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

SEP 14 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Sulfuryl Fluoride. ID No. 078003. Review of Toxicology Data Base to Determine Eligibility for Reregistration.

Tox. Chem. No.: 816A
PC No.: 078003
Barcode No.: D180762
Submission No.: S422075

FROM: Linnea J. Hansen, Ph.D. Linnea J. Hansen 8/31/92
Section IV, Tox. Branch I
Health Effects Division (H7509C)

TO: Larry Schnaubelt, Manager, PM Team 72
Don Mackey, PM Team 72
Reregistration Division (H7508W)

THRU: Marion P. Copley, D.V.M., D.A.B.T., Section Head KB 9/4/91
Section IV, Tox. Branch I Marion P. Copley 8/31/92
Health Effects Division (H7509C)

I. CONCLUSIONS:

A meeting with Dr. John Quast of DowElanco was held on July 16 to discuss the need for additional toxicology data to support reregistration of sulfuryl fluoride. The data requirements outlined in the reregistration standard for sulfuryl fluoride have been met; however, after consideration of the available data, HED requested additional neurotoxicity data (memo from L. Hansen to L. Rossi dated 7-31-92) and completion of the Reregistration Eligibility Document was postponed. The rationale for requiring these studies was discussed in detail in that memo.

To summarize, while the data base for sulfuryl fluoride is extensive, TB-I considers acute neurotoxicity endpoints necessary for realistic determination of short-term exposure risk following reentry, since neurotoxicity appeared to be the most sensitive toxicity endpoint for sulfuryl fluoride at subchronic exposures and no acute neurotoxicity data is available. MOEs based on available (subchronic) neurotoxicity data and measurements of sulfuryl fluoride following aeration down to limits of instrument detection are inadequate.

A toxicity profile of sulfuryl fluoride is attached to this

memo.

II. ACTION REQUESTED:

On July 2, 1992 DowElanco submitted a letter requesting eligibility of sulfuryl fluoride for reregistration based on the existing toxicology data base along with a summary of this data. A meeting with the Agency was requested to discuss whether additional data was necessary to support reregistration. SRRD also requested identification of all applicable data requirements and notation of those for which adequate data has not been submitted.

III. PRODUCT INFORMATION

Sulfuryl fluoride (SO_2F_2; MW 102.07) is a fumigant registered for uses in closed, sealed buildings (dwellings, garages, barns, storage buildings, etc.) for control of numerous pests, including drywood termites, powder post beetles, old house borers, bedbugs and clothes moths. Sulfuryl fluoride has no food or feed uses (including fumigation of grains). It is supplied as liquefied gas in pressurized steel cylinders which contain 99% sulfuryl fluoride/1% inert impurities. It is classified as a restricted use pesticide and may only be used by trained individuals wearing a self-contained breathing apparatus. Chlorpicrin is added as a warning agent.

The physical and chemical properties of sulfuryl fluoride gas are listed below:

Color:	colorless
Physical state:	gas at room temperature
Odor:	odorless
Solubility:	0.075 g/100 g in water (25°C);
	0.78 g/100 g in wesson oil (20°C);
	2.12 g/100 g in chlroform (22°C)
Melting point:	-136.67°C
Boiling point:	-55.21°C
Vapor pressure:	13,422 mm Hg at 25°C

The CAS Registry Number is 2699-78-8, ToxChem Number is 816A and the PC Number is 078003.

IV. REQUIREMENTS (CFR 158.135): Updated: 8-92

Sulfuryl Fluoride, Technical:

	Required	Satisfied
81-1 Acute Oral Toxicity	N[1]	-
81-2 Acute Dermal Toxicity	N[1]	-
81-3 Acute Inhalation Toxicity	Y[1]	Y
81-4 Primary Eye Irritation	N[1]	-
81-5 Primary Dermal Irritation	N[1]	-
81-6 Dermal Sensitization	N[1]	-
81-7 Acute Delayed Neurotox.(hen)	N[2]	-
81-8 Acute Neurotox. (rodent)	Y[2]	N
82-1 Subchronic Oral (rodent)	N[3]	-
82-1 Subchronic Oral (nonrodent)	N[3]	-
82-2 21-Day Dermal	N[3]	-
82-3 90-Day Dermal	N	-
82-4 90-Day Inhalation	Y	Y
82-5 90-Day Neurotoxicity (hen)	N[2]	-
82-5 90-Day Neurotoxicity (rodent)	Y[2]	N
83-1 Chronic Toxicity (rodent)	N[4]	-
83-1 Chronic Toxicity (nonrodent)	N[4]	-
83-2 Oncogenicity (rat)	N[4]	-
83-2 Oncogenicity (mouse)	N[4]	-
83-3 Teratogenicity (rodent)	Y	Y[5]
83-3 Teratogenicity (nonrodent)	N	Y[5]
83-4 Reproduction	N[4]	Y
83-5 Chronic/Oncogenicity		-
84-2 Mutagenicity-Gene Mutation	Y	Y
84-2 Mutagenicity-Struct. Chrom. Aber.	Y	Y
84-2 Mutagenicity-Other Genotoxic Effect	Y	Y
85-1 General Metabolism	N[3]	-
85-2 Dermal Penetration	N	-
86-1 Domestic Animal Safety	N	-
Special Studies:Ocular Effects		
Acute Oral (Rat)	N	-
Subchronic Oral (Rat)	N	-
Six month Oral (Dog)	N	-

Y= Yes; N= No

1 Sulfuryl fluoride is a gas and has no food uses.

2 Requested in a recent Data Call-in; 82-5 previously submitted but classified supplementary.

3 Gas with no food uses; oral/dermal exposure not anticipated

4 Chronic exposure to sulfuryl fluoride not anticipated

5 Data submitted by registrant

V. TOXICOLOGY PROFILE:

Updated August, 1992

STUDY;CLASSIFICATION; CATEGORY; STUDY #; DATE	RESULTS
Technical Sulfuryl fluoride	
81-3 Acute inhalation LC50 Species: rat Dow Chemical Co. ACC#1: 0238663 Date: 10/22/59 CORE - MINIMUM DOC#s: 002673	LC50 = 17.5 mg/L for 1 hr. exposure (= approx. 4200 ppm) Levels tested = 1000, 2000, 4000, 8000, 15,000 ppm
81-3 Acute inhalation LC50 Species: rat Dow Chem; Mammalian & Env. Tox Study#: K-016399 ACC#1: Date: 11/16/90 CORE - ACCEPTABLE DOC#s: 009393	LC50 > 9599 ppm (40,315 mg/m3). In Fischer 344 rats toxicity: Chromodacryorrhea and fecal soiling.
82-4a Inhalation-3 month Species: rat Dow Chemical Co. Study#: K-016399 MRID: 408909-02 Date: 11/16/87 CORE - MINIMUM DOC#s: 009479	NOEL = 30 ppm. LOEL = 100 ppm (M&F), based on fluorosis of teeth. The addition, at the 300 ppm there were significant body weight decrements, inflammation of the nasal passage, alveolar histiocytosis, & microscopic vacuolation of the caudate-putamen nucleus & white fiber tracts of the internal capsule of the brain (M&F), and very slight hyperplasia of the collecting ducts of the kidney (F). Fischer 344 rats were administered by inhalation, doses of: 0, 30, 100 and 300 ppm of sulfuryl fluoride for 6 hrs/day, 5 days/week for 13 weeks.
82-4b Inhalation-3 month Species: dog Dow Chemical, Mich. Study#: K-016399-041;-041A MRID: 422566-01 Date: 02/24/92 CORE - MINIMUM DOC#s: 009506	Doses administered: 0, 30, 100 & 200 ppm sulfuryl fluoride administered by inhalation (6 hr/day, 5 days/week) to young adult male & female dogs for 13 weeks. Systemic NOEL = 100 ppm. Systemic LOEL = 200 ppm, based on slightly decreased mean body weight/body weight gain & slight histopathology of the caudate nucleus of the basal ganglia in males & females (single incidence/sex) & transient neurological symptoms (lateral recumbency, tremors, followed by inactivity) in one male.
83-3(a) Developmental Toxicity Study Species: rat Dow Chemical Co. Study#: HET-K-16399-(15) MRID: 000900-15 Date: 10/26/81 CORE - MINIMUM DOC#s: 001421 009510	Maternal NOEL > 225 ppm (HDT) Fetotoxic NOEL > 225 ppm (HDT). Levels tested = 0,25,75,225 ppm gestation days 6-15 /6 hrs./day. Via inhalation in Fischer 344 rats. Reevaluation of this study (DER 009510) in support of reregistration agreed with previous review (DER 001421) assigning a Minimum Coregrade.

83-3(b)	Developmental Toxicity Study Species: rabbit Dow Chemical Co. Study#: HET-K-16399-(15) MRID: 000900-15 Date: 10/26/81 CORE - MINIMUM DOC#s: 001421 009510	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 in New Zealand White strain. Reevaluation of this study (DER 009510) in support of reregistration agreed with previous review (DER 001421) assigning a Minimum Coregrade.
83-4	Reproduction-2 generation Species: rat (inhalation) Dow Chemical, Texas Study#: K-016399-042 MRID: 412798-01 Date: 01/07/92 CORE - GUIDELINE DOC#s: 009479	Doses tested: 0, 5, 20 & 150 ppm via inhalation in Sprague-Dawley rats. Parental NOEL = 5 ppm. Parental LOEL = 20 ppm based on gross & microscopic lesions in the lung. At 150 ppm (HDT) there was decreased body weight, chronic pulmonary inflammation, vacuolation of the caudate putamen in the cerebrum and dental fluorosis. Reprod. NOEL = 20 ppm. Reprod LOEL = 150 ppm (decr. pup weight).
84-2(a)	Mutagenic-Ames Species: salmonella Dow Chemical Co. Study#: TXT:K016399-037 MRID: 416030-01 Date: 8/17/90 CORE - ACCEPTABLE DOC#s: 008247	Negative for inducing gene mutation in Ames tester strains of S. typh. exposed to test article up to toxic concentrations (30,000 - 50,000 ppm) with/without activation.
84-4	Mutagenic-micronucleus assay Species: mice Dow Chemical Co. Study#: TXT K-016839033 MRID: 414486-01 Date: 2/16/90 CORE - ACCEPTABLE DOC#s: 008067 008392	Reported negative, tested up to inhalation dose of 520 ppm; but evidence for MTD affecting bone not provided. Information provided 5/15/91, allowed an upgrade to acceptable.
84-4	Mutagenic-unscheduled DNA synt Species: rat hepatocytes Dow Chemical, Texas Study#: K-016399-043 MRID: 421798-02 Date: 10/07/91 CORE - ACCEPTABLE DOC#s: 009479	Doses tested: 0, 102, 204, 408, 612, 816, 1020 and 1530 ppm (0, 0.43, 0.85, 1.70, 2.65, 3.40, 4.25 & 6.37 mg/L) sulfuryl fluoride gas injected into primary rat hepatocyte cultures & exposed for 18-19 hrs. Doses of 1530 ppm & higher were too cytotoxic to assay for UDS. No evidence of increased unscheduled DNA synthesis over negative controls was observed up to 1020 ppm.

VI. DATA GAPS

The following data gaps have been identified for sulfuryl fluoride:

A. 81-8§§ Acute inhalation neurotoxicity study in rats. Required by recent Data Call-in to obtain neurotoxicity NOEL for short-term exposure.

B. 82-5§§ Chronic inhalation neurotoxicity study in rats. Required by recent Data Call-in to replace previously submitted study which showed some effects but was classified Core-supplementary.

VII. ACTION TAKEN TO REMOVE DATA GAPS AND OBTAIN ADDITIONAL INFORMATION:

The registrant should have been informed of studies needed to satisfy the remaining data requirements for registration of resmethrin through a recent data call-in notice.

VIII. REFERENCE DOSE (RfD):

An RfD has not been established for sulfuryl fluoride since there are no food uses.

IX. PENDING REGULATORY ACTIONS:

TB-I is not aware of any regulatory actions against sulfuryl fluoride at this time.

X. TOXICOLOGIC ISSUES:

A. Incident reports: There are two reports of fatalities following reentry into homes after fumigation with sulfuryl fluoride. Incidences of non-fatal sulfuryl fluoride poisoning have also been reported.

B. Margin of safety for exposure following reentry: Using a NOEL of 30 ppm (subchronic neurotoxicity, the most sensitive NOEL available at present for short- to mid-term exposure) and currently available data on sulfuryl fluoride concentrations following aeration (~1 ppm, at instrumentation limits of detection), the MOE is inadequate. Additional acute neurotoxicity data along with more sensitive determinations of sulfuryl fluoride and dissipation curves following aeration have been requested.