STRUCTURE ACTIVITY TEAM REPORT	ver. 04/98	[redacted]	
Case #:	P-10-0326	**DCN:**	
SAT Date:	4/16/2010	**SAT Chair:**	L. Keifer

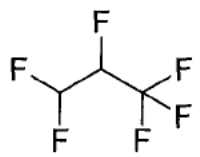
Submitter: [redacted]

Chemical Name:

Propane, 1,1,2,3,3-hexafluoro-

CAS RN:	**Trade Name:**
431-63-0	None

Structure



Molecular Formula:	$C_3H_2F_6$		
Molecular Wt. 152	**WT%<500:**	**WT%<1000:**	
MP:	**BP:** 760.000(	**Eq. Wt:**	
H2O Sol (g/L): 1.9300	**V.P.**	1507	
Max. Prod. Volume (kg/yr): [redacted]	**Physical State:**	Gas	

USE:

Chemical intermediate [redacted]
Synthetic Sequence P-10-326 [redacted]
[redacted] - Chemical intermediate for [redacted]
[redacted] is used as a chemical intermediate

Related Case Numbers	Case Role	Related Case Numbers	Case Role
[redacted]		[redacted]	

Focus Date: 4-29-10 Results: SR- Health

5 0 1 0 0 0 0 3 0 9 6

SAT Report

PMN Number: **P-10-0326**
SAT Date: **4/16/2010**
Print Date: **4/16/2010**

Related cases:

Health related cases: [redacted]
Ecotox related cases: Analogs: [redacted]

Concern levels:

Type of Concern:	**Health**	**Eco**	**Comments**
Level of Concern:	1-2	2	

Persistence	**Bioaccum**	**Toxicity**	**Comments**
3	1	1	

Exposure Based Review:

Health:
Ecotox: No

Routes of exposure:

Health: Inhalation
Ecotox: All releases to water
Fate: ;

Keywords:

Keywords: NEUROTOX; CARDIAC SENS; MALE REPRO; GLOBAL WARMING (UNCERT); AQUATOX

Summary of Assessment:

Fate:

Fate Summary: Gas

log Kow = 1.91 (E)
S = 1.93 g/L at 25 °C (M)
VP = 1507 torr at 25 °C (NOMO5)
BP = 6 °C (M)
H = 8.05 (E)
log Koc = 2.61 (E)
log Fish BCF = 0.92 (E)
log Fish BAF = 0.95 (E)
POTW removal (%) $\geq$ 90 via stripping
Time for complete ultimate aerobic biodeg > mo
Sorption to soils/sediments = low

Volatilization half-life from a standard river = 1 hrs
Volatilization half-life from a standard lake = 5 da
Atmospheric Oxidation Half-life = 24000 hr via OH radical
PBT Potential: P3B1
*CEB FATE: Migration to ground water = rapid

Health:

Health Summary: The PMN substance is a gas, as such, under ordinary conditions there should be no absorption through the skin or from the GI tract (pchem); absorbed from the lung (test data). Concern for neurotoxicity, cardiac sensitization, and male reproductive toxicity based on submitted test data.

Test Data: (-) Salmonella with and without activation; (-) E. coli with and without activation; (-) inhalation mouse micronucleus assay; (-) in a human lymphocyte assay with and without activation; rat 2-week inhalation NOEC = 5000 ppm, altered response to alerting stimulus at 20,000 and 50,000 ppm; dog cardiac sensitization NOEL = 2.5%, LOEL = 3.5%, 2/5 died at 10% [redacted]); rat inhalation LC50 = 85,000 ppm, narcosis at 24,000 ppm and higher [redacted] acute NOEC = 14,000 ppm); rat inhalation developmental NOEC = 50,000 ppm, maternal NOEC = 5000 ppm [redacted] rat 14-week (90-day) inhalation NOEC = 5000 ppm, effects on testes at 50,000 ppm, change in response to alerting stimulus at 20,000 and 50,000 ppm [redacted])

[redacted]

Ecotox:

Test Organism	Test Type	Test End Point	Predicted	Measured	Comments
fish	96-h	LC50	140		
daphnid	48-h	LC50	79		
green algal	96-h	EC50	36		
fish	_	chronic value	15		
daphnid	_	chronic value	9.0		
algal	_	chronic value	14		
Sewage Sludge	3-h	EC50	_		
Sewage Sludge	_	Chronic Value	_		

Ecotox Values Comments: Predictions are based on SARs neutral organic compounds; SAR chemical class = hydrofluorocarbon; MW 152; gas with unknown mp; S = 420 mg/L at 20 °C (P); pH7; effective concentrations based on 100% active ingredients and mean measured concentrations; hardness <150.0 mg/L as CaCO3; and TOC <2.0 mg/L;

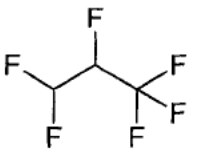
Factors	Values	Comments
Assessment Factor	10	
Concentration of Concern (ppb)	900	
SARs	neutral organic chemicals	
SAR Class	hydrofluorocarbon	

Ecotox Factors Comments:

SAT Chair: L Keifer 564-8916

NCSAB SAT REPORT		CBI? (Y/N):
PMN: P-10-0326	CAS RN:	431-63-(
Chemical Name: Propane, 1,1,2,3,3-hexafluoro-		Analogs:
		Production Volume: [redacted]

Structure:



Use:
Chemical intermediate [redacted]

Formula:	$C_3H_2F_6$		Eq Wt:		
Mol Weight:	152.04	Wt%<500:		Wt%<1000	
MP:		BP:	6.00	VP:	1507
H2O Sol (g/L):		Physical State:	Gas	Log P:	1.91 (E) 0.94 (ACD)

Endpoint (mg/L)	Est. Value	Meas. Value	Comments
Fish 96-h	140		
Daphnid 48-h	79		
Algal 96-h	36		
Fish ChV	15		
Daphnid ChV	9.0		
Algal ChV	14		
BCF			

CHEMICAL CLASS:				SAR: NO	
ECOTOX CONCERN	H	(M)	L	CONCERN CONCENTRATION	0.90
DATE 4/16/10				ASSESSOR: Gordon Cash	

GTOX Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 7 : 305
P-10-0326	0000431-63-0	04/02/10	Incomplet	

S/A: S

Name of Analog:

Reviewer: KEM

		with activation	without activation	Positive Strains
Salmonella Assay:		N	N	
Chromosomal Aberration	CHO:			
	CHL:			
	V79:			
E. coli Reverse Mutation:		N	N	
Mouse Micronucleus Assay:	Route:		N	
Rat Hepatocytes Unscheduled DNA Synthesis:				

Other GTOX Results

Route of exposure for the mouse micronucleus test was inhalation.
The PMN was negative for clastogenic effects with and without activation in an in vitro human lymphocyte test.

Comments

ECOTOX:

Fate:

WS/Log P: WS = 1.93 g/L @ 25C, 32.28 psia (M, p.13).

Toxicology Report [redacted]

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 7 : 298
P-10-0326	0000431-63-0	4/2/2010	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	298

Study Type	Species	Sex	Route
STOXRPDS	RATS	MF	INHL

Test Substance Description

liquid gas; 99.9% purity.

Test Conditions

Four groups of 5 male and 5 female Crl:CD BR rats (age: 44-days; weights: males 210-240 g, females 161-188 g) were exposed by inhalation for 6 hours a day, 5 days a week for 2 weeks to 0 (control), 5000, 20000, or 50000 ppm test substance (analytically determined concentrations: 0, 5000, 20000, and 49700 ppm). Rats were weighed and observed for clinical signs during and after exposure. Immediately following the last exposure, rats were sacrificed and necropsied.

Results

No effects to bodyweight, no abnormal clinical signs, no compound-related effects noted during clinical pathology evaluation, and no mortality were observed. The NOAEL was 5000 ppm.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 7 : 299
P-10-0326	0000431-63-0	4/2/2010	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	299

Study Type	Species	Sex	Route
OTHR	DOGS	M	INHL

Test Substance Description

colorless gas

Test Conditions

In a nose-only inhalation cardiac sensitization potential study, 8 male beagle dogs (age: 9-14 months; weight: 11350-15600 g) were first exposed to epinephrine following 2 minutes of air exposure. Five minutes later (Minute 7) dogs were exposed to test substance gas at 1.25, 2.5, 3.5, 5.0, or 10% concentrations (12500, 25000, 35000, 50000, and 100000 ppm, respectively). The challenge epinephrine dose was administered following five minutes of exposure to test substance (Minute 12). Exposure to test gas was terminated after an additional five minutes (Minute 17). The tests were conducted in the 8 dogs on different and multiple days using different concentrations resulting in at least 5 dogs being exposed to each concentration. Electrocardiographic (ECG) data were recorded continuously throughout the aforementioned procedures. ECG recordings taken during the challenge epinephrine dose (during test gas exposure) were compared to the ECG recordings taken after the first epinephrine dose (during air exposure) and inspected for responses indicative of cardiac sensitization. Thus, each dog served as its own control. Complete necropsies were performed on all study animals. Tests were conducted from 12/3/1994 to 1/6/1995.

Results

Two dogs died during exposure to 10% test substance and a single dog died during exposure to 5% test substance. No gross necropsy findings were observed in deceased animals. No adverse effects were observed in the remaining surviving animals. Animals exposed to 10% test substance responded positively for cardiac sensitization. Based on protocol criteria, there were 0/5, 0/5, 1/5, 4/6, and 5/5 positive responders at the 1.25, 2.5, 3.5, 5, and 10% concentrations, respectively. The NOAEL and LOAEL were considered to be 2.5% and 3.5%, respectively. The EC50 was 4.4%.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 7 : 300
P-10-0326	0000431-63-0	4/2/2010	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	300

Study Type	Species	Sex	Route
ATOX	RATS	M	INHL

Test Substance Description

liquid gas; 99.8% purity.

Test Conditions

Groups of 3 male Crl:CD BR rats (age: young adult; weight: 226-316 g) were exposed whole body to 15000, 25000, 50000, and 100000 ppm test substance gas (corresponding analytical concentrations of 13586, 23588, 44813, and 84927 ppm) for 4 hours. Use of a control group was not indicated. Rats were observed 4 days following exposure for clinical signs and mortality.

Results

No mortality was observed up to the highest dose tested (85,000 ppm). The test substance (HFC-236ea) caused symptoms of narcosis at concentrations of 24,000 ppm or greater. Rats recovered within 1 hour of cessation of exposure and no delayed effects were seen in a 1- to 4-day recovery period.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 7 : 301
P-10-0326	0000431-63-0	4/2/2010	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	301

Study Type	Species	Sex	Route
RTOXTERA	RATS	F	INHL

Test Substance Description

Test Conditions

OECD TG 404 (Developmental Toxicity Study) - The test substance was administered by inhalation to groups of 25 Crl:CD BR female rats (age: 63 days; weight: 192.6-226.2 g) on days 7 to 16 of gestation at daily concentrations of 0 (control), 5000, 20000, or 50000 ppm for 6 hours/day. Observations for morbidity and mortality were made daily up to gestation day (GD) 22. On GD 22 females were euthanized and a gross pathologic exam was conducted. The uterus was assessed for live and dead fetuses and resorptions.

Results

At 50000 ppm, there were significant dose-related decreases in maternal body weight gain and maternal food consumption. At 20000 and 50000 ppm, diminished alerting responses were observed during GD 7 to 16. No evidence of maternal toxicity was detected at 5000 ppm and the NOAEL was considered 5000 ppm. There was no evidence of developmental toxicity at all tested concentrations and the NOAEL was considered 50000 ppm.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 7 : 302
P-10-0326	0000431-63-0	4/2/2010	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	302

Study Type	Species	Sex	Route
STOXRPDS	RATS	MF	INHL

Test Substance Description

Liquefied gas; >99.9% purity.

Test Conditions

Four groups of 10 male and 10 female Crl:CD BR rats (age: NS; weight: males 201-240 g, females 152 to 190 g) were exposed by inhalation for 6 hours a day, five days a week over a 14 week period (65 exposures) to 0 (control), 5000, 20000, or 50000 ppm test substance (corresponding analytically determined mean concentrations of 0, 5010, 20100, and 50100 ppm). The rats were weighed weekly and were observed for clinical signs at weighing and following exposure. Additional observations included response to alerting stimulus, ophthalmological examination, and clinical pathology evaluation. All animals were necropsied and subjected to gross and microscopic examination at study termination.

Results

The test substance had no effect on food consumption, food efficiency, or body weight; produced no ophthalmological aberrations; and did not induce hepatic peroxisome proliferation at any test concentration. A transient diminution or absence of an alerting response was observed at 20000 and 50000 ppm, which resolved within 30 to 50 minutes after cessation of exposure. A slight increase in urinary fluoride concentrations was reported. Male rats exposed to 50000 ppm exhibited increased testicular weights, increased testes-to-brain weight ratios, and dilation of the seminiferous tubules. No effects to germ cells or Sertoli cells were reported in these animals, and the epididymides appeared unaffected. The reported NOAEL was 5000 ppm for males and females based on the reduced or absent response to an alerting stimulus and testicular effects.

OPPT STRUCTURE ACTIVITY TEAM (SAT) MEETING DATE 4-16-10

ATTENDEES	SIGNATURE
CHEMISTRY	
___ Paul Bickart	
___ Diana Darling	
___ Rich Engler	
___ Greg Fritz	
___ Daniel Lin	
✓ Kathy Schechter	Kathy Schechter
✓ Richard Fehir	
✓ Justin Roberts	
✓ Myrta R. Christian	Myrta R. Christian
ENVIRONMENTAL FATE	
___ Bob Boethling	
___ Jed Costanza	
___ Wen-Hsiung Lee	
___ Laurence Libelo	
___ David Lynch	
___ Andy Mamantov	A. Mamantov
HEALTH	
___ Katherine Anitole	
✓ Michael Cimino	
✓ Steve Cragg	Steve Cragg
___ Leonard Keifer	
___ David Lai	
✓ Jim Murphy	
✓ Ronald Ward	
✓ Yin Tak Woo	
___	
ENVIRONMENTAL EFFECTS	
✓ Gordon Cash	Gordon Cash
___ Jeff Gallagher	
___ Maggie Johnson	
___ Sara Pollack	
SAT CHAIR/OTHER	
___ Rebecca Jones	
✓ Leonard Keifer	
___ Jim Kwiat	
___	
___	