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Data Evaluation Report on the stability of Penoxsulam in water

PMRA Submission Number {.....} EPA MRID Number 45830803

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:

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Dynamac Corporation

Signature:
Date:

Secondary Reviewer: Lucy Shanaman
EPA Reviewer

Signature: Lucy Shanaman
Date: January 22, 2004

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

CITATION: Thomas, A.D., A.M. Miller and D.A. Lindsay. 2002. 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), XDE-638 TPSA and 2-amino-8-methoxy (5-OH-2-amino-TP) in water -- Interim Report. Unpublished study performed by Regulatory Laboratories, Dow AgroSciences LLC, Indianapolis, IN; sponsored and submitted by Dow AgroSciences, LLC, Indianapolis, IN. Study ID: 010106. Experiment initiated August 24, 2001. Study in-progress, no completion date reported (p.3). Interim report issued on August 29, 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 water that was treated at 0.03 mg a.i./L and stored refrigerated (*ca.* 4°C) for up to 284 days, or frozen (-20°C) for up to 221 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-XDE-638);
- 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);
- (5,8-dimethoxy[1,2,4-triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid (TPSA);
- 2-amino-8-methoxy[1,2,4-triazolo[1,5-c]pyrimidin-5-ol (5-OH-2-amino-TP);

were also studied in water that was treated at 0.03 mg a.i./L and stored refrigerated (*ca.* 4°C) for up to 284 days. No significant degradation was observed during storage of the refrigerated transformation products. Penoxsulam showed no significant degradation for 130 days when stored refrigerated and no significant degradation was observed in frozen storage for up to 221 days. Recoveries from the refrigerated water treated with penoxsulam after 130 days averaged 100.0% of the applied, frozen recoveries averaged 96% after 221 days. Recoveries after 284 days of refrigerated storage averaged 100%, 104%, 91%, 106%, 119%, 99% and 116% of the applied, in the 5-OH-XDE-638, sulfonamide, BTSCA, BSA, 2-amino-TP, TPSA, and 5-OH-2-amino-TP, respectively.

METHODOLOGY:

The test system consisted of glass vials (40 mL) containing 25 mL of water from Sutter County California (pp.14, 15). The water was treated with either penoxsulam or the transformation products: 5-OH-XDE-638, sulfonamide, BTSCA, BSA, 2-amino-TP, TPSA, and 5-OH-2-amino-TP, at 0.03 mg a.i./L, ten times the limit of quantification (0.003 mg a.i./L; p.12). A total of 0.10 µL of the appropriate 7.5 µg/mL test solution was added to the each aliquot of water. The vials were capped and stored in the refrigerator at *ca.* 4°C within 15 minutes of treatment (p.16). Additional samples treated with penoxsulam were also stored in the freezer at *ca.* -20°C. Also, additional water samples were prepared and stored without treatment. These samples were spiked and analyzed at the time of sampling to determine concurrent recoveries.

Triplicate vials of the treated water and one untreated water were collected after 0, 130, 229, and 284 days of refrigerated storage (pp 12-13). Duplicate vials of the penoxsulam treated water and untreated water were collected after 0 and 221 days of frozen storage. Two vials (10 mL) of untreated water were treated with 0.03 µL of either penoxsulam or its transformation products (p.16).

An aliquot (25.0 mL) of the fortified/stored and freshly fortified water samples were transferred to clean, glass GC vials and analyzed immediately by LC with ion electrospray tandem mass spectrometry (LC/MS/MS; p.17). Penoxsulam and the transformation product 2-amino-TP were analyzed operating in positive ion mode. All other transformation products were analyzed by LC/MS/MS operated in negative ion 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 water were performed using power regression (pp.18-19).

RESULTS:

Penoxsulam was relatively stable during 221 days of frozen storage, with recoveries averaging 96% of the applied at 221 days (Table 18, p.44). Recoveries of the frozen fortified samples averaged 104% (Table 19, p.45). In water that was treated and stored under refrigeration, penoxsulam recoveries averaged 100% of the applied after 130 days of storage (Table 2, p.28). Recoveries of the fortified samples ranged from 76-105% (Tables 10-17, pp.36-43). Recoveries for the penoxsulam transformation products 5-OH, sulfonamide, BSTCA, BSA, 2-amino-TP, TPSA, and 5-OH-amino-TP averaged 100%, 104%, 91%, 106%, 119%, 99% and 116%, respectively (Tables 3-9, pp.29-35).

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

Penoxsulam	Sampling time (days)		
	0	130	221
Frozen (n = 3)	108.7 ± 3.8	---	96.0 ± 1.7
Refrigerated (n =32)	107.7 ± 18.2	100.7 ± 3.8	---

Data obtained from Table 2, p.28, Table 18, p.44 in the study report.

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Table 2. Recovery of penoxsulam transformation products in refrigerated water, expressed as a percentage of the applied (mean ± sd, n = 3).

	Sampling time (days)			
	0	130	229	284
5-OH	100.2 ± 2.3	114.7 ± 1.5	97.7 ± 1.5	99.7 ± 0.6
Sulfonamide	108.3 ± 3.2	115.7 ± 2.9	103.0 ± 1.0	103.3 ± 0.6
BSTCA	85.3 ± 0.6	94.3 ± 0.6	86.3 ± 0.6	90.7 ± 0.6
BSA	102.0 ± 1.0	113.7 ± 2.5	104.3 ± 1.5	106.0 ± 2.0
2-amino-TP	107.3 ± 4.7	123.3 ± 1.2	104.7 ± 1.2	118.7 ± 3.2
TPSA	98.7 ± 1.5	107.3 ± 1.2	93.3 ± 2.5	99.3 ± 2.5
5-OH-amino-TP	105.3 ± 4.0	110.3 ± 0.6	111.7 ± 1.5	116.7 ± 3.5

Data obtained from Tables 3-9, pp.29-35 in the study report.

REVIEWER'S COMMENTS:

1. Recoveries for refrigerated samples treated with penoxsulam averaged 67% and 69% of the applied at 229 and 284 days, respectively (Table 2, p.28). Frozen samples averaged 61% of the applied at 320 days (Table 18, p.44). The study author stated that there was a problem with the fortification solution for samples analyzed after 229 and 284 days (p.23). No further details were provided.

2. The submitted report was a preliminary report. The study is to be conducted over approximately a two year period (p.12).

3. The water was treated at a rate of 0.03 mg a.i./L for each test substance, which is 10X the validated limit of quantitation (0.003 mg a.i./kg; p.12).

4. The storage conditions were reported to be typical of storage conditions employed for long term storage of water samples (p.12).

5. This experiment was conducted to fulfill requirements in EPA Subdivision N 164-2 Guidelines and in compliance with EPA and OECD GLP Standards (pp.3, 13).

Attachment 1

Excel Spreadsheets

Chemical: Penoxsulam
MRID: 45830803
PC: 119031

Penoxsulam

	Frozen	Refrigerated
0	113	124
0	107	111
0	106	88
Average	108.67	107.67
SD	3.79	18.23
130		98.00
130		105.00
130		99.00
Average		100.67
SD		3.79
221	95	
221	95	
221	98	
Average	96.00	
SD	1.73	

Data obtained from Table 2, p. 28 and Table 18, p. 44 in the study report.

Transformation products

	5-OH	Sulfonamide	BSTCA	BSA	2-amino-TP	TPSA	5-OH-2-amino-TP
0	103	106	86	101.00	109.00	99	109
0	99	112	85	103	111	100	101
0	99	107	85	102	102	97	106
Average	100.33	108.33	85.33	102.00	107.33	98.67	105.33
SD	2.31	3.21	0.58	1.00	4.73	1.53	4.04
130	116	119	95	114	122	106	110
130	115	114	94	111	124	108	110
130	113	114	94	116	124	108	111
Average	114.67	115.67	94.33	113.67	123.33	107.33	110.33
SD	1.53	2.89	0.58	2.52	1.15	1.15	0.58
229	99.00	103	86	103	104	93	110
229	98.00	104	87	106	104	91	113
229	96.00	102	86	104	106	96	112
Average	97.67	103.00	86.33	104.33	104.67	93.33	111.67
SD	1.53	1.00	0.58	1.53	1.15	2.52	1.53
284	100	103	90	106	115	102	120
284	100	104	91	108	121	97	117
284	99	103	91	104	120	99	113
Average	99.67	103.33	90.67	106.00	118.67	99.33	116.67
SD	0.58	0.58	0.58	2.00	3.21	2.52	3.51

Data obtained from Tables 3-9, pp. 29-35 in the study report.

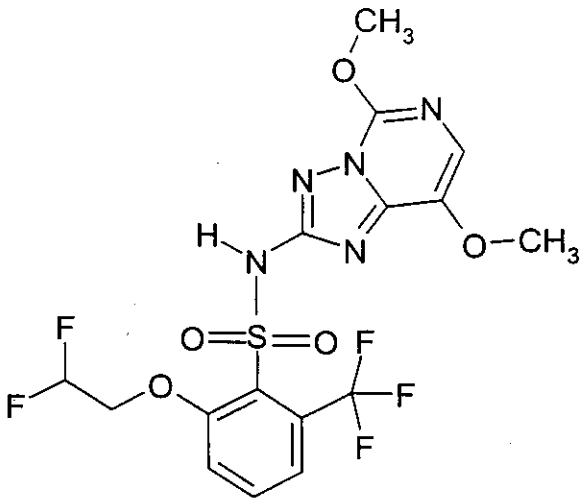
Attachment 2

Structures of Parent and Transformation Products

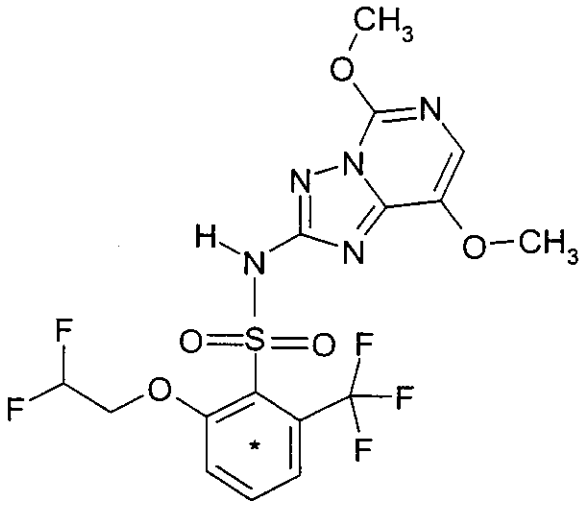
Penoxsulam

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

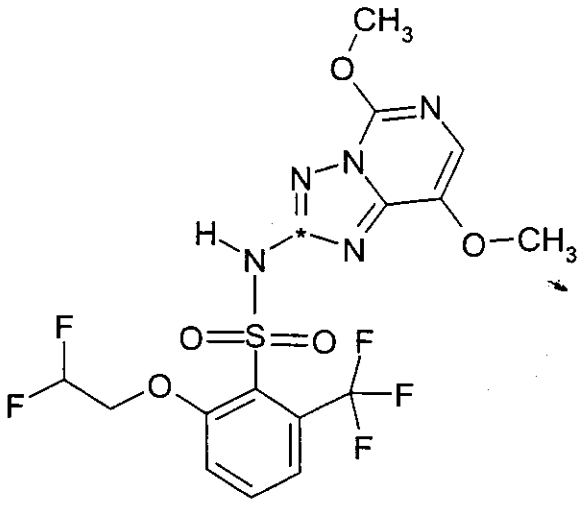
Unlabeled



[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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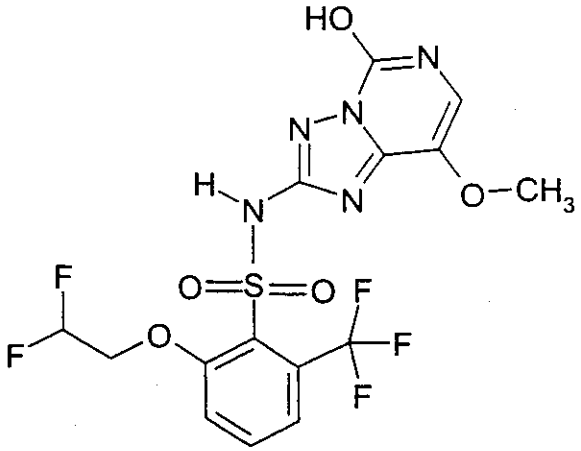
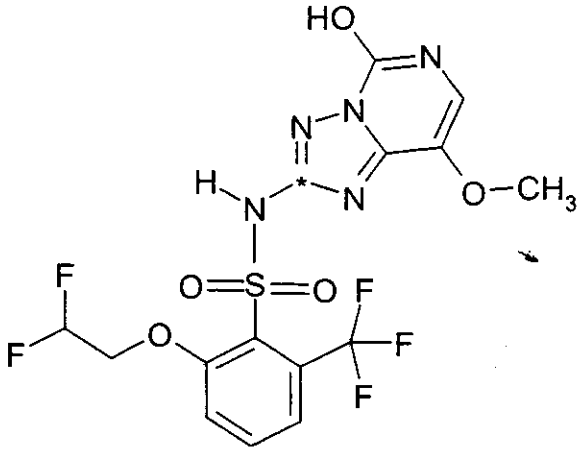


[Triazolopyrimidine-2-^{14}C] label



* Position of the radiolabel.

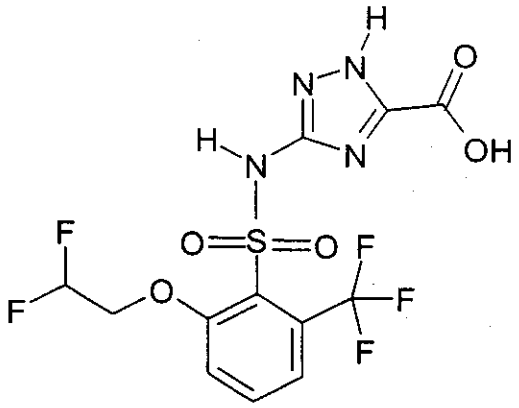
BSTCA

IUPAC name: 3-[6-(2,2-Difluoroethoxy)-α,α,α-(trifluoro-o-toluenesulfonamido]-s-triazole-5-carboxylic acid

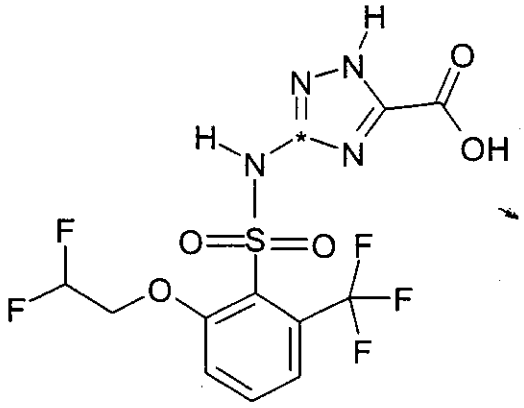
CAS name: 3-[[[2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)phenyl]-sulfonyl]amino]-1H-1,2,4-triazole-5-carboxylic acid

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

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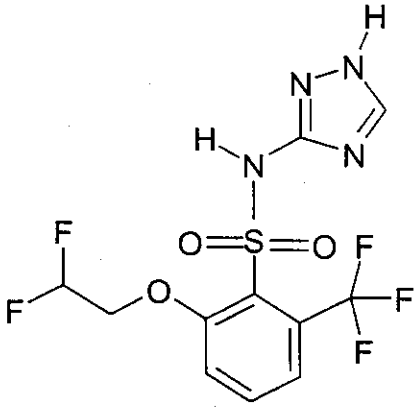
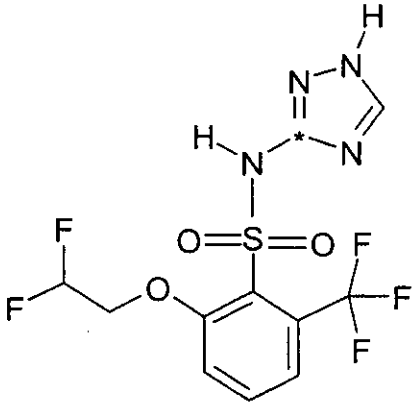


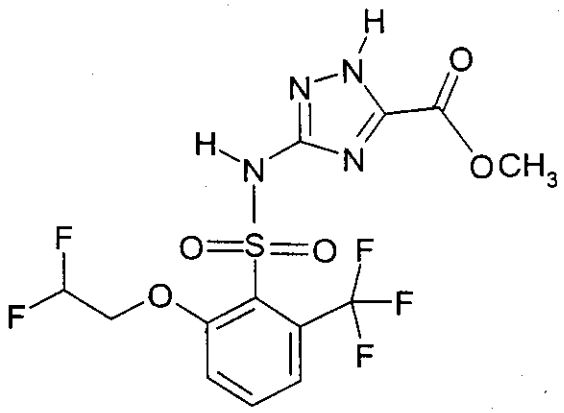
[Triazolopyrimidine-2-^{14}C] label



* Position of the radiolabel.

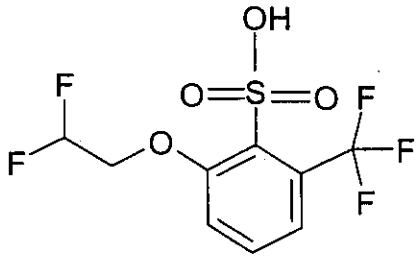
BSTCA-methyl

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



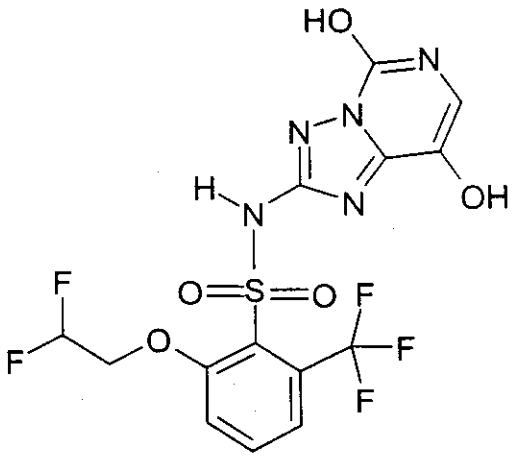
BSA

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



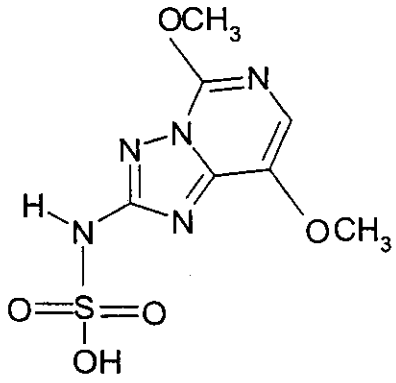
5,8-diOH

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



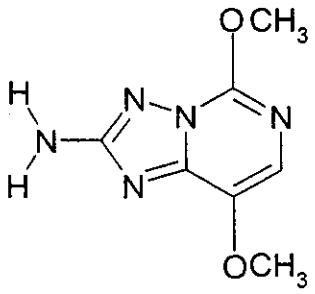
TPSA

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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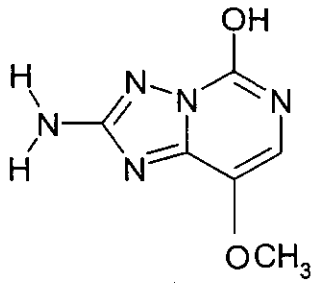
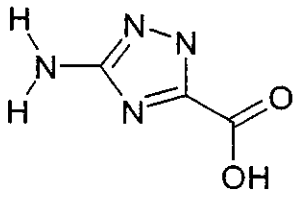
CAS No: NA



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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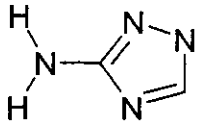
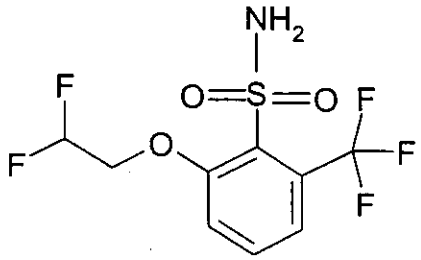


Sulfonamide

IUPAC name: 2-(2,2-Difluoroethoxy)-6-(trifluoromethyl)-benzenesulfonamide
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