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

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JL 31 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA File Symbol 11273-LT
Ditek 80DF Fungicide

FROM: Mary L. Waller
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

MLW E 8/7/86

TO: Henry M. Jacoby, PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: Pylon Corporation
525 California Avenue
Palo Alto, CA 94304

ACTIVE INGREDIENT:
Thiophanate-methyl(dimethyl[(1,2-phenylene)-bis
(iminocarbonothioyl)]-bis[carbamate]) 80.0%
INERT INGREDIENTS. 20.0%

BACKGROUND:

The applicant has submitted acute oral, acute dermal, primary skin irritation, and primary eye irritation studies. The studies were conducted by Biosearch Incorporated. The data Accession Number is 263488. The method of support is owner-submission.

RECOMMENDATION:

FHB/TSS finds the data acceptable to support registration. The signal word is "WARNING" based on the primary eye irritation study. The applicant must submit acute inhalation toxicity and dermal sensitization studies.

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005998

The Product Manager should inform the registrant that in future primary skin irritation studies, when testing solids (which may be pulverized, if necessary), the test substance should be moistened sufficiently with water, or, where necessary, a suitable vehicle, to ensure good contact with the skin. When vehicles are used, the influence of the vehicle on irritation of the skin should be taken into account.

LABELING:

1. The signal word must be changed from "CAUTION" to "WARNING."

2. The heading Precautionary Statements should appear immediately above the subheading "Hazards to Humans and Domestic Animals."

3. Delete the following sentences from the precautionary statements and place them under the Directions for Use: "Do not contaminate feed or food. Keep children and pets out of treated areas until material is completely dry."

4. Revise and reorder precautionary statements as follows:

   Causes substantial but temporary eye injury. Harmful if swallowed, inhaled, or absorbed through skin. Do not get in eyes or on clothing. Wear goggles, face shield, or safety glasses. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.

5. Place the Storage and Disposal heading and information under the Directions for Use. The Storage and Disposal instructions should be placed directly under the Misuse Statement or it should be placed at the end of the Directions for Use.

6. The Statements of Practical Treatment or First Aid instructions should be organized so that the various exposure routes of greater hazard requiring the most urgent treatment are listed first. Therefore, the statements should be reordered and revised as follows:

   If in Eyes: Flush with plenty of water. Call a physician.

If Swallowed: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger, or, if available, by administering syrup of ipecac. Do not induce vomiting or give anything by mouth to an unconscious person.

If on Skin: Wash immediately with soap and water.

REVIEW:

(1) Acute Oral Toxicity Study: Biosearch Incorporated; Project No. 86-4968A; April 10, 1986.

PROCEDURE:

Groups of five male and five female albino rats were administered by gavage a single oral dose of test material as follows: five groups of females (5/group) received either 2.51, 3.16, 3.98, 4.47, or 5.00 g/kg of 25% w/v suspension of test material in deionized water; four groups of males (5/group) received either 5.00, 5.62, or 6.31 g/kg of 25% w/v suspension of test material in deionized water, and three groups of males (5/group) received either 7.94, 10.00, or 12.60 g/kg of 50% w/v suspension of test material in deionized water. Animals were observed frequently on the day of dosing and twice per day thereafter for 14 days. Observations were conducted once/day on weekends and holidays. All animals were necropsied at study conclusion.

RESULTS:

No deaths occurred at 5.00, 5.62, and 7.94 g/kg in the males and at 2.51 and 3.16 g/kg in the females. At 6.31 and 10.0 g/kg, 1/5 males died. At 12.6 g/kg, 3/5 males died. At 3.98 g/kg, 1/5 females died. At 4.47 g/kg, 2/5 females died. At 5.00 g/kg, 5/5 females died. The LD_{50} for males was reported to be 13.20 g/kg with 95% confidence limits of 9.12 to 19.11 g/kg. The LD_{50} for females was reported to be 4.42 g/kg with 95% confidence limits of 3.90 to 5.01 g/kg.

Toxic symptoms included hypoactive state, tremors, increased responsiveness to external stimuli, convulsions, and comatose condition. Gross necropsy revealed pale kidneys, congested lungs, distended stomach, tan liquid in gastro-intestinal tract, nasal discharge, and stained genital area.

005998

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(2) Acute Dermal Toxicity Study: Biosearch Incorporated; Project No. 86-4968A; April 10, 1986.

PROCEDURE:

Five male and five female New Zealand White rabbits each received 5000 mg/kg of test material moistened with 5 ml of physiological saline. The dose of moistened test material was applied to the previously shaven backs of each animal under occlusive wrap. After 24 hours of exposure, the wrap was removed and the remaining test material was removed. Animals were observed frequently on day of dosing and twice/day thereafter for 14 days (observed once/day on weekends and holidays). Body weights were measured prior to dosing, and at 7 and 14 days. All animals were submitted for gross necropsy.

RESULTS:

No deaths occurred. The dermal LD_{50} was reported to be > 5000 mg/kg. Toxic symptoms included mild erythema and edema in the males which cleared by day 4 and mild erythema and edema in the females which cleared by 24 hours, nasal discharge, diarrhea, and loss of body weights. Gross necropsy revealed liquid in the gastrointestinal tract of 1/5 females and clear nodules on the surface of the kidneys in 1/5 females.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category IV - CAUTION.

(3) Primary Skin Irritation Study: Biosearch Incorporated; Project No. 86-4968A; April 10, 1986.

PROCEDURE:

Six New Zealand White rabbits each received 0.5 g of test material applied to a previously shaven test site on the animals' backs. The test material was held in place with semiocclusive wrap for 4 hours. Adjacent untreated areas of skin were covered with wrap and served as a control. After removal of wrap the test sites were washed with deionized water. Skin irritation at the test sites were scored within 30 to 60 minutes after wrap removal and at 24, 48, and 72 hours.

RESULTS:

At 30 to 60 minutes, 1/6 animals exhibited very slight erythema which persisted through to 24-hour reading and was cleared by the 48-hour reading. The primary irritation score was 0.09.

STUDY CLASSIFICATION:

Core Guideline Data. See comments under Recommendation.

TOXICITY CATEGORY: Category IV - CAUTION.

(4) Primary Eye Irritation Study: Biosearch Incorporated; Project No. 86-4968A; April 10, 1986.

PROCEDURE:

Six New Zealand White rabbits each received 0.1 g of test material which was placed in one eye. The other untreated eye of each animal served as a control. The treated eyes were examined and eye irritation scored at 1 hour, and at 1, 2, 3, 4, 7, 14, and 21 days.

RESULTS:

Eye irritation was scored as follows: at 24 hours, conjunctivae redness (5/6 = 1), chemosis (5/6 = 1) and discharge (2/6 = 1); at 7 days, conjunctivae redness (4/6 = 1) and discharge (1/6 = 1); at 14 days, conjunctivae redness (2/6 = 1) and discharge (1/6 = 1); and at 21 days, conjunctivae redness (1/6 = 1).

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category II - WARNING.

89252:Waller:CBI-A:KENCO:8/5/86:8/13/86:dej:LMF

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Thiophanate-methyl tox review

Page _____ is not included in this copy.

Pages 7 through 8 are not included in this copy.

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 product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

X A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

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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.
