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TOX-5/87

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

005437

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: June 27, 1985

SUBJECT: EPA File Symbol: 10182-EUP-GO
Paclobutrazol

FROM: Deloris F. Graham
FHB/TSS
Registration Division (TS-767C)

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767C)

Applicant: ICI Americas, Inc.
Agricultural Chemicals Division
Concord Pike and New Murphy Road
Wilmington, DE 19897

Active Ingredient:
(2RS, 3RS)-1-(4-chlorophenyl)-4,
4-dimethyl-2-(1H-1,2,4-triazol-1-yl
pentan-3-ol 22.94%
Inert ingredients 77.06%

Background:

Submitted Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation, Primary Skin Irritation, and Dermal Sensitization Studies. Studies conducted by Imperial Chemical Industries PLC, Central Toxicology Laboratory, Alderly Park, Macclesfield, Cheshire, UK. Data under Accession Number 257548. Method of support not indicated.

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Recommendations:

1. FHB/TSS finds all studies except Acute Oral acceptable to support conditional registration of this product. In the Acute Oral the appropriate toxicity category could not be accurately determined until acceptable LD_{50} for male rats are submitted.

2. It appears the appropriate signal word is CAUTION, however, this may change upon submission of acute oral information requested.

Label:

1. The statement "Keep Out of Reach of Children" and the signal word should precede active ingredient statement.

2. Additional label precautions may be necessary upon submission of acute oral information requested.

Review:

1. Acute Oral Toxicity Study: ICI PLC, Central Toxicology Lab.; Report No. CTL/P/872; August 4, 1983.

Procedure:

Seven groups consisting of five male and five female rats each received one of the following doses: 0.5, 1.0, 2.5, 4.0, 5.0, 7.5, or 10.0 ml/kg of the test material orally. Observations made frequently on day of dosing, then daily thereafter up to 15 days posttreatment. Necropsy performed on all surviving animals.

Results:

At 1.0 ml/kg, 1/5 M and 2/5 F died; at 2.5 ml/kg, 3/5 M and 2/5 F died; at 4.0 ml/kg, 1/5 M and 5/5 F died; at 5.0 ml/kg, 2/5 M and 4/5 F died; at 7.5 ml/kg, 0/5 M and 3/5 F died; at 10.0 ml/kg, 3/5 M and 5/5 F died.

Clinical signs reported included activity decrease, abdominal tone decreased, ptosis both eyelids, comatosed, dehydrated, hypothermia, piloerections, scouring, sides pinched in, hair loss, stains around snout, upward curvature of spine, corneal reflex (loss of), loss of righting reflex, decreased breathing rate, increased breathing depth, loss of stability, chromodacryorrhea, lachrymation, stained around mouth, urinary incontinence, labored breathing.

Necropsy report revealed very pale colored livers and kidneys.

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LD_{50} for females reported to be 2.14 ml/kg (2.31 g/kg) with 95 percent confidence limits between 0.85 and 3.73 ml/kg. Due to the distribution of observed mortalities in male the LD_{50} could not be determined.

Study Classification:

Core Supplementary Data. The toxicity category cannot be accurately determined until LD_{50} for males is submitted.

2. Acute Dermal Toxicity Study: ICI PLC, Central Toxicology Lab.; Report No. CTL/P/872; August 4, 1983.

Procedure:

Five male and five female rats received 4.0 ml/kg of the test material at intact skin site under occlusive wrap for 24-hour exposure. Observations made for 2 to 4 hours after application and daily thereafter up to day 15. Necropsy performed on all animals.

Results:

No mortalities reported. Clinical signs reported chromodacryorrhea, urinary incontinence, desquamation, skin eruptions, scouring, stains around mouth/snout. No abnormalities reported at necropsy. LD_{50} reported to be greater than 4.0 ml/kg (4.35 g/kg).

Study Classification:

Core Guideline Data

Toxicity Category:

III-CAUTION

3. Primary Skin Irritation Study: ICI PLC, Central Toxicology Lab; Report No. CTL/P/872; August 4, 1983.

Procedure:

Six rabbits received 0.5 ml of the test material under occlusive wrap for 4-hour exposure. Observations made at 1, 20, 48, and 68 hours after treatment.

Results:

At one hour, 5/6 had slight erythema and 4/6 slight to well-defined edema at 20 hours, 2/6 had erythema and edema. However, irritation had cleared at 68 hours.

Study Classification:

Core Guideline Data

Toxicity Category:

IV-CAUTION

4. Eye Irritation Study: ICI PLC, Central Toxicology Lab.; Report Co. CTL/P/872; August 4, 1983.

Procedure:

Six rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed with lukewarm tapwater 30 to 60 seconds after treatment. Observations made through 7 days posttreatment.

Results:

At 1 to 2 hours, 3/3 unwashed and 3/3 washed had conjuctive irritation (3/3 unwashed had cumulative score of 8.0 and 3/3 washed score of 3.3). Irritation cleared by day 1.

Study Classification:

Core Guideline Data

Toxicity Category:

IV-CAUTION

5. Dermal Sensitization Study: ICI PLC Central Toxicology Laboratory; Report No. CTL/P/1109; August 26, 1984.

Procedure:

Twenty male guinea pigs received 0.4 ml topical application of the test material under occlusive wrap for 6-hour exposure once a week for 3 weeks during induction phase. Two weeks after final induction phase application, a 0.2 ml challenge dose was applied. Observations made at 24 and 48 hours after application. A group of 10 male guinea pigs were treated in manner to previously mentioned group except no test material applied until challenge dose, these animals served as control group.

Results:

"One test animal died prior to challenge application, but it was not thought to be compound related." No irritation reported in test or control group. Therefore it was concluded that this product does not elicit a sensitizing response.

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Study Classification:

Core Guideline Data

Toxicity Category:

Non-sensitizing

6. Acute Inhalation Toxicity Study: ICI PLC Central Toxicology Lab.; RT No. CTL/P/1223; January 30, 1985.

Procedure:

Five male and five female rats were exposed nose only ~~for~~ to a 250 mg/m^3 maximum concentration that could be generated. 22.5 to 34 percent of product contained respirable particles (< 2.5 µm aerodynamic equivalent diameter). Average room temperature was 21 ± 2 °C and relative humidity 40 to 70 percent. Observation made frequently during exposure then daily for 14 days post-exposure. Necropsy performed on all animals. A control group treated in similar manner as previous group except exposed to air only.

Results:

No mortalities reported. Clinical signs reported included red stains around nose, chromodacryorrhea, wet fur, reduced response to sound, hunched posture, piloerection, stains around the nose, stained coat seen in both test and control animals; absence of pinna reflex, reduced righting reflex, subdued behavior, abnormal respiratory noise and single incidences, reduced foot withdrawal reflex, lachrymation noted in test group. Necropsy report revealed kidney: slight pelvic dilation: LC_{50} reported to be greater than 250 mg/m^3.

Study Classification:

Core Guideline Data

Toxicity Category:

IV-CAUTION

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RD/FRB:JOB-96304:Graham:CBI-10:Kendrick:898-1270:7/3/85:Del.7/16/85:lc

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