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TXR-2392

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

002392

6 DEC 1982

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Franklin Gee
Product Manager, No. 17
Registration Division (TS-767)

THRU: Christine F. Chaisson, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Methoprene; Zoecon RF 179 Methoprene Concentrate, An Insecticide For Formulation Use Only, EPA Registration No. 2724-288

Registrant:

Zoecon Industries
Dallas, Texas 75234

Action Requested:

1. Review and evaluation of materials submitted in complience with the Agency's requirements in connection with the Methoprene Registration Standard.

2. Ammended Registration

Recommendations:

The data submitted by the registrant support the registration of this product. However the label can not be approved until dermal sensitization data are submitted to the Agency.

Review

I. Acute Oral Toxicity

Text material:

Methoprene concentrate (~~13~~ 17% methoprene, ~~87~~ 83% methylene chloride), F-143-183-1, RD No. 8456, density is 1.2 g/ml.

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Testing Laboratory:

Elars Bioresearch Laboratories, Project No 1538D, June 27, 1980.

Test Animal:

Sprague-Dawley rats with an average body weight of 200-400 gms.

Procedure:

Test materials was administered at dosage levels of 2, 3, 3.4, 3.7, 4 and 5.1 g/kg. Five males and five femals were used for each dose level. The rats were observed daily for 14 days for toxic signs and body weight was recorded once a week. All rats including those succumbed during the study were subject to necropsy.

Results:

1. Mortalities were 10%, 0%, 50%, 60%, 70%, and 70% for the dosage levels of 2, 3, 3.4, 3.7, 4 and 5.1 g/kg respectively. The LD_50 was determined to be 3.73 g/kg (P-0.95), the chemical can be classified as Tox. Category III.

2. Small number of animals lost weight at the middle two dosage levels, however loss of body weight was obvious in the highest two dosage levels especially in females.

3. Animals of the 2.0 g/kg group showed homorrhagic lungs and congested kidneys. Dose levels of 3 g/kg or higher, caused ataxia, lethargy, conclusion, shallow respiration, and slight diarrhea. Animals died in day 2 from the 3.4/kg or higher groups showed hemorrhagic stomachs, kidneys, and livers. In addition the lungs were congested, and the non-glandular esophageal part of the stomach had numerous adhesions, some of which involved the surrounding tissues, the spleen and the liver. The mucosal surface of the stomach appeared white and rough according to the report.

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Core Classification:

Core-minimum

Acute Dermal Toxicity:

Test Materials:

Methopren Concentrate (17% methoprene, 83% methylene chloride), F-143-183-1, RD No. 8456, liquid with a density of 1.2 g/ml.

Testing Laboratory:

Elars Bioresearch Laboratories, Project No. 1538-C, June 27, 1980.

Test Animal:

New Zealand white rabbits, approximately 2-3 kg.

Procedure:

The material was tested at two dose levels 2.1 g/kg and 5.1 g/kg, and ten animals (5 males and 5 females) were used for each dose level. A control was also included. Ten percent of the total body surface area. The test material was applied to the abraded test sites in a single dose in a guage sponge backed with plastic wrap. The test material remained in contact with the body for 24 hours after which the skin was wiped out. The animals were observed for toxic signs and mortality for 14 days. All animals were subjected to necropsy. Tissues with abnormal appearance were taken for histopathologic examination.

Results:

According to the author, no abnormalities were noted in the low dose group during the observation period. Necropsy, however, showed inflamation of stomach linings in several animals, and slightly congested kidneys in one animal.

The high does group showed signs of skin irritation, including erythemea, edema, and skin discoloration. Gross necropsy of this group revealed evidence of gross toxicity of the kidneys of several animals. The acute dermal toxicity was considered to be greater than 5.1 g/kg under test conditions. The chemical may be placed in Tox. Cat. III.

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Core Classification:

Core - Minimum

Primary Dermal Irritation:

Test Chemicals:

Methoprene Concentrate (17% methoprene, 83% methylene chloride), F-143-183-1, RD No. 8456

Testing Laboratory:

Elars Biorearch Laboratory, Project No. 1538-A, June 25, 1980

Test Animal:

New Zealand White Rabbits

Procedure:

The back of the animals (3 males and 3 females) were clipped free of hair in the area extended from the shoulders to the hips. Four test sites were designated for each animal. Two sites were abraded on each animal. A dose of test material equal to 0.5 ml. was applied to each site using one-inch square gauze patches backed by plastic wrap. The test material was kept in contact with the skin for 24 hours after which the test site was wiped to remove excess test material. At 24 and 72 hours and 4 through 21 days post dose. animals were observed and dermal irritation signs were scored..

Results:

At 24 hours, slight edema edema and moderate erythma were observed in the intact and abraded skin. At 72 hours, slight to moderate erythma and edema were seen in 5 out of six test animals. Moderate to severe erythema persisted for 13 days in only one animal Edema was not observed after 10 days. The scores for abraded skin was always higher than these for the intact skin. The author concluded that this material is to be considered mildly irritating, with primary irritating score of 2.12.

Core Classification:

Core-minimum.

Primary Eye Irritation:

Test Material:

Methoprene Concentrate (17% methoprene, 83% methylene chloride), Lot3 No. F-143-183-1, RD No. 8456.

Testing Laboratory:

Elars Bioresearch Laboratories, Project No. 1538-B, May 22, 1980.

Test Animals:

Adult New Zealand white rabbits.

Procedure:

A dose of 0.1 ml of the undiluted test substance was placed on the everted lower lid of the right eye of each of the nine animals used (5 males, 4 females). The eyes of three rabbits (2 males, one female) were flused for one minute with warm water 30 seconds after application. The untreated left eye of each rabbit served as a control. Scoring of ocular lesions was done at 24, 48, and 72 hours and then at 4, 7, 10, 13, 16, 19 and 22 days, according to Draize (1959).

Results:

All rabbits showed varying degrees of opacity, with four of them recovered by day 7. Three rabbits had irreversible corneal damage. Eight rabbits exhibited iridial irritation that gradually cleared by day 10. Varying degree of conjunctival irritation were seen in all rabbits and gradually cleared by day 22. The rinsed eyes generally scored less than the unrinsed group at all times.

The chemcial is considered potential eye irritant with a 24 hours average of 51.44, and can be classified as Tox. Category I for eye irritation.

Core Classification:

Core minimum.

Acute Inhalation Toxicity:

The registrant claims that worker inhalation exposure to respirable mist, fog, and/or aerosol prticulates from normal manufacturing use and handling of this product will be non-existent. However, based on the physical chemical properties of the solvent system in the product, methylene chloride, it is possible for workers to be exposed to the muthylene chloride vapors.

The registrant provided calculation and figures indicating that essentially no methoprene will be in the vapor was calculated to be 3.2×10^{-7}%. Based on the above facts, inhalation studies required on this manufacturing use product to determine label precautions and workers safety should be done on the methylene chloride and the label will reflect a warning signal based on the LC_{50} value for the solvent rather than the active ingredient, which is found to be 14,000 ppm in mice or 50 mg/L (according to the registrant). Furthermore, the Safety and Health Administration has set a standard for methylene chloride in workplace air at 500 ppm. (HEW Publications No. (NIOSH) 76-183.

With this consideration in mind we therefore concluded that more testing is not required to assess the human hazard, and the warning signal will be based on the LC_{50} for methylene chloride and therefore the product can be placed in Tox. Category IV.

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