 25°C in pH 5, pH 7 and pH 9 buffer solutions (Table 8, pp.30-31). Penoxsulam concentrations were slightly, however there was no indication of a pattern of decline at any pH level for either label. At pH 5 (both labels), penoxsulam ranged from 97.0-104.0% of the applied. At pH 7 (both labels), penoxsulam ranged from 95.5-104.8%. At pH 9 (both labels), penoxsulam ranged from 92.5-102.1%. In natural water (both labels), penoxsulam ranged from 93.6-100.7% of the applied.

HALF-LIVES/DT50: [^{14}C]Penoxsulam was stable at 25°C at pH 5, pH 7, pH 9, and natural water, therefore half-lives were not calculated.

Half-lives/DT50s/DT90s

Temperature	First order linear			DT50	DT90
	Half-life	Regression equation	r^2		
25°C, [Triazolopyrimidine-3- ^{14}C]- and [phenyl-U- ^{14}C]-labeled penoxsulam					
pH 5	Stable			NA	NA
pH 7	Stable			NA	NA
pH 9	Stable			NA	NA
natural water	Stable			NA	NA

* Data obtained from Table 8, pp.30-31.
NA = Not applicable.

TRANSFORMATION PRODUCTS: No transformation products were reported. The study authors only provided data for the total recovery and parent (Table 8, pp.30-31). The reviewer calculated the residual radioactive fraction from the difference between the total recovery and the parent as percent of the applied. The residual radioactivity (both labels) was ≤3.7% of the applied for all buffer solutions and the natural water.

VOLATILIZATION: Volatiles were not collected.

TRANSFORMATION PATHWAY: No transformation pathway was reported, however penoxsulam was stable in all experimental aqueous solutions at 25°C (p.17).

Table 5: Chemical name and CAS number for the transformation products of penoxsulam.

Applicant's Code Name	CAS Number	Chemical Name	Chemical formula	Molecular weight (g/mol)	SMILES string
None.					

D. SUPPLEMENTARY EXPERIMENT-RESULTS: No supplementary experiments were reported.

III. STUDY DEFICIENCIES: No major study deficiencies were noted.

IV. REVIEWER'S COMMENTS:

1. No justification for the nominal application rate of the test material was reported. The nominal application rate was 1 mg/L in the definitive study, 1 mg/L (pH 4 and pH 9) and 10 mg/L (pH 7 and natural water) in the preliminary study (p.14). Clarification is needed.

2. The Limits of Detection and Limits of Quanitification for LSC and HPLC were not reported.

3. Only single samples of each radiolabel were collected and reported (Table 8, pp.30-31). Duplicate samples collected at each sampling interval for each label would be preferable.

4. The volume and concentration of test material applied to each treatment of buffer solution or natural water, and the amount of co-solvent (acetonitrile) in the stock and/or test solutions was not reported. More details involving the preparation of the test medium should have been included.

5. The material balance was reported as percent applied. However, the percent radioactivity of the parent is presented as the "% Parent in Chromatogram". The reviewer assumed this corresponded to the percent recovery of the parent and calculated the percent applied based on the total radioactivity (Table 8, pp.30-31). The residual radioactivity was calculated as the difference between the material balance and parent as percent of applied.

6. Based on statistical analysis (t-test performed using Microsoft Excel spreadsheet, v. 7.0), the study author concluded that degradation did not occur in any buffer solutions or natural water at the 99% confidence limit (pp.16-17; Table 9, p.32).

7. It was not clear if TLC analysis was used to confirm the identity of the parent in the preliminary and definitive studies. The TLC analysis was not reported in the materials and methods of the study and no data or example chromatographs are reported. However, a TLC method was reported as part of the study's "Analytical Methods and Calculations" section (pp.14, 15; Appendix A, pp.43-45). The method reported involved using TLC with silica gel, phosphorescent plates (20 cm x 20 cm; Whatman LK6F) which were developed using a toluene:ethyl acetate:acetic acid mobile phase (45:55:1). Identification was by comparison of R_f values with non-radiolabeled reference standard.

8. The method of pH measurement (definitive study) and the aliquot size for HPLC measurements (preliminary and definitive studies) were not reported by the study authors (pp.14, 15).

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V. REFERENCES:

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 161-1. Hydrolysis studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.

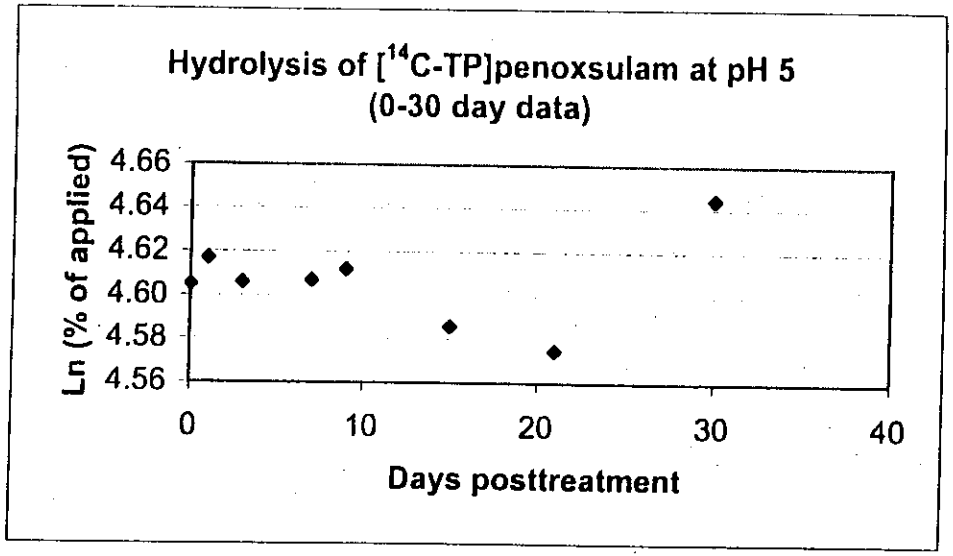
3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

Attachment 1

Excel Spreadsheets

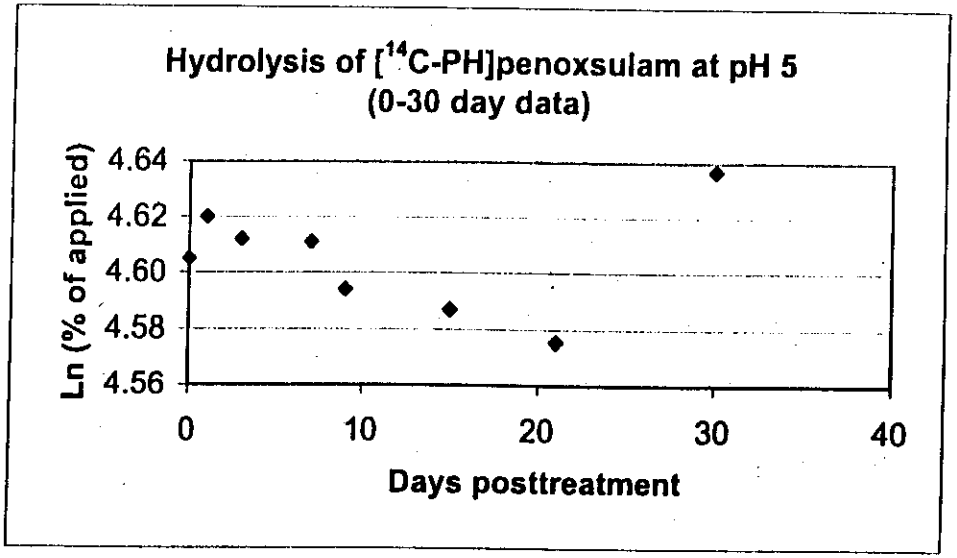
Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
pH 5
[^{14}C-TP]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
1	101.2	4.6171
3	100.1	4.6062
7	100.2	4.6072
9	100.7	4.6121
15	98.1	4.5860
21	97.0	4.5747
30	104.0	4.6444



[^{14}C-PH]XDE-638 Experiment

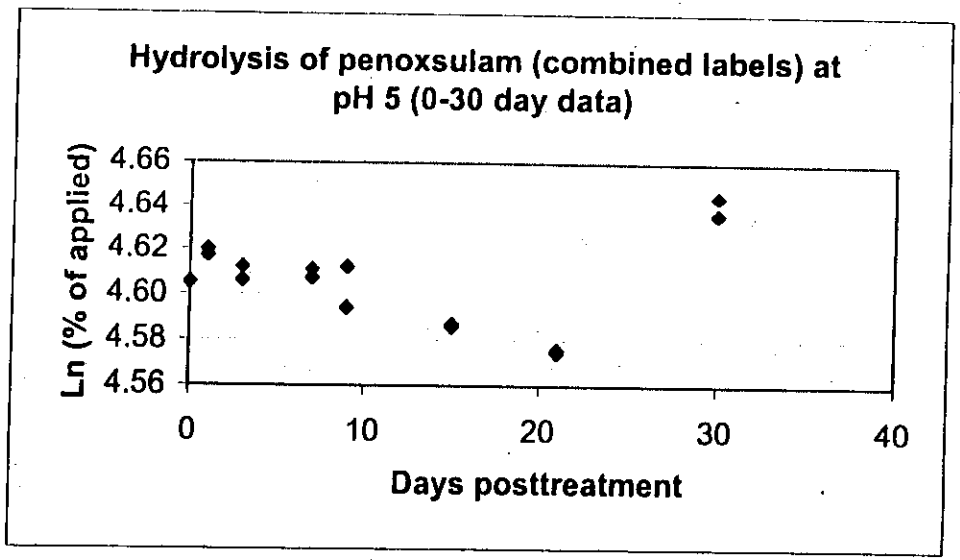
Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
1	101.5	4.6201
3	100.7	4.6121
7	100.6	4.6112
9	98.9	4.5941
15	98.2	4.5870
21	97.1	4.5757
30	103.2	4.6367



16

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
pH 5
Combined labels

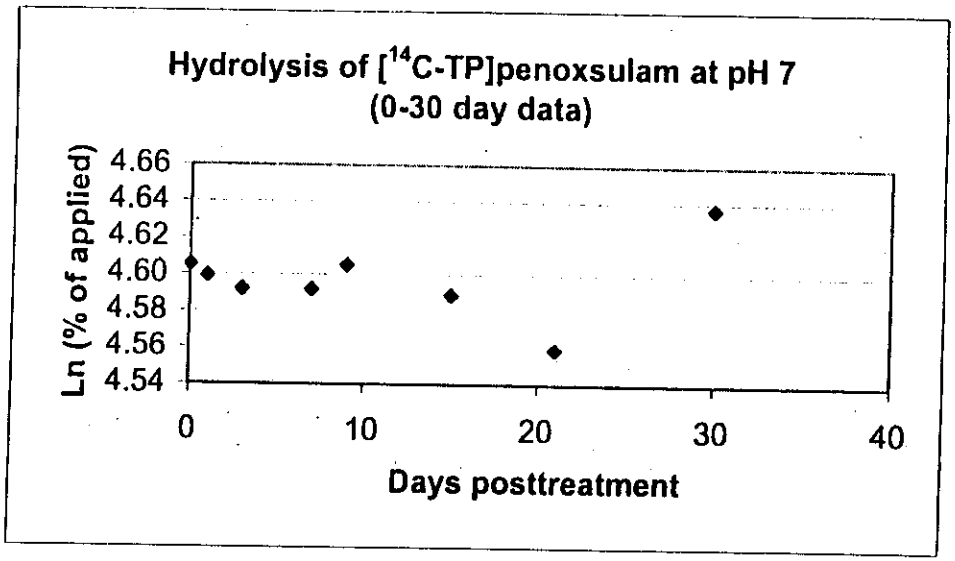
Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
0	100.0	4.6052
1	101.2	4.6171
1	101.5	4.6201
3	100.1	4.6062
3	100.7	4.6121
7	100.2	4.6072
7	100.6	4.6112
9	100.7	4.6121
9	98.9	4.5941
15	98.1	4.5860
15	98.2	4.5870
21	97.0	4.5747
21	97.1	4.5757
30	104.0	4.6444
30	103.2	4.6367



17

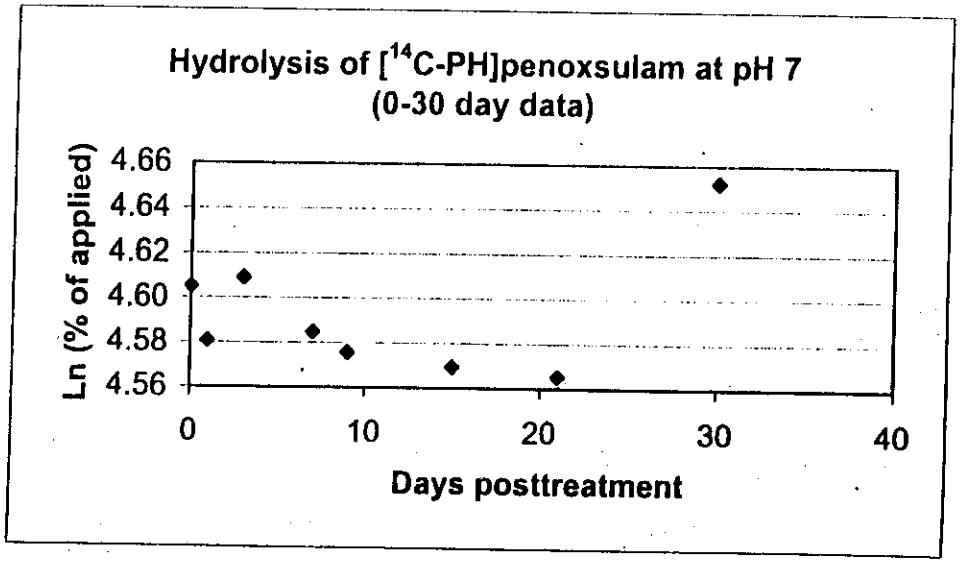
Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
pH 7
[^{14}C-TP]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
1	99.4	4.5992
3	98.7	4.5921
7	98.7	4.5921
9	100.0	4.6052
15	98.4	4.5890
21	95.5	4.5591
30	103.2	4.6367



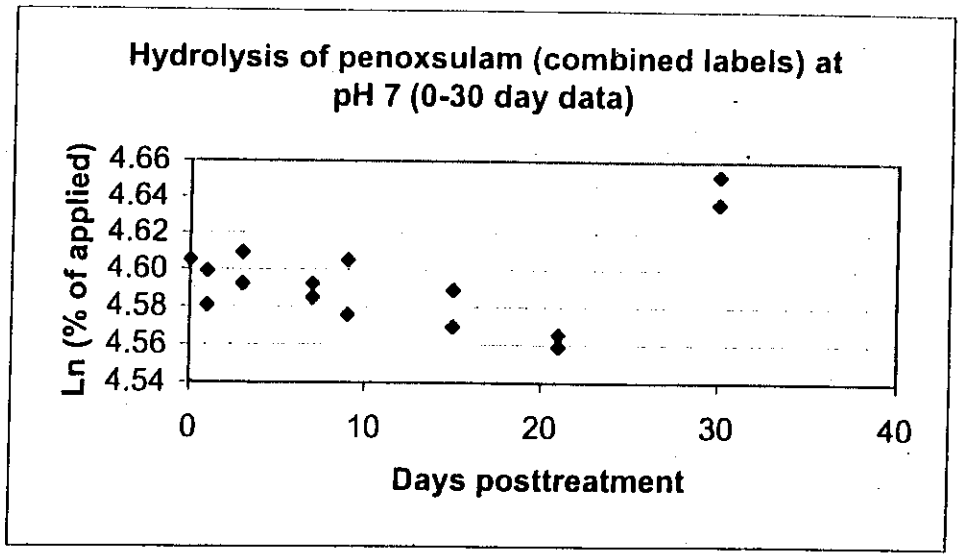
[^{14}C-PH]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
1	97.6	4.5809
3	100.4	4.6092
7	98.0	4.5850
9	97.1	4.5757
15	96.5	4.5695
21	96.1	4.5654
30	104.8	4.6521



Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
pH 7
Combined labels

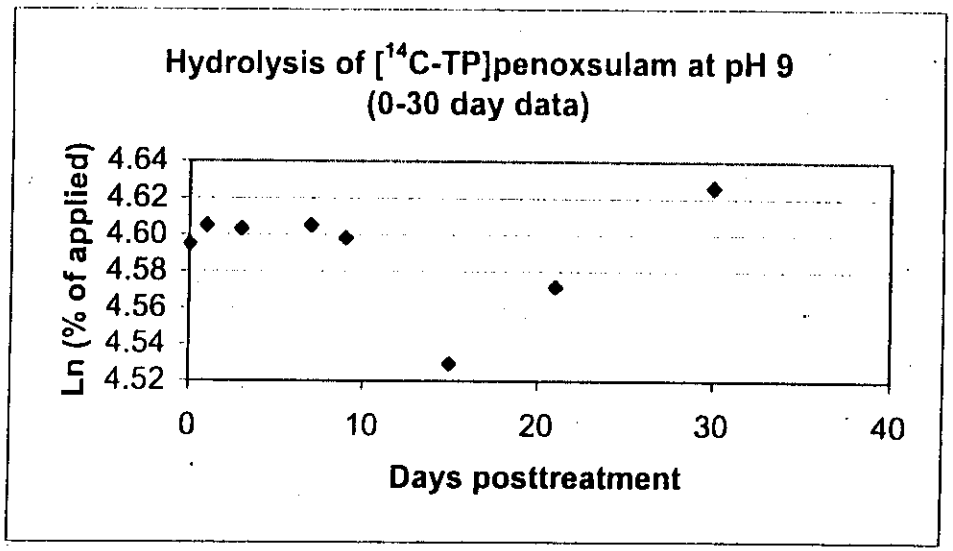
Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
0	100.0	4.6052
1	99.4	4.5992
1	97.6	4.5809
3	98.7	4.5921
3	100.4	4.6092
7	98.7	4.5921
7	98.0	4.5850
9	100.0	4.6052
9	97.1	4.5757
15	98.4	4.5890
15	96.5	4.5695
21	95.5	4.5591
21	96.1	4.5654
30	103.2	4.6367
30	104.8	4.6521



Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
pH 9

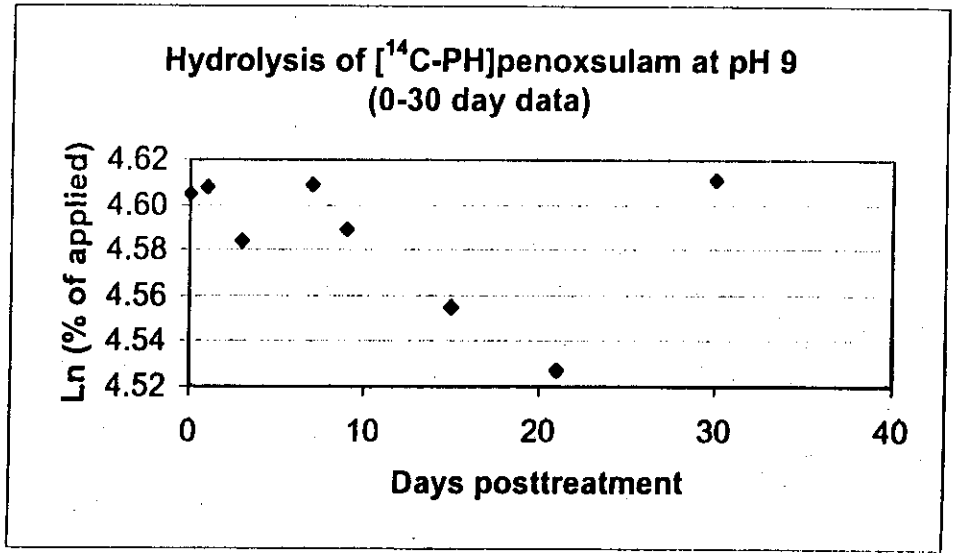
[^{14}C-TP]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	99.0	4.5951
1	100.0	4.6052
3	99.8	4.6032
7	100.0	4.6052
9	99.3	4.5981
15	92.7	4.5294
21	96.7	4.5716
30	102.1	4.6260



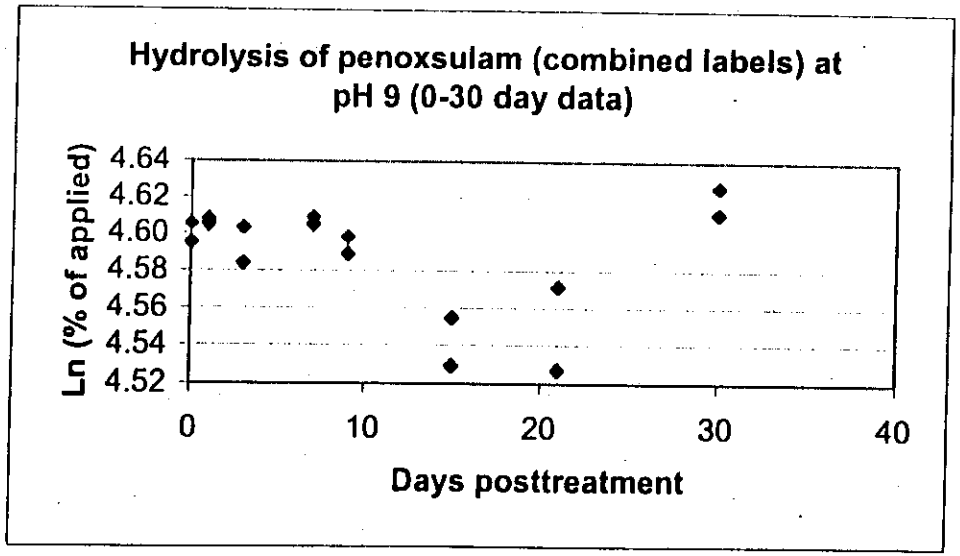
[^{14}C-PH]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	100.0	4.6052
1	100.3	4.6082
3	97.9	4.5839
7	100.4	4.6092
9	98.4	4.5890
15	95.1	4.5549
21	92.5	4.5272
30	100.3	4.6112



Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
pH 9
Combined labels

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	99.0	4.5951
0	100.0	4.6052
1	100.0	4.6052
1	100.3	4.6082
3	99.8	4.6032
3	97.9	4.5839
7	100.0	4.6052
7	100.4	4.6092
9	99.3	4.5981
9	98.4	4.5890
15	92.7	4.5294
15	95.1	4.5549
21	96.7	4.5716
21	92.5	4.5272
30	102.1	4.6260
30	100.6	4.6112



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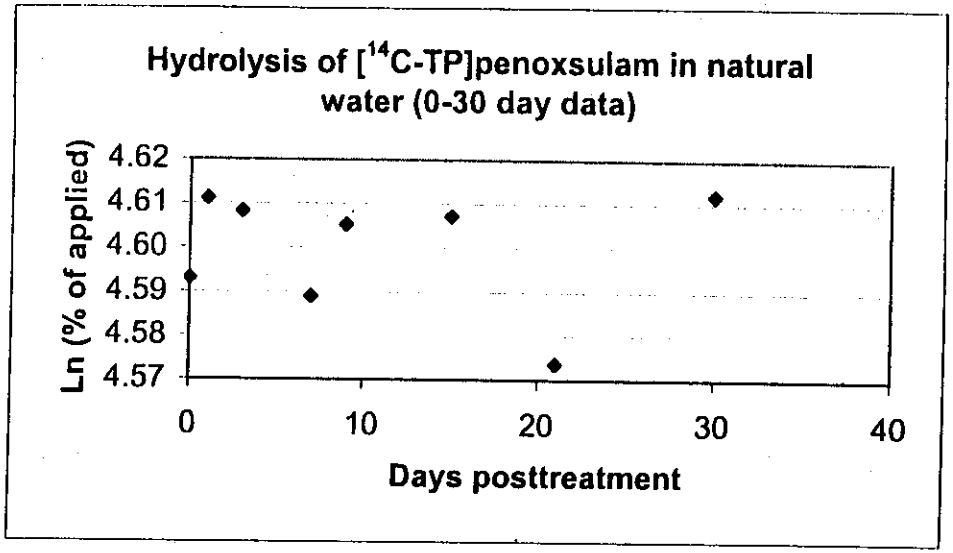
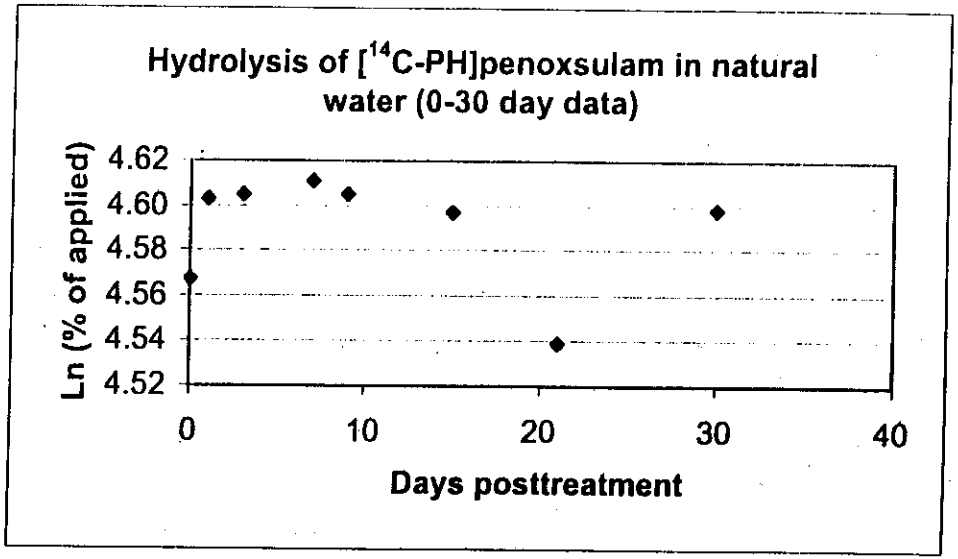
Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
Natural Water
[^{14}C-TP]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	98.8	4.5931
1	100.6	4.6112
3	100.3	4.6082
7	98.4	4.5890
9	100.0	4.6052
15	100.2	4.6072
21	96.9	4.5737
30	100.7	4.6121



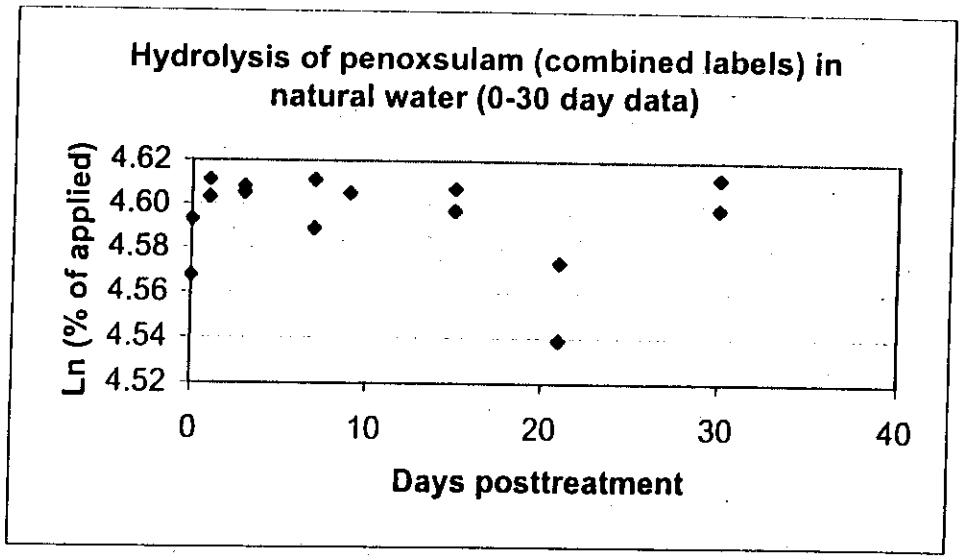
[^{14}C-PH]XDE-638 Experiment

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	96.3	4.5675
1	99.8	4.6032
3	100.0	4.6052
7	100.6	4.6112
9	100.0	4.6052
15	99.2	4.5971
21	93.6	4.5390
30	99.3	4.5981



Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1
Natural water
Combined labels

Days	XDE-638 (% applied)	ln (% applied XDE-638)
0	98.8	4.5931
0	96.3	4.5675
1	100.6	4.6112
1	99.8	4.6032
3	100.3	4.6082
3	100.0	4.6052
7	98.4	4.5890
7	100.6	4.6112
9	100.0	4.6052
9	100.0	4.6052
15	100.2	4.6072
15	99.2	4.5971
21	96.9	4.5737
21	93.6	4.5390
30	100.7	4.6121
30	99.3	4.5981



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Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

[^{14}C-TP]XDE-638 Experiment **pH 5**

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
1	101.2	1.012	100.0	101.2	0.0
3	101.2	1.012	98.9	100.1	1.1
7	100.2	1.002	100.0	100.2	0.0
9	100.7	1.007	100.0	100.7	0.0
15	98.1	0.981	100.0	98.1	0.0
21	97.0	0.97	100.0	97.0	0.0
30	104.0	1.04	100.0	104.0	0.0
Mean	100.3				
SD	2.1				

[^{14}C-PH]XDE-638 Experiment **pH 5**

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
1	101.5	1.015	100.0	101.5	0.0
3	100.7	1.007	100.0	100.7	0.0
7	100.6	1.006	100.0	100.6	0.0
9	100.2	1.002	98.7	98.9	1.3
15	98.2	0.982	100.0	98.2	0.0
21	97.1	0.971	100.0	97.1	0.0
30	103.2	1.032	100.0	103.2	0.0
Mean	100.2				
SD	1.9				

Overall	100.2
St. Dev.	1.9

Data obtained from Table 8, p. 30 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

[^{14}C-TP]XDE-638 Experiment **pH 7**

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
1	100.3	1.003	99.1	99.4	0.9
3	100.1	1.001	98.6	98.7	1.4
7	98.7	0.987	100.0	98.7	0.0
9	100.0	1	100.0	100.0	0.0
15	98.4	0.984	100.0	98.4	0.0
21	95.5	0.955	100.0	95.5	0.0
30	103.2	1.032	100.0	103.2	0.0
Mean	99.5				
SD	2.2				

[^{14}C-PH]XDE-638 Experiment **pH 7**

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
1	100.4	1.004	97.2	97.6	2.8
3	100.4	1.004	100.0	100.4	0.0
7	99.1	0.991	98.9	98.0	1.1
9	99.6	0.996	97.5	97.1	2.5
15	97.5	0.975	99.0	96.5	1.0
21	96.1	0.961	100.0	96.1	0.0
30	104.8	1.048	100.0	104.8	0.0
Mean	99.7				
SD	2.5				

Overall	99.6
St. Dev.	2.3

Data obtained from Table 8, p. 30 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

[^{14}C-TP]XDE-638 Experiment **pH 9**

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	99.0	99.0	1.0
1	100.0	1	100.0	100.0	0.0
3	99.8	0.998	100.0	99.8	0.0
7	100.0	1	100.0	100.0	0.0
9	99.3	0.993	100.0	99.3	0.0
15	94.7	0.947	97.9	92.7	2.0
21	96.7	0.967	100.0	96.7	0.0
30	102.1	1.021	100.0	102.1	0.0
Mean	99.1				
SD	2.3				

[^{14}C-PH]XDE-638 Experiment **pH 9**

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
1	100.3	1.003	100.0	100.3	0.0
3	99.0	0.99	98.9	97.9	1.1
7	100.4	1.004	100.0	100.4	0.0
9	99.3	0.993	99.1	98.4	0.9
15	95.1	0.951	100.0	95.1	0.0
21	95.6	0.956	96.8	92.5	3.1
30	102.2	1.022	98.4	100.6	1.6
Mean	99.0				
SD	2.4				

Overall	99.0
St. Dev.	2.3

Data obtained from Table 8, p. 31 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

[^{14}C-TP]XDE-638 Experiment — Natural Water

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	98.8	98.8	1.2
1	100.6	1.006	100.0	100.6	0.0
3	100.3	1.003	100.0	100.3	0.0
7	100.6	1.006	97.8	98.4	2.2
9	100.0	1	100.0	100.0	0.0
15	100.2	1.002	100.0	100.2	0.0
21	96.9	0.969	100.0	96.9	0.0
30	100.7	1.007	100.0	100.7	0.0
Mean	99.9				
SD	1.2				

[^{14}C-PH]XDE-638 Experiment — Natural Water

Days	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	96.3	96.3	3.7
1	99.8	0.998	100.0	99.8	0.0
3	100.0	1	100.0	100.0	0.0
7	100.6	1.006	100.0	100.6	0.0
9	100.0	1	100.0	100.0	0.0
15	99.2	0.992	100.0	99.2	0.0
21	95.4	0.954	98.1	93.6	1.8
30	100.2	1.002	99.1	99.3	0.9
Mean	99.4				
SD	1.7				

Overall	99.7
St. Dev.	1.4

Data obtained from Table 8, p. 31 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

Preliminary Study at 50°C

[^{14}C-TP]XDE-638 Experiment — pH 4

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
2	90.8	0.908	98.6	89.5	1.3
4	94.2	0.942	98.8	93.1	1.1
24	89.9	0.899	100.0	89.9	0.0
120	90.7	0.907	100.0	90.7	0.0
Mean	93.1				
SD	4.2				

[^{14}C-PH]XDE-638 Experiment — pH 4

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
2	98.9	0.989	100.0	98.9	0.0
4	108.5	1.085	100.0	108.5	0.0
24	113.5	1.135	100.0	113.5	0.0
120	105.0	1.05	100.0	105.0	0.0
Mean	105.2				
SD	6.1				

Overall	99.2
St. Dev.	8.0

Data obtained from Table 7, p. 28 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

Preliminary Study at 50°C

[^{14}C-TP]XDE-638 Experiment pH 7

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
2	103.0	1.03	98.9	101.9	1.1
4	101.2	1.012	100.0	101.2	0.0
24	106.3	1.063	100.0	106.3	0.0
120	90.4	0.904	100.0	90.4	0.0
Mean	100.2				
SD	6.0				

[^{14}C-PH]XDE-638 Experiment pH 7

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
2	104.4	1.044	100.0	104.4	0.0
4	103.4	1.034	100.0	103.4	0.0
24	103.6	1.036	100.0	103.6	0.0
120	93.3	0.933	98.5	91.9	1.4
Mean	100.9				
SD	4.6				

Overall	100.6
St. Dev.	5.0

Data obtained from Table 7, p. 28 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

Preliminary Study at 50°C

[^{14}C-TP]XDE-638 Experiment pH 9

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
2	102.8	1.028	100.0	102.8	0.0
4	108.3	1.083	100.0	108.3	0.0
24	106.7	1.067	100.0	106.7	0.0
120	108.5	1.085	98.9	107.3	1.2
Mean	105.3				
SD	3.7				

[^{14}C-PH]XDE-638 Experiment pH 9

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	100.0	100.0	0.0
2	101.2	1.012	100.0	101.2	0.0
4	108.0	1.08	100.0	108.0	0.0
24	107.3	1.073	100.0	107.3	0.0
120	108.6	1.086	100.0	108.6	0.0
Mean	105.0				
SD	4.1				

Overall	105.1
St. Dev.	3.7

Data obtained from Table 7, p. 29 of the study report.

Chemical Name: Penoxsulam
PC Code: 119031
MRID: 45830721
Guideline No.: 161-1

Preliminary Study at 50°C

[^{14}C-TP]XDE-638 Experiment — Natural Water

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	98.8	98.8	1.2
2	102.4	1.024	100.0	102.4	0.0
4	92.6	0.926	100.0	92.6	0.0
24	91.6	0.916	100.0	91.6	0.0
120	93.0	0.93	98.6	91.7	1.3
Mean	95.9				
SD	4.9				

[^{14}C-PH]XDE-638 Experiment — Natural Water

Hours	Total (% applied)	% Total	XDE-638 (% recovered)	XDE-638 (% applied)	Radioactive Fraction (% applied)
0	100.0	1	99.0	99.0	1.0
2	100.1	1.001	100.0	100.1	0.0
4	98.6	0.986	100.0	98.6	0.0
24	99.5	0.995	100.0	99.5	0.0
120	96.5	0.965	100.0	96.5	0.0
Mean	98.9				
SD	1.5				

Overall	97.4
St. Dev.	3.8

Data obtained from Table 7, p. 29 of the study report.

Attachment 2

Structures of Parent and Transformation Products

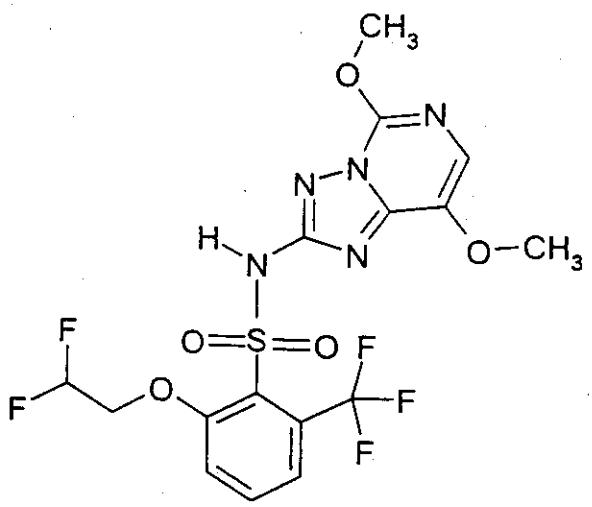
Penoxsulam

IUPAC name: 3-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide

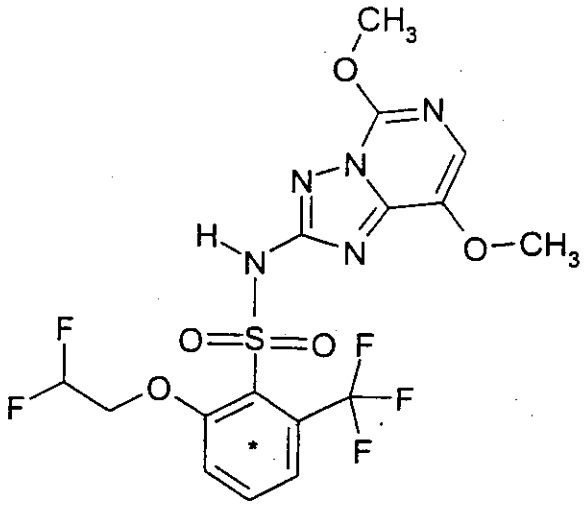
CAS name: 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide

CAS No: 219714-96-2

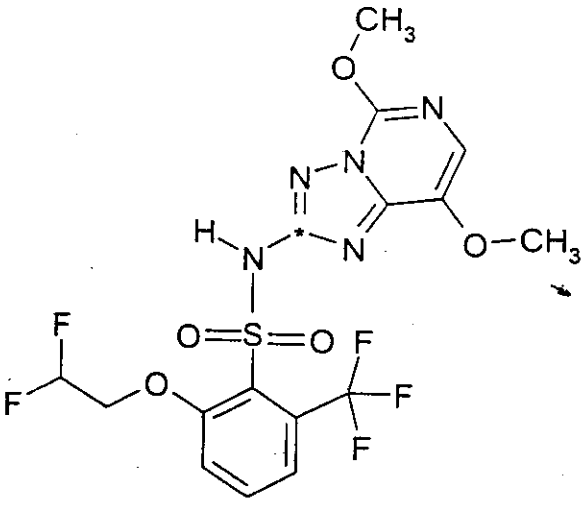
Unlabeled



[Phenyl-U-^{14}C] label



[Triazolopyrimidine-2-^{14}C] label



* Position of the radiolabel.

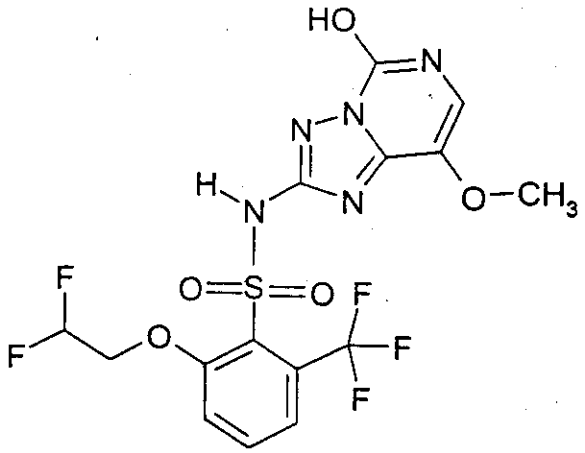
5-OH-XDE-638

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

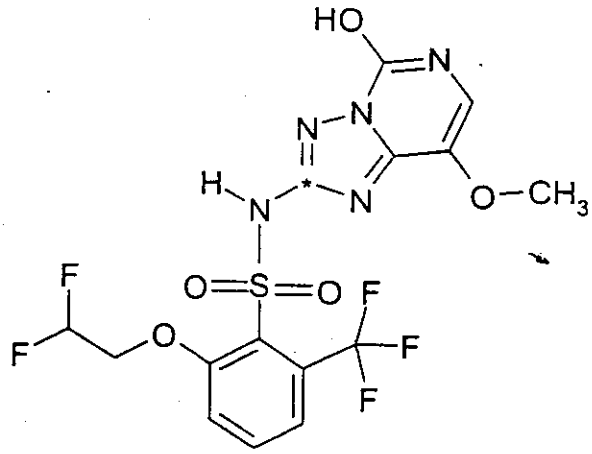
CAS name: 2-(2,2-Difluoroethoxy)-N-(5,6-dihydro-8-methoxy-5-oxo[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide

CAS No: NA

Unlabeled



[Triazolopyrimidine-2-^{14}C] label

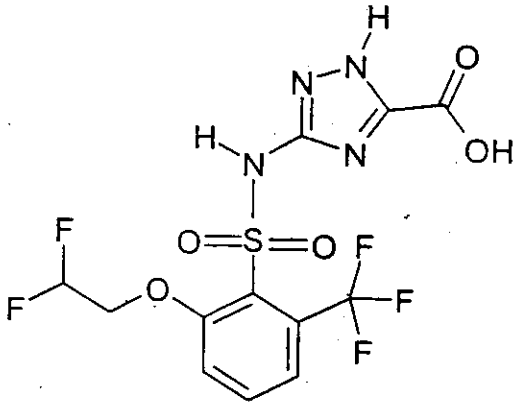


* Position of the radiolabel.

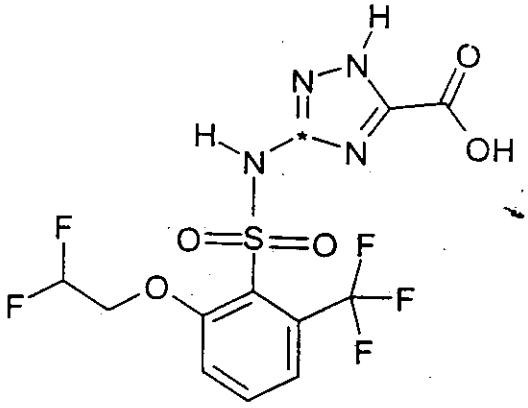
BSTCA

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 No:	NA

Unlabeled



[Triazolopyrimidine-2-^{14}C] label



* Position of the radiolabel.

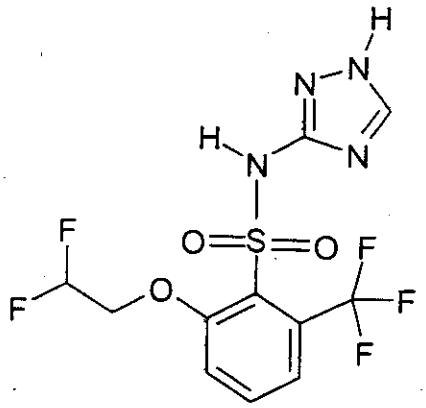
BST

IUPAC name: 6-(2,2-Difluoroethoxy)-α,α,α-trifluoro-N-s-triazol-3-yl-o-toluenesulfonamide

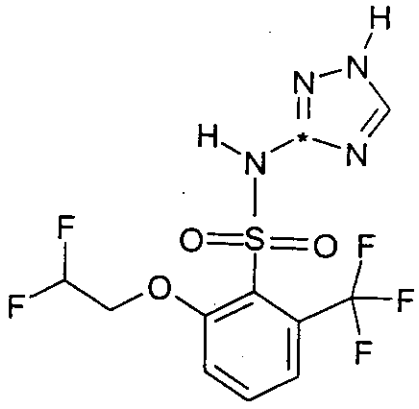
CAS name: 2-(2,2-Difluoroethoxy)-N-1H-1,2,4-triazole-3-yl-6-(trifluoromethyl)benzenesulfonamide

CAS No: NA

Unlabeled



[Triazolopyrimidine-2-^{14}C] label



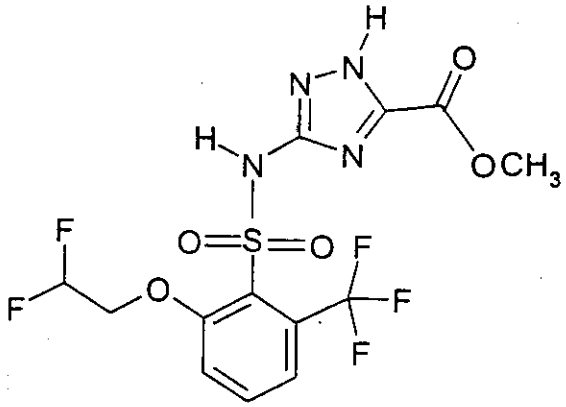
* Position of the radiolabel.

BSTCA-methyl

IUPAC name: Methyl 3-[6-(2,2-difluoroethoxy)-α,α,α-trifluoro-o-toluenesulfonamido]-s-triazole-5-carboxylate

CAS name: Methyl 3-[[[2-(2,2-difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylate

CAS No: NA

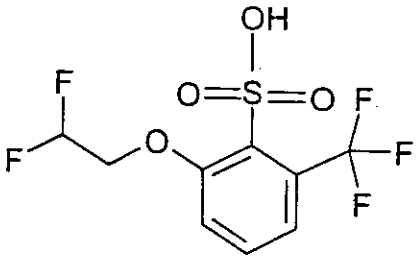


BSA

IUPAC name: 6-(2,2-Difluoroethoxy)-α,α,α-trifluoro-o-toluenesulfonic acid

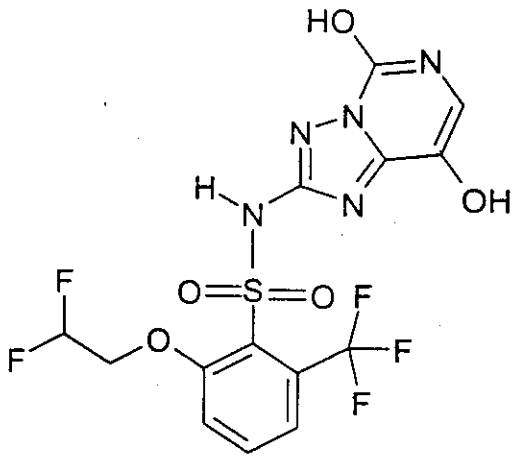
CAS name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid

CAS No: NA



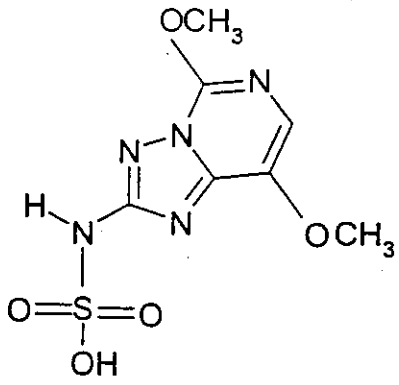
5,8-diOH

IUPAC name: NA
CAS name: 2-(2,2-Difluoroethoxy)-6-trifluoromethyl-N-(5,8-dihydroxy-[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)benzenesulfonamide
CAS No: NA



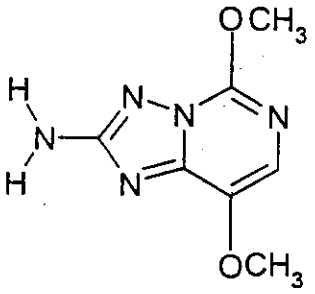
TPSA

IUPAC name: NA
CAS name: 5,8-Dimethoxy[1,2,4]triazolo-[1,5-c]pyrimidin-2-yl-sulfamic acid
CAS No: NA



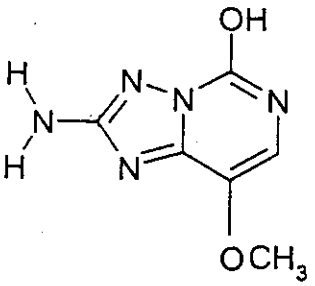
2-Amino TP

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 No:	NA



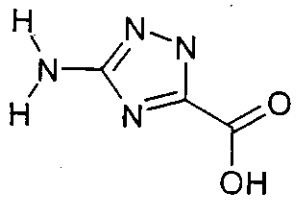
5-OH, 2-Amino TP

IUPAC name:	NA
CAS name:	8-Methoxy[1,2,4]triazolo-[1,5-c]pyrimidin-5-ol-2-amine
CAS No:	NA



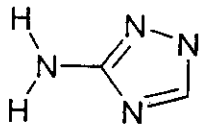
2-Amino TCA

IUPAC name: NA
CAS name: 2-Amino-1,3,4-triazole-5-carboxylic acid
CAS No: NA



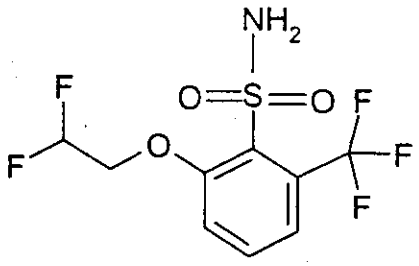
2-Amino-1,3,4-triazole

IUPAC name: NA
CAS name: 2-Amino-1,3,4-triazole
CAS No: NA



Sulfonamide

IUPAC name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide
CAS name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide
CAS No: NA



Sulfonylformamidine

IUPAC name: 2-(2,2-Difluoroethoxy)-N-[(E)iminomethyl-6-(trifluoromethyl)benzenesulfonamide
CAS name: 2-(2,2-Difluoroethoxy)-N-(iminomethyl-6-(trifluoromethyl)-benzenesulfonamide
CAS No: NA