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

008247

JAN 29 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Sulfuryl Fluoride - Toxicology Data Submitted
Under MRID No. 416030-01
EPA-ID No. 078003

Chemical (Caswell) No.: 816A
RD Record No.: 268478
HED Project No.: 0-2050

FROM: Irving Mauer, Ph.D., Geneticist 01/25/91
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

TO: D. Mackey, PM 74
Reregistration Branch
Special Review and Reregistration Division (H7508C)

THRU: Karl P. Baetcke, Ph.D., Chief 1/26/91
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

Registrant: DowElanco, Indianapolis, IN

Request

Review and evaluate the following mutagenicity study performed by the Health and Environmental Sciences-Texas Center (TXT) of Dow Chemical, Freeport, TX;

Evaluation of Sulfuryl Fluoride in the Ames Salmonella/Mammalian-Microsome Bacterial Mutagenicity Assay, Study ID TXT:K-016399-037, dated August 17, 1990. (EPA MRID No. 416030-01.)

0001 M10

TB Conclusion

This study is judged ACCEPTABLE in demonstrating negative results in Ames testing up to toxic concentrations (30,000 ppm), with/without metabolic activation (rat liver S9).

(Detailed review attached to this memorandum.)

Attachment (DER)

CONSULTATION NOTE:

SUBJECTS: Sulfuryl fluoride Salmonella Ames test: Dow study TXT:K--16399-037.

TO: Irving Mauer, Toxicology Branch (H7509C)

FROM: Stanley Gross, Toxicology Branch (H7509C) 1/17/91

cc: Marion Copely, Toxicology Branch (H7509C)

Request: Was the exposure to SF adequate?

Comments:

1) Cultures of Salmonella were prepared and placed in a sealed desiccator jar. The air in the desiccator above the petri dishes was replaced with SF to expose the bacteria. Four concentrations in the air above the petri dishes were analyzed for SF but SF in the media itself was not measured. Therefore Dow did not measure the concentrations to which the bacteria were exposed.

2) If the toxicity to the bacteria was demonstrated, then the mutagenicity testing could be adequate. However, it is not possible to determine the concentrations of SF to which the bacteria were exposed based on the information provided (pages 7, 10, 11, 13 and 21).

SF-cnslt, January 17, 1991

Reviewed By: Irving Mauer, Ph.D., Geneticist 01/25/91
Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief 1/26/91
Toxicology Branch I - IRS (H7509C)

DATA EVALUATION RECORD 00824,

I. SUMMARY

MRID (Acc) No.: 416030-01
ID No.: 078003
RD Record No.: 268478
Caswell No.: 816A
Project No.: 0-2050

Study Type: Mutagenicity - Ames Test

Chemical: Sulfuryl fluoride

Synonym: Vikane Gas Fumigant

Sponsor: DowElanco, Indianapolis, IN

Testing Facility: Health and Environmental Sciences-Texas (TXT), Lake Jackson Research Center, Dow Chemical, Freeport, TX

Title of Report: Evaluation of Sulfuryl Fluoride in the Ames Salmonella/Mammalian Microsome Mutagenicity Assay.

Authors: B.B. Gollapudi, Y.E. Samson, and J.A. Zempel

Study Number: TXT:K-016399-037

Date of Issue: August 17, 1990

TB Conclusions:

Negative for inducing gene mutation in the battery of Ames bacterial tester strains of S. typhimurium exposed up to toxic concentrations (30,000 ppm), with/ without metabolic activation (rat liver S9).

Classification (Core-Grade) - ACCEPTABLE

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II. DETAILED REVIEW

A. Test Material - Sulfuryl fluoride (SO_2F_2) supplied by Dow Chemical

Description: Colorless gas
Batch (Lot): 874
Purity (%): 99.6% per supplier; tested at 96.5% ai with 3.5% air
Solvent/Carrier/Diluent: Sterile compressed air

B. Test Organism - Bacterial cultures

Species: Salmonella typhimurium LT2
Strains: TA98, TA100, TA1535, TA1537 (all his^-)
Source: Dr. Bruce N. Ames, UCal (Berkeley)

C. Study Design (Protocol) - This study was designed to assess the mutagenic potential of sulfuryl fluoride when administered in vitro to a battery of four his^- strains of Salmonella typhimurium, according to standardized procedures (referenced publications).

Statements of Quality Assurance measures (inspections/audits) as well as of adherence to Good Laboratory Practice (GLP) were both provided.

D. Procedures/Methods of Analysis - Following preliminary dose-selection testing (with only TA100 exposed to test article at 1000, 10,000, and 50,000 ppm), groups of triplicate cultures of the four Ames tester strains (characterized in Report Table 1) in open Petri dishes were each exposed for 4 hours to six concentrations of the gas in sealed desiccators modified for use as exposure chambers (Report Figure 1). After exposure, cultures were removed, covered, and reincubated for an additional 2 days. The test treatments were conducted both in the absence and presence of mammalian metabolic activation provided by commercially purchased hepatic microsomes from Sitek Labs (Rockville, MD)[1], plus NADP(H)-generating cofactors added just before use (as summarized in Report Table 2). In addition to sham-treated (compressed air only) and untreated cultures serving as negative controls,

[1]Rat liver homogenate (S9) prepared from adult Sprague-Dawley males pretreated with Aroclor 1254.

other groups of cultures were treated with strain-specific mutagens (listed in Report Table 3)[2] to serve as positive controls.

After the 2-day posttreatment incubation, all cultures were scored for revertant (his$^+$) colonies, either manually or by electronic counter (Artek 880). A test material is considered a bacterial mutagen in this system by these investigators if it induces a reproducible threefold plus increase in reversions at more than one (preferably sequential) concentration, when tested in the absence of overtly severe toxicity.

E. Results - Distribution and concentration of 100 ppm sulfuryl fluoride introduced into this type of modified dessicator was measured prior to the assay during a 1- to 5-hour exposure period, as follows (taken from Report Table 4):

Exposure Time (hr)	Location Inside Chamber	Observed Concentration* (uL/L)
1	Top	102 ± 6.0
1	Middle	94.2 ± 13.0
1	Bottom	95.6 ± 3.1
5	Bottom	87.0 + 4.6

*Mean of 3 samples per location

In preliminary cytotoxicity testing, the test material was severely toxic at 50,000 ppm (HDT), as evidenced by the absence of background bacterial lawn, accompanied by the production of "microcolonies" and a reduction in mean revertant count (Report Table 5). The next lower dose, 10,000 ppm, produced only minimal effects. Hence the highest dose chosen for the mutagenicity assay per se was 30,000 ppm, accompanied by five lower doses, namely: 10,000, 3000, 1000, 300, and 0 ppm (the last, untreated control).

[2]Non-activation: TA1535, TA100: Sodium azide (NaN_3, 25 ug/plate): TA98: 2-Nitrofluorene (2NF, 100 ug/plate); TA1537: ICR-191 (10 ug/plate).
Activation: For all strains, 2-anthramine (2AA, 3 ug/plate).

In independent repeat assays, the highest concentration, 30,000 ppm, produced slight to moderate toxicity, but at no concentration did sulfuryl fluoride induce consistent evidence of mutagenicity (Summary Report Tables 6 and 7--attached to this DER--constructed from Report Tables 9 through 16, representing individual plate counts). Sporadic increases of revertant frequency in SO_2F_2-treated cultures (i.e., small but greater than 3X the value among specifically dosed untreated negative controls) were recorded,* but discounted by the investigators because they were:

1. Within the overall range of untreated values under activation, namely 1-7; and/or,

2. Non-reproducible (between repeat assays); and/or,

3. Not dose-dependent (within assays); and/or,

4. Comparable increases were seen in sham-treated (compressed air) controls (0 ppm SO_2F_2).

By contrast, highly significant increases in revertants were found in all positive control cultures.

Hence, the investigators concluded that sulfuryl fluoride was not mutagenic in Ames testing, as performed in this lab.

F. TB Evaluation - ACCEPTABLE. This study was conducted according to adequate procedures under such control conditions (including analytical verification of the homogeneity of the test article concentration inside the exposure chambers) as to render the resulting negative response valid.

Attachments (Summary Report Tables 6 and 7)

*Activated TA1537 at 10,000 ppm (4 vs. 1, Table 7 Assay 2e).
Non-activated TA1535 at 300 ppm (Table 6).

ATTACHMENT - 1

Summary Data Tables

VIKANE (Sulfuryl fluoride) TX Review 008247

Page ____ is not included in this copy.

Pages 9 through 10 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

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____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

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