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

MAR 15 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE:

SUBJECT: Request To Review An Acute Inhalation Study Using KELTHANE.

TO: Jay Ellenberger, PM #12
Registration Division (TS-767)

FROM: Carolyn Gregorio, Toxiocologist CG 3-13-85
Toxicology Branch/ HED (TS-769)

THRU: Clint Skinner, Ph.D. C.S. 3-14-85
Section Head,
and
Theodore M. Farber, Ph.D.
Branch Chief,
Toxicology Branch/ HED (TS-769)

Chemical: KELTHANE, dicofol

Caswell No.: 93

Petitioner: Makhtesim-Agan (America)

Petition No.: 11603-26

Accession No.: 256514

Action Requested: The Petitioner has submitted the following study for review: Rosenfeld,G. 4-Hour Acute Aerosol Inhalation Toxicity In Rats. Sponsor: Makhteshim-Agan (America). Study No. 1176C. Conducted by Cosmopolitan Safety Evaluation, Inc. CSE #S1429-25. January 8, 1985.

Conclusion: The submitted study is sufficient to establish the acute inhalation LC50 in male and female Sprague-Dawley rats is greater than 4.2 mg/liter; Toxicity Category III.

Chemical: Kelthane, Dicofol, Acarin

Caswell No.: 93

Formulation: Technical (85% Active Ingredient)

Citation: Rosenfeld, G. 4-Hour Acute Aerosol Inhalation Toxicity Study In Rats. Sponsor is Makhteshim-Agan (America) Inc., Study No. 1176C. Conducted by Cosmopolitan Safety Evaluation, Inc. CSE # S1429-25. January 8, 1985

Petitioner: Makhtesim-Agan (America)

Accession No.: 256514

Reviewed By: Carolyn Gregorio, Toxicologist 3-12-85
Toxicology Branch/HED (TS-769)

Secondary Review: Clint Skinner, Ph.D. C.S. 3-14-85
Section Head
Toxicology Branch/HED (TS-769)

Material and Methods: "The test article, MITIGAN TECH 85% (dicofol), a brown transparent semi-solid, was tested for acute inhalation toxicity in conformity with the Health Effects Test Guidelines, August 1982 at a dose concentration of 10.2 mg/l. The test article as supplied was unsuited to nebulization and was diluted using 140 g test article q.s. to 280 g xylene to form a 50% w/w concentration. This preparation was agitated in the nebulizer container until uniform and was maintained on the stir plate during dosing.

"Five male and five female healthy young adult rats (Sprague-Dawley derived) were exposed for 4 hours to an atmosphere containing a nominal concentration of 10.2 mg of the diluted test article per liter of air, which was the maximum attainable concentration of aerodynamic particles. The actual concentration of diluted test article measured gravimetrically twice during exposure was 4.15 mg/l and 4.25 mg/l equivalent to a mean concentration of 4.2 mg of the test article per liter of air. The mass median diameter of the particles was 0.6 microns at approximately 1-1/2 hours 0.6 microns at 3 hours. A similar control group which did not receive test article or diluent was also used."

Animals were observed for body weight changes, clinical signs of toxicity and mortality. Gross necropsy was performed on all animals.

Results:

Clinical Signs: "During exposure there was reduced response to sound and, later, incoordination. [These signs were attributed to the vehicle.]" After return to the cages clinical signs were ataxia, (4/5 males; 2/5 females) prostration (1/5 males; 4/5 females) and lacrimation (1/5 males; 4/5 females). The rats "recovered from ataxia and prostration within 5 hours and the rest recovered overnight; chromorhinorrhea and sporadic perineal staining lasted until Day 4 except in one male found dead on Day 5. Surviving rats appeared normal from Day 5 to Day 14."

Body Weight: "Rats exposed to the test article lost weight in the first 2 days after exposure then gained weight, but the overall gain was less than in controls."

Mortality: "One male was found dead on morning of Day 5. This was the only death."

Pathology: "At gross necropsy, no pathognomonic signs in survivors to term. The rat which died had edematous lungs and slight intestinal congestion."

Conclusion: Based on the conditions of this study, Mitigan Technical as a 50% w/w solution in xylene, the acute inhalation for male and female Sprague-Dawley rats is greater than 4.2 mg/liter.

Toxicity Category: III

Core Classification: Minimum.