1-26-04

Data Evaluation Report on the stability of Penoxsulam in soil

PMRA Submission Number {.....} EPA MRID Number 45830718

Data Requirement: PMRA Data Code:
EPA DP Barcode: D288160
OECD Data Point:
EPA Guideline: Non-guideline (Storage stability)

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 (Petitioner's code).
SMILES string: n1c(nc2n1c(ncc2OC)OC)NS(=O)(=O)c3c(cccc3C(F)(F)F)OCC(F)F.

Primary Reviewer: Dana Worcester
Dynamac Corporation

Signature:
Date:

QC Reviewer: Joan Gaidos
Dynamac Corporation

Signature:
Date:

Secondary Reviewer: Lucy Shanaman
EPA Reviewer

Signature: Lucy Shanaman
Date: January 26, 2004

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

CITATION: Thomas, A.D., A.M. Miller and D.A. Lindsay. 2002. Frozen storage stability of XDE-638, 5-hydroxy-XDE-638, XDE-638 sulfonic acid (BSA), XDE-638 sulfonamide, triethylammonium of XDE-638 (BSTCA), 5,8-dimethoxy XDE-638 (2-amino-TP) in soil – Interim Report. Unpublished study performed by Regulatory Laboratories, Dow AgroSciences LLC, Indianapolis, IN; sponsored and submitted by Dow AgroSciences, LLC, Indianapolis, IN. Study ID: 010096. Experiment initiated July 27, 2001. Study in-progress, no completion date reported (p.3). Interim report issued on August 16, 2002.

(1)

EXECUTIVE SUMMARY:

The stability of 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, DE-638; purity 99.1%) was studied in soil that was treated at 0.03 mg a.i./kg and stored frozen (*ca.* -20°C) for up to 327 days. The penoxsulam transformation products:

- 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-hydroxy-XDE-638, 5-OH);
- 2-(2,2-difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonic acid (XDE-638 sulfonic acid, BSA);
- 2-(2,2-difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide (sulfonamide);
- 3- [[[2-(2,2-difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylic acid (BSTCA, triethylammonium of XDE-638);
- 5,8-dimethoxy[1,2,4-triazolo[1,5-c]pyrimidin-2-amine (2-amino-TP);

were also studied in soil that was treated at 0.03 mg a.i./kg and stored frozen (*ca.* -20°C) for up to 327 days. No significant degradation was observed during the frozen storage of penoxsulam, 5-OH, sulfonamide, BSA and 2-amino-TP. BSTCA degrade from an average of 88.7% of the applied at day 0 to 76.7% at 327 days. Recoveries after 327 days of frozen storage averaged 97.3%, 82.0%, 96.3%, 76.7%, 107.7% and 52.3% of the applied in the penoxsulam, 5-OH-XDE-638, sulfonamide, BTSCA, BSA, and 2-amino-TP, treated soils, respectively.

METHODOLOGY:

The test system consisted of tin containers (1/4 pint) containing 5.0 ± 0.1 g of soil from Sutter County California (pp.13, 14). The soil was treated with either penoxsulam or the transformation products 5-OH-XDE-638, sulfonamide, BTSCA, BSA, or 2-amino-TP at 0.03 mg a.i./kg, ten times the limit of quantitation (0.003 mg a.i./kg; p.14). A total of 0.10 µL of the appropriate 1.5 µg/ mL test solution was added to each soil sample. The tins were capped, placed in cardboard boxes and stored in the freezer at *ca.* -20°C within 15 minutes of treatment (pp.14, 15). Additional soil samples were prepared and stored without treatment; these samples were spiked and analyzed at the time of sampling to determine concurrent recoveries.

Duplicate tins of the treated soil and one untreated soil were collected after 0, 91, 182, 196, and 327 days of frozen storage (p.11). One tin of untreated soil was treated with 0.03 mg/kg of penoxsulam or its transformation products (p.14).

The fortified/stored and freshly fortified soil samples were extracted with acetonitrile:1.0N HCl (25 mL, 90:10, v:v) by shaking for 60 minutes. The procedure was repeated a second time with 15 mL of extraction solutions for 30 minutes (pp.15-16). The extracts were combined and an aliquot (4.0 mL) evaporated to near dryness under pressure (20 psi) at 40°C. The resulting residues were

acidified with 0.1N HCl, eluted with acetonitrile:methanol:water with 0.1% acetic acid (5:5:90, v:v:v) and analyzed by LC/MS/MS operated in the positive ion electrospray mode. Penoxsulam and its transformation products were identified by comparison to reference standards. A series of calibration curves were included in each chromatographic run. Calculations for determination of penoxsulam and its transformation products in soil were performed using power regression (pp.17-18).

RESULTS:

No significant degradation of either penoxsulam or its transformation products 5-OH, sulfonamide, BSA and 2-amino-TP was observed during storage. However, BSTCA declined from an average 88.7% of the applied to 76.7% at study termination (Table 5, p.29).

[^{14}C]Penoxsulam averaged 83.3% of the applied at day 0 and 97.3% at 327 days posttreatment (Table 2, p.26).

[^{14}C]5-OH averaged 76.7% of the applied at day 0 and 82.0% at 327 posttreatment (Table 3, p.27).

[^{14}C]Sulfonamide averaged 99.0% of the applied at day 0 and 96.3% at 327 posttreatment (Table 4, p.28).

[^{14}C]BSTCA averaged 88.7% of the applied at day 0 and 76.7% at 327 posttreatment (Table 5, p.29).

[^{14}C]BSA averaged 98.0% of the applied at day 0 and 107.7% at 327 posttreatment (Table 6, p.30).

[^{14}C]2-Amino-TP averaged 53.0% of the applied at day 0 and 52.3% at 327 posttreatment (Table 7, p.31).

Table 1. Percent recovery in treated soil, expressed as a percentage of the applied (mean ± sd).

	Sampling time (days)				
	0	91	182	196	327
Penoxsulam	83.3 ± 1.2	80.7 ± 4.3	84.3 ± 6.1	80.3 ± 9.3	97.3 ± 13.6
5-OH	76.7 ± 0.6	71.7 ± 4.0	73.7 ± 3.2	70.0 ± 1.7	82.0 ± 1.0
Sulfonamide	99.0 ± 1.0	95.7 ± 2.5	97.0 ± 12.2	89.7 ± 6.8	96.3 ± 4.3
BSTCA	88.7 ± 2.5	80.0 ± 1.7	89.3 ± 3.8	64.3 ± 3.1	76.7 ± 0.6
BSA	98.0 ± 1.0	91.7 ± 1.5	89.7 ± 0.6	104.7 ± 1.5	107.7 ± 4.2
2-amino-TP	53.0 ± 1.7	42.7 ± 0.6	42.7 ± 3.1	44.3 ± 0.6	52.3 ± 2.1

Data obtained from Tables 2-7, pp.26-31 in the study report.

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REVIEWER'S COMMENTS:

1. It was reported that, "All samples were ... analyzed using the Dow AgroSciences method GRM 01.31". However, no written outline of that method accompanies the submitted study report.

2. Initial recoveries for penoxsulam, 5-OH, BSTCA and 2-amino-TP were below 90% (Tables 2-7, pp.26-31). Recoveries were based on the nominal concentration.

3. Fresh fortified recoveries averaged 76 ± 14%, 82 ± 6%, 75 ± 5%, 77 ± 4%, 81 ± 5%, 75 ± 5% for penoxsulam, 5-OH, sulfonamide, BSTCA, BSA and 2-amino-TP, respectively (Tables 8-13, pp.32-37).

4. On p.11 the storage temperature was reported as 20°C rather than *ca.* -20°C.

5. The submitted report was a preliminary report. The study is to be conducted over approximately a two year period (p.11).

6. The soil was treated at a rate of 0.03 mg a.i./kg for each test substance, which is 10X the validated limit of quantitation (0.003 mg a.i./kg; p.11).

7. The storage conditions were reported to be typical of storage conditions employed for long term storage of soil samples (p.11).

8. The test soils were stored in temperature controlled refrigeration at *ca.* 4°C (p.14). The length of storage was not reported.

9. Fortified stock solutions were diluted with acetonitrile:methanol:water (5:5:90, v:v:v containing 0.1% acetic acid; p.14).

10. This experiment was conducted to support rice paddy studies and fulfill requirements in EPA OPPTS 860.1380 Storage Stability Data, Residue Chemistry Test Guidelines and stability requirements in EC Commission Directive 96/68/EC (p.12). The study was conducted in compliance with EPA GLP Standards (p.3).

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Attachment 1

Excel Spreadsheets

Chemical: Penoxsulam
MRID: 45830718
PC: 119031

	Penoxsulam	5-OH Sulfonamide		BSTCA	BSA	2-amino-TP
0	82	77	99	91	97	55
0	84	77	98	89	99	52
0	84	76	100	86	98	52
Average	83.33	76.67	99.00	88.67	98.00	53.00
SD	1.15	0.58	1.00	2.52	1.00	1.73
91	75.00	74.00	96	79	92	42
91	83.00	74.00	98	82	93	43
91	84.00	67.00	93	79	90	43
Average	80.67	71.67	95.67	80.00	91.67	42.67
SD	4.93	4.04	2.52	1.73	1.53	0.58
182	85	70	91	85	90	42
182	87	76	111	92	89	46
182	81	75	89	91	90	40
Average	84.33	73.67	97.00	89.33	89.67	42.67
SD	3.06	3.21	12.17	3.79	0.58	3.06
196	83	69	92	65.00	106.00	44
196	70	72	82	61	105	45
196	88	69	95	67	103	44
Average	80.33	70.00	89.67	64.33	104.67	44.33
SD	9.29	1.73	6.81	3.06	1.53	0.58
327	90	83	99	77	111	50
327	89	81	99	77	103	54
327	113	82	91	76	109	53
Average	97.33	82.00	96.33	76.67	107.67	52.33
SD	13.58	1.00	4.62	0.58	4.16	2.08

Data obtained from Tables 2-7, pp. 26-31 in the study report.

Attachment 2

Structures of Parent and Transformation Products

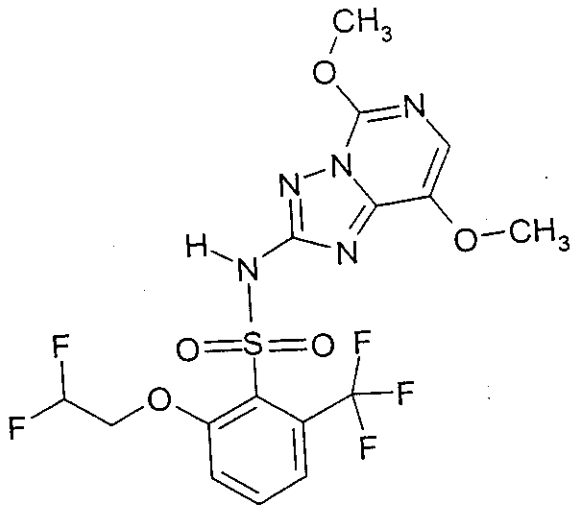
Penoxsulam

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

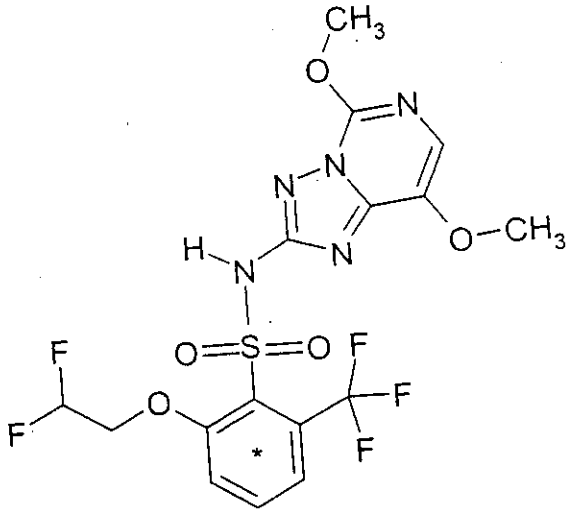
CAS name: 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide

CAS No: 219714-96-2

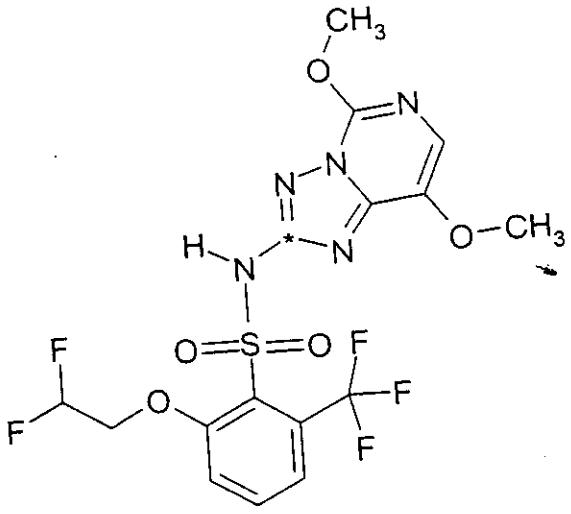
Unlabeled



[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

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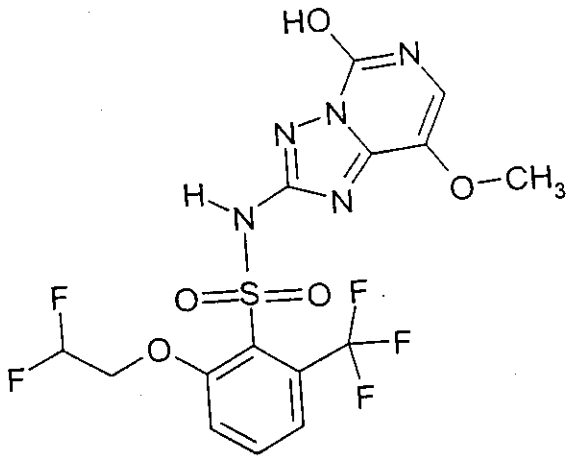

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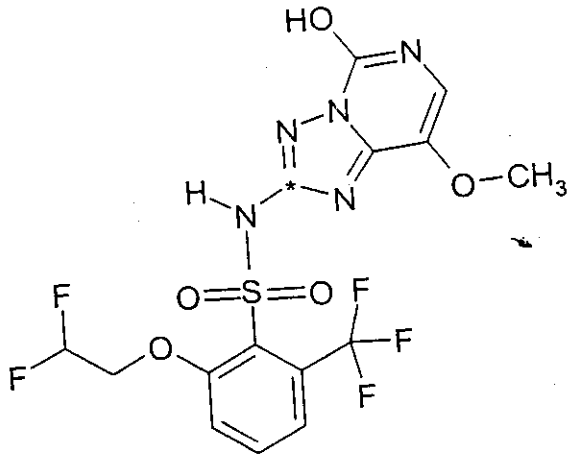

* Position of the radiolabel.

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

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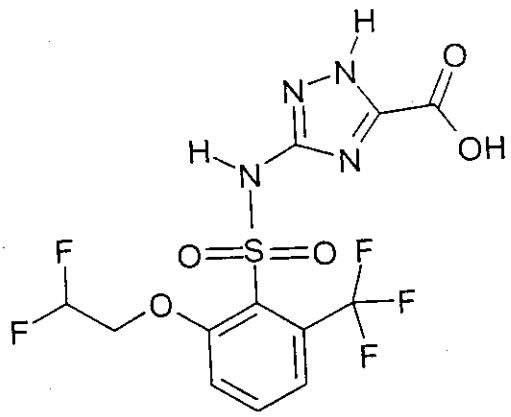
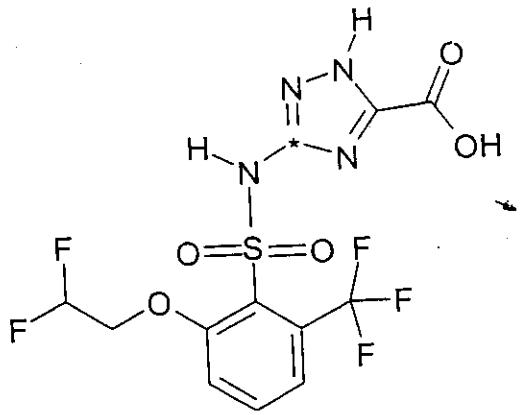


[Triazolopyrimidine-2-^{14}C] label



* 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

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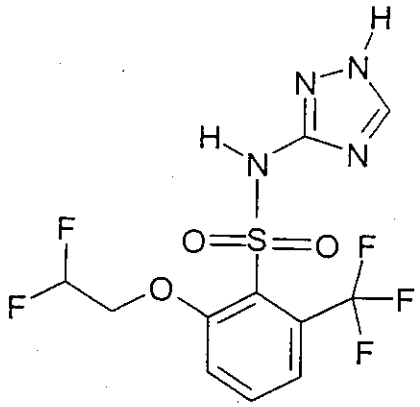
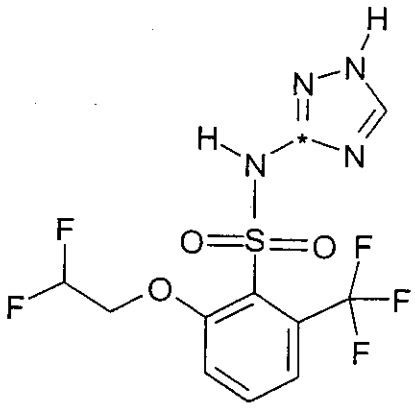


[Triazolopyrimidine-2-^{14}C] label



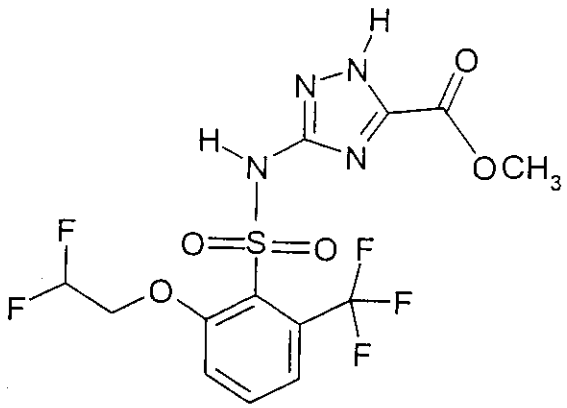
* Position of the radiolabel.

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

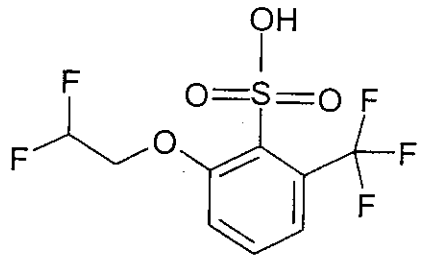


BSA

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

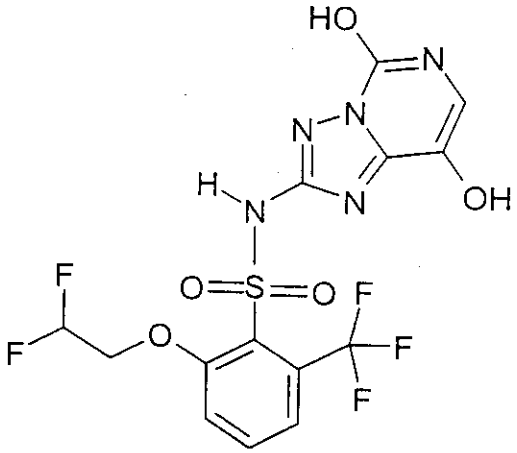
CAS name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid

CAS No: NA



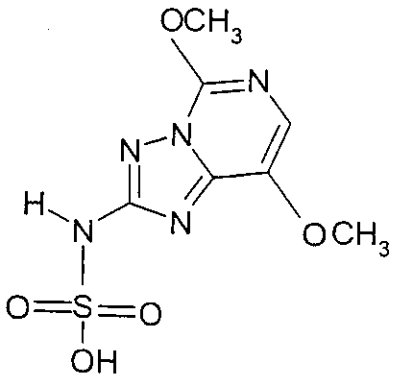
5,8-diOH

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



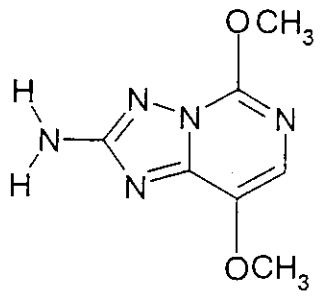
TPSA

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
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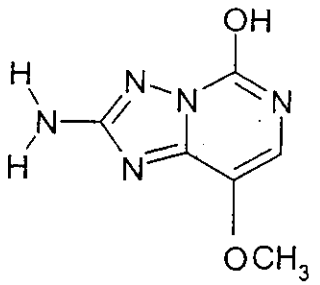
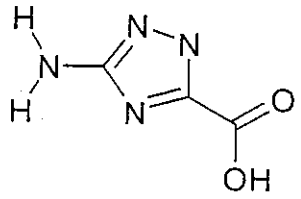
CAS No: NA



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
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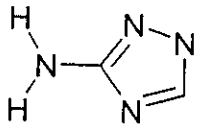

Sulfonamide

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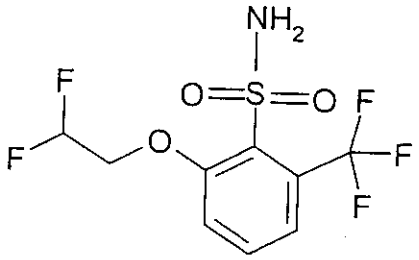
CAS No: NA



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