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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Sulfuryl Fluoride
TOX Chem. 816A

TO: William Miller, PM #16
Registration Division (TS-767)

THRU: Robert B. Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

FROM: Ray Landolt
Review Section #1
Toxicology Branch/HED (TS-769)

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The Toxicology Chapter to the Registration Standard for Sulfuryl Fluoride is enclosed.

Sulfuryl fluoride (Vikane) is an odorless and colorless gas without adequate warning properties. It is practically insoluble in water, slightly soluble in organic solvents and vegetable oils. Its properties include a high vapor pressure, nonflammability, stable to heat and reactive with strong bases⁽¹⁾. Vikane is marketed as a gas in 125 pound pressurized cylinders. With consideration given to the high volatility of sulfuryl fluoride, ingestion is unlikely and topical exposure to skin or eyes would result in injury from freezing of the contact area. Vikane is relatively low in acute inhalation toxicity with a rat inhalation LC₅₀ of 17.5 mg/l (4200 ppm) for a one hour exposure. The signs of toxicity observed at the lethal concentration were tremors, urination, salivation, chromodacryorrhea accompanied by repeated convulsions (characterized by opisthotonus) and death within three hours (2).

Studies on the effectiveness of respiratory protective equipment has shown that commercial black organic vapor (charcoal) canisters were effective for a limited period of time. An organic vapor canister (black) will permit about five minutes protection at 8000 ppm or for 30 minutes at a concentration of 1000 ppm (3). The use of a NIOSH or MSHA approved positive pressure self-contained breathing apparatus is recommended.

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The threshold limit value (TLV) of 5 ppm (20 mg/m³) for sulfur dioxide is the time-weighted average concentration for a normal 8 hour workday and a 40 hour work week, to which nearly all workers may be repeatedly exposed, day after day, without adverse effects. The short term exposure limit (STEL) of 10 ppm (40 mg/m³) for sulfur dioxide is the time-weight average concentration to which a worker can be exposed continuously for a short period, not to exceed 15 minutes, without adverse effects during an eight hour working day (4).

Teratology:

Four groups of 28 to 29 artificially inseminated New Zealand white rabbits per group were exposed via inhalation under dynamic conditions to 0, 25, 75 or 225 ppm of the test material for six hours per day during days 6 through 18 of gestation. Air concentrations were determined 1 to 2 times per hour by infrared spectrophotometry. Sulfur dioxide was reported to be negative for teratogenicity at 225 ppm, the highest level tested. Decreased maternal and fetal body weight were observed at the 225 ppm level accompanied by a decrease in fetal crown-rump length. The 75 ppm level was without effects for maternal and fetotoxicity (5).

Four groups of 35 to 36 pregnant Fisher 344 rats per group were exposed via inhalation under dynamic conditions to 0, 25, 75 or 225 ppm of the test material for six hours per day during days 6 through 15 of gestation. Air concentrations were determined 1 to 2 times per hour by infrared spectrophotometry. Sulfur dioxide was reported to be negative for teratogenicity at 225 ppm, the highest level tested. The 225 ppm level was without effects for maternal and fetotoxicity (5).

Registered Uses:

This fumigant is registered for structural fumigation of dwellings by professional applications. Sulfur dioxide does not fulfill the requirements for restricted classification (40 CFR 162.11). The recommendation for the use of sulfur dioxide to fumigate dwellings where food and furnishings are likely to be exposed are of concern with respect to the residual deposit likely to be available for human exposure. With reference to the literature, it was determined that sulfur dioxide at a concentration of 35 mg per liter penetrates 4-mil polyethylene sheeting at a rate of 6.2 mg per square meter per hour (6). This permeability of sulfur dioxide lends support to the removal of food-stuffs from the dwelling prior to fumigation rather than to store the commodity in polyethylene plastic bags

during fumigation. Sulfuryl fluoride residues were reported to be detectable 40 days post fumigation in concentrations greater than 1 ppm in feathers, leather, rayon, black sponge rubber and wool (7). The affinity of sulfuryl fluoride for these materials as the result of structural fumigation raises the question as to the potential hazard from dermal exposure of the occupants to the residues deposited.

The nature of these residues on household items need to be characterized along with a quantitative determination of the residue deposited as the result of structural fumigations at 1X and 10X the use concentration. Based on this information additional toxicity data may be necessary. Determination of test substance and relevant toxicity studies cannot be ascertained until this information is made available.

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BIBLIOGRAPHY

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2. Dow Chemical Company (1959) The Acute Vapor Toxicity of Vikane As Determined on Male and Female Rats: Single Exposures of Groups of Rats to High Concentrations of Vikane in Air. (Unpublished study received on unknown date under 464-236; CDL:022799-F). MRID No. 00072289.
3. Dow Chemical Company (1959) Toxicological Studies with Vikane (Sulfuryl fluoride). (Compilation; unpublished study received Oct. 22, 1959 under 464-236; CDL:104918-A). MRID No. 00043314.
4. TLVs Threshold Limit Values for Chemical Substances in the Work Environment Adopted by ACGIH for 1983-84.
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7. Meikle, R.; Stewart, D. (1962) The residue potential of sulfuryl fluoride, methyl bromide, and methanesulfonyl fluoride in structural fumigations. *Agricultural and Food Chemistry* 10(5): 393-397. (Also in unpublished submission received 1962 under unknown administration No.; submitted by Dow Chemical U.S.A., Midland, MI; CDL:121956-A). MRID No. 0010496.

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GENERIC DATA REQUIREMENTS FOR SULFURYL FLUORIDE

Data Requirement	Composition	1/ Use Patterns	2/ Requirement? (Yes, No or Partially)	Does EPA Have Data To Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? <u>3/</u>
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§158.135 Toxicology

ACUTE TESTING: 4/

81-1 - Acute Oral Toxicity		NA				
81-2 - Acute Dermal Toxicity		NA				
81-3 - Acute Inhalation Toxicity - (rat)	TCAL	I	YES	00072269		NO
81-4 - Primary Eye Irritation		NA				
81-5 - Primary Dermal Irritation		NA				
81-6 - Dermal Sensitization		NA				
81-7 - Acute Delayed Neurotoxicity - Hen		NA				
<u>SUBCHRONIC TESTING: 4/</u>						
82-1 - 90-Day Feeding - Rodent		NA				
Non-rodent (dog)		NA				
Non-rodent (guinea pig)		NA				
82-2 - 21-Day Dermal		NA				
82-3 - 90-Day Dermal		NA				
82-4 - 90-Day Inhalation - Rat		NA				
82-5 - 90-Day Neurotoxicity- Hen/Mammal	CA	NA				

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GENERIC DATA REQUIREMENTS FOR SULFURYL FLUORIDE

Data Requirement #	Composition	Use 1/ Pattern 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?
<u>1158.135 Toxicology (continued)</u>					
<u>CHRONIC TESTING: 4/</u>					
83-1 - Chronic Toxicity -	Rodent (rat)	NA			
Non-rodent (dog)		NA			
<u>83-2 - Oncogenicity</u>					
Rat		NA			
Mouse		NA			
<u>83-3 - Teratogenicity -</u>					
Rat	TGAI	I	YES	0090015	NO
Rabbit	TGAI	I	YES	0090015	NO
<u>83-4 - Reproduction, 2-generation</u>					
		NA			
<u>MUTAGENICITY TESTING 4/</u>					
84-2 - Gene Mutation		NA			
84-2 - Chromosomal Aberration		NA			
84-2 - Other Genotoxic Effects					
<u>SPECIAL TESTING: 4/ 6</u>					
85-1 - General Metabolism					[may also include Dermal Penetration, Immunotoxicity Studies, etc]

GENERIC DATA REQUIREMENTS FOR SULFURYL FLUORIDE

Data Requirement	Composition	1/ Use 2/	Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 2/
<u>5158.135 Toxicology</u> (continued)						
<u>CHRONIC TESTING: 4/</u>						
83-1 - Chronic Toxicity -			NA			
Rodent (rat)						
Non-rodent (dog)			NA			
83-2 - Oncogenicity						
Rat			NA			
Mouse			NA			
83-3 - Teratogenicity -						
Rat	TGAI	I		YES	0090015	NO
Rabbit	TGAI	I		YES	0090015	NO
83-4 - Reproduction, 2-generation			NA			
<u>MUTAGENICITY TESTING 4/</u>						
84-2 - Gene Mutation			NA			
84-2 - Chromosomal Aberration			NA			
84-2 - Other Genotoxic Effects						
<u>SPECIAL TESTING: 4/ ~J</u>						
85-1 - General Metabolism	[may also include Dermal Penetration, Immunotoxicity Studies, etc]					

TABLE A
GENERIC DATA REQUIREMENTS FOR SULFURYL FLUORIDE

- 1/ Composition: Material to be tested is technical grade unless otherwise specified in footnotes. PAI= Pure Active Ingredient. PAIRA= Pure Active Ingredient, Radio-Labeled.
- 2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-food; C = Aquatic, Food Crop; D = Aquatic, Non-Food; E = Greenhouse, Food Crop; F = Greenhouse, Non-Food; G = Forestry; H = Domestic Outdoor, I = Indoor; IP = Industrial Preservative.
- 3/ Unless otherwise specified, data must be submitted no later than six months after publication of this Standard.
- 4/ Additional toxicity data are contingent upon the characterization and quantitative determination of the residues deposited on household items as the result of structural fumigation at 1 and 10 times the use concentration.

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DATA EVALUATION REPORT

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STUDY: Subacute InhalationLABORATORY: Dow Chemical Co.DATE: October 22, 1959STUDY NUMBER:MRID NUMBER: 00G72290MATERIAL TESTED: Sulfuryl fluoride (Vikane)ANIMALS: Rats, Guinea Pigs, Mice, Rabbits and Monkeys

METHODS: Groups of the above species received an inhalation exposure of 7 hours/day 5 days/week for six months at 0, 20, 50, 100, 150 and 200 ppm followed by a recovery period of 0, 3 and 6 months after the last exposure. The number of animals and species exposed varied with the concentration of the test material.

RESULTS:CONCLUSIONS:TOXICITY CATEGORY:CORE RATING: Supplementary

- DEFICIENCY:
1. Actual exposure concentrations and frequency of monitoring air concentration is questionable.
 2. Number of survivors per air concentration of questionable value.
 3. Detailed histopathological evaluation was not included.

DATA EVALUATION REPORT

STUDY: Subacute Dietary

LABORATORY: Dow Chemical Co.

DATE: October 22, 1959

STUDY NUMBER:

MRID NUMBER: 00072288

MATERIAL TESTED: Sulfuryl fluoride (Vikane)

ANIMALS: Rats

METHODS: Five groups of 10 male and 10 female rats per group were fed fumigated feed at dietary levels of 0, 19, 53, 350 and 704 ppm for 66 days.

RESULTS:

CONCLUSIONS:

TOXICITY CATEGORY:

CORE RATING: Supplementary

- DEFICIENCY:
1. Dietary concentrations were not monitored during the study.
 2. Detailed histopathological evaluation was not included.

Study/Lab/Study #/Date	Material	No.	LD ₅₀ , LC ₅₀ , PIS, NOEL, LEL	Category	Doc. No.
Registration standard Teratology - rabbit; Dow Chemical; #HET-K-16399-(15); 10/26/81	Gas Lot #217	246489	Teratogenic NOEL > 225 ppm (HDT) Maternal NOEL = 75 ppm Maternal LEL = 225 ppm (decreased body weight gain) Fetotoxic NOEL = 75 ppm Fetotoxic LEL = 225 ppm (decreased fetal body weight and decreased rump-crown length). Levels tested = 0, 25, 75, 225 ppm during days 6-18 of gestation for 6 hrs./day by inhalation.		004281 Minimum 001421
Teratology - rat; Dow Chemical; #HET-K-16399-(15); 10/26/81	Gas Lot #217	246489	Teratogenic NOEL > 225 ppm (HDT) Maternal NOEL > 225 ppm (HDT) Fetotoxic NOEL > 225 ppm (HDT) Levels tested = 0, 25, 75, 225 ppm during days 6-15 of gestation for 6 hrs./day. Via inhalation.		Minimum 001421
1-Month inhalation - rat ; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = 200 ppm LEL = 400 ppm (mortality, pulmonary hemorrhages and cloudy swelling of the kidneys) Levels tested = 200, and 400 ppm for 7 hrs/day/5 days/wk for 5 wks.		Supplementary 002674
1-Month inhalation - rabbit; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = 200 ppm LEL = 400 ppm (loss of control, tremors of the hind quarters, lung, liver & kidney pathology and weight loss) Levels tested = 200, and 400 ppm for 7 hrs/day/5 days/wk for 5 wks.		Supplementary 002674
1-Month inhalation - guinea pig; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = < 200 ppm (congestive liver) Levels tested = 200, and 400 ppm for 7 hrs/day/5 days/wk for 5 wks.		Supplementary 002674

Study/Lab/Study #/Date	Material	No.	LD ₅₀ , IC ₅₀ , PIS, NOEL, LEL	Category	Doc. No.
66 Day Feeding - rat; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072288	NOEL = 19 ppm LEL = 53 ppm (Decreased growth and body weight gain) Levels tested = 19, 53, 350, and 704 ppm		Supplementary 002674 Supplementary 004281
6-Month inhalation - rat ; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = 100 ppm LEL = 200 ppm (mortality, decrease in body wt. increase in fluoride in urine, blood, bone, lungs and teeth) Levels tested = 100, and 200 ppm 7 hr/day/5 days/wk for six months plus a 30 day recovery period for 1/2 the test groups.		Supplementary 002674 Supplementary 004281
6-Month inhalation - rat ; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = < 20 ppm (increased fluoride in bone) Levels tested = 0, 20, 50, 150 ppm		Supplementary 002674 Supplementary 004281
6-Month inhalation - mice; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = < 20 ppm (elevated heart to body weight and elevated lung to body weight)		Supplementary 002674 Supplementary 004281
6-Month innalation - rabbit; Dow Chemical Co. ; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL < 100 ppm (slight liver damage) Levels tested = 100 and 200 ppm 7 hr/day/5 days/wk for six months plus a 30 day recovery period for 1/2 the test groups.		Supplementary 002674 Supplementary 004281

Tox Chem No. 816A- Sulfuryl fluoride

Study/Lab/Study #/Date	Material	EPA Accession No.	LD ₅₀ , LC ₅₀ , PIS, NOEL, LEL	Results:	TOX Category	CORE Grade/Doc. No.
6-Month inhalation - guinea pig; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = < 100 ppm (depressed growth, mortality, increased fluoride in bone and reversible liver damage) Levels tested = 100 and 200 ppm 7 hr/day/5 days/wk for six months plus a 30 day recovery period for 1/2 the test groups.		Supplementary 002674 Supplementary 004281	
6-Month inhalation - guinea pig; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = > 150 ppm (HDT) Levels tested = 0, 20, 50, 150 ppm		Supplementary 002674 Supplementary 004281	
6-Month inhalation - monkey; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	Two monkeys exposed at 100 ppm exhibited no adverse effects.		Supplementary 002674 Supplementary 004281	
1-Year inhalation - rat ; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072290	NOEL = < 20 ppm (increased fluoride in bone) Levels tested = 0, 20, 50, and 150 ppm (females)		Supplementary 002674	
1-Year inhalation - mice ; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072990	NOEL = < 20 ppm Levels tested = 0, 20, 50, 150 ppm		Supplementary 002674	
1-Year inhalation - guinea pig; Dow Chemical Co.; 10/22/59	Vikane 99% a.i.	00043314 00072990	NOEL = > 150 ppm (HDT) Levels tested = 0, 20, 50, 150 ppm		Supplementary 002674	
Acute oral LD ₅₀ - rat; Dow Chemical; 10/22/59	Vikane 99% a.i.	238663 00043314 00072990	LD ₅₀ = approx. 100 mg/kg (both male and female) Levels tested: male = 50, 100, 200, 400 mg/kg female = 40, 80, 160 mg/kg Dosing is by feeding in corn oil.		Supplemen- tary 002673	

Study/Lab/Study #/Date	Material	EPA Accession No.	Results:		TOX Category	CORE Grade/Doc. No.
			LD ₅₀ , LC ₅₀ , PIS, NOEL, LEL			
Acute oral LD ₅₀ - guinea pig; Dow Chemical; 10/22/59	Vikane 99% a.i.	238663 00043314 00072990	LD ₅₀ = approx. 100 mg/kg (female) Levels tested = 50, 100, 200, 400 mg/kg by feeding in corn oil.			Supplementary 002673
Acute inhalation LC ₅₀ - rat; Dow Chemical; 10/22/59	Vikane 99% a.i.	238663 00043314 00072990	LC ₅₀ = 17.5 mg/L for 1 hr. exposure (= approx. 4200 ppm) Levels tested = 1000, 2000, 4000, 8000, 15,000 ppm		III	Minimum 002673