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

009393

MAR 30 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Sulfuryl Fluoride (SF). 4 hour dermal vapor exposure study in rats.
ID #1062719-00004
HED # 2-0109
Tox Chem No. 816A
S 40 1150

TO: Ruth Douglas (PM-32)
Disinfectants Branch
Registration Division (H7505W)

FROM: Stanley B. Gross, PhD, DABT, CIH
Toxicologist/Hygienist
Toxicology Branch I
Health Effects Division (H7509C)

THRU: Joycelyn Stewart, PhD
Acting Head, Section II, Toxicology Branch I
Health Effects Division (H7509C)

THRU: Karl P. Baetcke, PhD
Chief, Toxicology Branch I
Health Effects Division (H7509C)

Submitted Study:

"Sulfuryl Fluoride: Four-Hour Dermal Vapor Exposure in Fischer 344 Rats," by G. J. Bradley, T.D. Landry, J. E. Battjes and J. F. Quast of the Dow Chemical Company, Study ID# K-016399-036. MRID #417120-01.

The study was reviewed by Clement International Corporation, contractor for HED. The Clement review is attached to this memorandum.

Study Summary.

The purpose of this study was to determine any toxic effects from the absorption of SF vapor through the intact skin of rats while preventing the animals from breathing the SF to which their skins were exposed. Thus the animals were placed in a inhalation exposure chambers with their bodies inside the chambers and their heads outside in a reversed head only exposure position. The bodies were then exposed for 4 hours to SF at 9599 ppm SF. No adverse effects were observed from these exposures.

1 of 14

Conclusions.

Based on the results of this study, the dermal vapor LC50 of SF in rats is greater than 9599 ppm (40.3 mg/L). No TOXICITY CATEGORY can be assigned to this study because we have no corresponding category. Based on the methods and observations used, the study is ACCEPTABLE.

Comments:

This study is not typical of guideline specifications; however it met its objectives of assessing the possible toxicity from dermal exposures to high concentrations of SF. The vapor exposures were well performed and characterized. Whole animal toxicity of ~~evalu~~ation along with possible skin and internal organ pathology.

Note; A one-liner summary for this study was attached with the SF/RED toxicology summary prepared for FIFRA 1988 review of SF.

009393

DOC920123

FINAL

DATA EVALUATION REPORT

SULFURYL FLUORIDE

Study Type: Dermal Vapor Exposure in Rats

Study Title: Sulfuryl Fluoride: Four-Hour Dermal Vapor Exposure in Fischer 344 Rats

Prepared for:

Health Effects Division
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031-1207

Principal Reviewer	Jessica Kidwell Jessica Kidwell	2/11/92 Date
Independent Reviewer	Nancy McCarroll Nancy McCarroll	2/11/92 Date
QA/QC Manager	Sharon Segal Sharon Segal	2/11/92 Date

Contract Number: 68D10075
Work Assignment Number: 1-35
Clement Number: 91-127
Project Officer: James E. Scott

009393

EPA Reviewer: Stanley Gross, Ph.D.
Review Section II, Toxicology Branch I/HED

Signature: Stanley Gross
Date: 3/24/92

EPA Section Head: Joycelyn Stewart, Ph.D.
Review Section II, Toxicology Branch I/HED

Signature: Joycelyn Stewart
Date: 3/24/92

DATA EVALUATION REPORT

STUDY TYPE: Modified Guideline Series 81-2: Acute Dermal Toxicity Study in Rats

EPA IDENTIFICATION NUMBERS

Tox. Chem. Number:
MRID Number: 417120-01

TEST MATERIAL: Sulfuryl fluoride

SYNONYMS: VIKANE® gas fumigant

SPONSOR: DowElanco, Midland, MI

STUDY NUMBER: K-016399-036

TESTING FACILITY: The Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI

TITLE OF REPORT: Sulfuryl Fluoride: Four-Hour Dermal Vapor Exposure in Fischer 344 Rats

AUTHOR: G.J. Bradley, T.D. Landry, J.E. Battjes, and J.F. Quast

STUDY COMPLETED: November 16, 1990

CONCLUSIONS: The dermal vapor LC_{50} for sulfuryl fluoride in male and female rats is greater than 9599 ppm (40,315 mg/m^3).

ONE-LINER: The No-Observed-Effect Level (NOEL) for dermal exposure to sulfuryl fluoride vapor in rats is 9599 ppm (40,315 mg/m^3).

CORE CLASSIFICATION: This study is acceptable (modified guideline series 81-2).

TOXICITY CATEGORY: Not applicable

4

A. MATERIALS

1. Test Material

Compound: Sulfuryl fluoride (SO_2F_2)
Purity of material: 99.67%
Physical description: Colorless gas
Lot no.: 880329 752
Storage conditions: Not reported

2. Controls

Materials: None
Animals: None

3. Test Animals

Species: Rats
Strain: Fischer 344
Source: Charles River Breeding Laboratories, Inc., Kingston, NY
Receipt date: Not reported
Sex: Male and female
Numbers: 10 males, 10 females
Housing: Double
Age: 6-8 weeks at time of exposure
Weight: Preexposure: 101.2-122.9 g (males), 90.5-126.8 g (females)
Feeding: Feed and water ad libitum
Assignment: Computer-generated randomization

4. Exposure

Limit test:

Route of administration: Dermal vapor

Dose level: 987 ppm (5 males)
1013 ppm (5 females)
9599 ppm (5 animals/sex)

B. TEST PERFORMANCE

Prior to exposure, the dorsal surface of each rat was shaved with electric clippers.

Exposure Concentration

Groups of five male or five female rats were dermally exposed (body only) to 987 ppm and 1013 ppm of sulfuryl fluoride, respectively, for a single 4-hour period. Since no effects were noted from this exposure, another group of five rats/sex/dose group were dermally exposed to 9599 ppm for

4 hours. This concentration (9599 ppm) was reported to be approximately 10-fold greater than the whole-body inhalation LC_{50}.[1]

Chamber

A stainless steel and glass, 157-liter, Rochester-type chamber (50 cm x 50 cm x 50 cm) was used. The chamber was modified so that the heads of the rats protruded through an elastic dental dam, which served as a barrier between the test material and the breathing air for the rats. A ventilated enclosure (≈30 liters/minute) surrounded the protruding heads to allow monitoring of the air the animals were breathing. Chamber air was controlled by a system designed to maintain temperature and humidity at 22°C and 50%, respectively. Air flow through the chamber was maintained at approximately 30 liters per minute. Rats were dermally exposed to vapors of the test material and were housed individually to minimize crowding during the exposure period. A diagram of the exposure chamber was provided.

Vapor Generation

Sulfuryl fluoride vapors were generated by metering from a gas sampling bag made of SARAN® resin with an FMI pump (Fluid Metering Inc., Oyster Bay, NY) to a J-tube. Compressed air was mixed with the sulfuryl fluoride gas in the glass J-tube assembly to attain the desired chamber concentration.

Chamber Monitoring

Air flow through the chamber was determined with a precalibrated manometer prior to study initiation. Temperature, relative humidity, and air flow values were recorded every 30 minutes during the 4-hour exposure. The analytical concentration of sulfuryl fluoride in the chamber was measured at least once per hour with a MIRAN 1A infrared spectrophotometer. The breathing area of the rats was checked at least once per hour to determine if there was significant inhalation exposure to sulfuryl fluoride (minimum analytical sensitivity was <20 ppm). A distribution check of test material in the breathing zone was performed prior to exposure of the animals to the test material. Results showed that vapor concentrations in the four sampling ports ranged from 102% to 104% of the standard.

Observations

Animals were weighed and examined prior to test material exposure (day 1). All rats were weighed on test days 2, 4, 8, 11, and 15 during the 2-week postexposure period. Animals were observed during exposure and daily during the 2-week postexposure period. Fur, eyes, mucous membranes, and respiration were examined. Behavior pattern and nervous system activity

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[1]Miller, R.R., Calhoun, L.L., Keyes, D.G., and Kociba, R.J. 1980a. Sulfuryl Fluoride (VIKANE® fumigant): An LC_{50} Determination. Report of the Dow Chemical Company Toxicology Research Laboratory, Midland, MI.

were also assessed by observing for tremors, convulsions, salivation, lacrimation, diarrhea, lethargy, and other signs of altered central nervous system function.

All rats were subjected to gross necropsy on test day 15; brain and samples of clipped and unclipped skin were saved. Multiple sections of brain and clipped and unclipped skin from each animal in the 9599-ppm group were processed by routine histologic procedures. No gross pathologic observations were noted in any rats; therefore, no other tissues were microscopically examined.

C. RESULTS AND STUDY AUTHORS' CONCLUSIONS

Tables were presented for chamber atmosphere conditions during exposure, clinical observations, body weights, gross pathology, and histopathologic observations. Findings were as follows:

Analytical Determinations

Test atmospheres in the exposure chamber were reported to be 987±21, 1013±9, and 9599±142 ppm. Chamber temperature (23-24°C) and relative humidity (33-39%) were generally comparable for each exposure.

Animal Observations

Since no compound-related effects were noted in the five male and five female rats exposed to 987 ppm and 1013 ppm, respectively, an additional group of five rats/sex/dose were dermally exposed to 9599 ppm for 4 hours.

Animals in all groups survived the 4-hour exposure and the 14-day postexposure period. The majority of rats in all exposure groups exhibited chromodacryorrhea and fecal soiling. The study authors reported that these findings were related to the method of restraint during the exposure period.

Average body weights decreased slightly (<3%) from pretreatment values immediately following exposure to all concentrations of the test substance. The study author reported that this weight loss was not treatment related. Similar weight losses occurred during a preliminary assessment performed on rats in the chamber prior to the study. By day 4, all animals exceeded their pretreatment weights and continued to gain weight throughout the remainder of the study.

Gross pathological examinations of all animals were normal. Histopathologic examinations of brain and skin samples taken from animals exposed to 9599 ppm revealed no treatment-related lesions.

D. REVIEWERS' COMMENTS

Based on the results of this study, the dermal vapor LC_{50} of sulfuryl fluoride in rats is greater than 9599 ppm. No toxicity category was

7

assigned to this study because there is no corresponding category. Based on the observations and methods used, this study is acceptable.

One-Liner

Based on the results of this study, the NOEL for dermal exposure to sulfuryl fluoride vapor in rats is 9599 ppm (40,315 mg/m^3).

E. QUALITY ASSURANCE MEASURE

A signed Quality Assurance Statement, dated 11/16/90, was presented. A Good Laboratory Practice compliance statement was included.

F. CBI APPENDIX

CBI Materials and Methods, pp. 8-13.

8

VIKANE (Sulfuryl fluoride) Tof Review 009393

Page ____ is not included in this copy.

Pages 9 through 14 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

__✓__ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
