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

007300

JUN 30 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Azinphos-Methyl

Project No. 9-1345
TOX Chem No.: 374

FROM: Ray Landolt 6/6/89
Review Section I
Toxicology Branch II - Herbicide, Fungicide, and
Antimicrobial Support
Health Effects Division (H7509C)

TO: Dennis H. Edwards, Jr., PM 12
Insecticide-Rodenticide Branch
Registration Division (H7505C)

THRU: Mike Ioannou, Section Head J.M. Ioannou 6-20-89
Review Section I
Toxicology Branch II - Herbicide, Fungicide, and
Antimicrobial Support
Health Effects Division (H7509C)

and

Marcia van Gemert, Acting Chief
Toxicology Branch II - Herbicide, Fungicide, and
Antimicrobial Support
Health Effects Division (H7509C)

Registrant: Mobay Corporation, letter of April 7, 1989

Action Requested

Review a Dermal Sensitization Study in guinea pigs submitted in response to the Registration Guidance Document dated September 11, 1986.

Conclusion

Classification of Data - Guideline.

Positive for skin sensitization when tested by the Buehler Patch Test method at 12.5 % concentration during the induction phase followed by a challenge dose of 6.0%. A second challenge with a 0.6% concentration was comparable to the vehicle control response.

There is no evidence in the Toxicology Data File (No. 374) of a review of the Dermal Sensitization Study, Mobay Report No. 94697 (MRID No. 402553-02) cited in Mobay Corporation's letter of April 7, 1989.

Reviewed By: Ray Landolt 6/4/89
Section I, Toxicology Branch II - HFAS (H7509C)
Secondary Reviewer: Y. M. Ioannou 6/12/89
Section I, Toxicology Branch II - HFAS (H7509C)

007300

DATA EVALUATION REPORT

Study Type: Dermal Sensitization (81-6)
Project No.: 9-1345
Test Material: Azinphos-methyl (92.4%)
TOX Chem No.: 374
Synonyms: Guthion, E1582 Technical
MRID No.: 410644-01
Study Number: 98565
Study Date: 11/05/87
Sponsor: Mobay Corporation
Testing Facility: Bayer AG Fachbereich Toxikologie
Title of Report: Study of Skin Sensitization Effect on Guinea Pigs.
Author: K.G. Heimann

Conclusions:

1. Classification of Data - Guideline
2. Positive for skin sensitization when tested by the Buehler Patch Test method at 12.5% concentration during the induction phase followed by a challenge dose of 6.0%. A second challenge with a 0.6% concentration was comparable to the vehicle control response.

A. Method:

A modified method of "The Epidermal Patch Test Method of Buehler (Arch. Dermatol. 91:171-175 (1965)" was used.

1. Materials

   a. The technical E1582, formulated with Cremophor EL (2 % v/v) in sterile physiological saline solution, was applied at a constant volume of 0.5 mL during the induction and challenge phase. A hypoallergenic patch of the test material was placed on the shaven flank of each animal of the respective groups and secured in place for 6 hours with a Saniplast elastic wrap.

   b. Animals - Thirty-six SPF-bred guinea pigs, weighing between 309 to 373 g, were used in this study.

2. Study Design - Three groups of 12 animals per group were dosed at 12.5% (induction), 6.0% (first challenge) and 0.6% (second challenge).

   a. Epicutaneous Induction - Three epidermal inductions of 12.5% test material were applied to the left flank of 12 animals once a week for 3 weeks. Twelve control (group 1) animals were treated with the vehicle in the same manner.

   b. First Challenge - Five weeks after the start of induction, the first challenge of 6.0% was applied to the left flank of the test and control (group 1) animals. The right flank served as the vehicle control for comparison.

   c. Second Challenge - Seven weeks after the start of induction, the second challenge of 0.6% was applied to the left flank of the test and control (group 2) animals. The right flank served as the vehicle control for comparison.

3. Skin reactions were scored 48 and 72 hours after the wrap was removed. "The results were evaluated by subtracting the number of animals with an irritant reaction on the control side from the number of animals with an irritant reaction on the test compound side. This calculation was done both for the animals of the test compound group and for the animals of the control group. . . . Body weights were determined prior to the start of the experiment and weekly thereafter, as well as on Day 31 and Day 45."

4. "The sensitivity of this guinea pig strain was verified in a Magnusson-Kligman test using formaldehyde" (Bayer No. 13252, February 1, 1985). Formaldehyde induced a positive response in 7/20 animals when challenged with a concentration of 2.0 and 0.5%.

B. Results:

1. No signs of toxicity* or mortality were observed in the test or control groups except for "increased circulation in the hairless body parts" of a control group animal during days 8 to 10 of the induction phase.

2. A normal body weight gain was reported for the test and control groups during the experimental period.

3. Evaluation of Skin Reaction - Dermal application of a 12.5% concentration of azinphos-methyl by the Buehler Patch Test method induced skin sensitization in approximately 50 percent of the animals when challenged with a 6.0% concentration of azinphos-methyl. The second challenge with a 0.6% concentration of azinphos-methyl elicited in a mild reaction similar between the test and control response.

The following table from this report summarizes the results of this study.

First Challenge (Concentration: 6%)

Number of Animals with Skin Reactions

Test Compound Group (12 Animals)		Control Group 1 (12 Animals)	
Test Compound Patch	Control Patch	Test Compound Patch	Control Patch
6	1	2	2

*The application of 0.5 mL of a 12.5% concentration results in a total dose of 62.5 mg/animal. The average body weight of the 12 animals receiving the first induction dose was 0.347 kg for an approximate dermal application of 180 mg/kg once a week for 3 weeks.

Second Challenge (Concentration: 0.6%)

Number of Animals with Skin Reactions

Test Compound Group (12 Animals)		Control Group 2 (10 Animals)	
Test Compound Patch	Control Patch	Test Compound Patch	Control Patch
1	0	2	0