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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

APR 20 1988

SUBJECT: EPA Registration Number 10182-119
Prelude Herbicide

FROM: Mary L. Waller
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C) mlw 5/4/88 E 5/4/88

TO: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: ICI Americas, Inc.
Agricultural Products
Concord Pike & New Murphy Road
Wilmington, DE 19897

ACTIVE INGREDIENTS:

| | |
|---|---|
| Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridium dichloride) | 7.86% |
| Linuron | 2.84% |
| 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide | 22.75% |
| INERT INGREDIENTS: | 66.55% |

BACKGROUND:

The registrant has submitted a revised acute oral toxicity study which was previously reviewed on 4-27-87. The study was conducted by ICI Central Toxicology Laboratory. The MRID number is 404006-01. The registrant has also submitted an acute dermal toxicity study as requested by the TSS review of 4-27-87. The study was conducted by Food & Drug Research Laboratories, Inc. The registrant has also requested a waiver of the primary eye irritation study. The method of support was not indicated.

RECOMMENDATION:

FHB/TSS findings are as follows:

1. The acute oral and acute dermal toxicity studies are acceptable. Regarding the acute oral, the registrant has indicated that the formulation was tested and not the active ingredients.

2. The primary eye irritation study is waived based on the fact that the product is a severe dermal irritant. See TSS review of 4-27-87.

3. The signal word is "DANGER" based on the 4-27-87 TSS review of the acute inhalation toxicity study.

LABELING:

1. All Statements of Practical Treatment for routes of exposure falling in Toxicity Category I (inhalation & eye) must appear on the front panel of the label and must be grouped with the signal word and child hazard warning.

2. Move the "NOTE TO PHYSICIAN" out of the Statement of Practical Treatment. The "NOTE TO PHYSICIAN" must appear near the Statement of Practical Treatment but must be clearly distinguished from it.

3. Add the following sentence to the Statement of Practical Treatment for oral exposure "Do not induce vomiting or give anything by mouth to an unconscious person."

4. Revise Statements of Practical Treatment for skin, eye and inhalation exposures as follows:

   "SKIN CONTACT: Wash with plenty of water. Get medical attention.

   INHALATION: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth to mouth. Get medical attention.

   EYE CONTACT: Flush eyes with plenty of water. Call a physician."

5. The Precautionary Statements should be revised to read as follows:

"Causes irreversible eye damage. Fatal if inhaled. Harmful or fatal if swallowed or absorbed through skin. Do not breathe mist. Do not get in eyes, on skin or on clothing. Wear a mask or pesticide respirator jointly approved by the Mining Enforcement and Safety Administration and the National Institute for Occupational Safety and Health. Wear goggles, a face shield or safety glasses. Wear protective clothing and rubber gloves. Wash thoroughly with soap and water after handling and before eating or smoking. Remove contaminated clothing and wash before reuse. This product may cause an allergic skin reaction."

6. Supplemental labeling must have the same Statements of Practical Treatment and Precautionary Statements as recommended above.

REVIEW:

(1) Acute Oral Toxicity Study: ICI Central Toxicology Laboratory; I.D. CTL/P/1664 (second revision); MRID No. 404006-01; 7-21-87.

PROCEDURE:

Three groups of five male and five female albino rats were each administered by gavage a single oral dose of either 800, 1200, or 2400 mg/kg of test material suspended in deionized water. Animals were observed frequently on day of dosing and once daily thereafter for 15 days. Animals were weighed prior to exposure and on days 3, 8 and 15. Animals were necropsied at study conclusion.

RESULTS:

At 800 mg/kg, 1/5 females died. At 1200 mg/kg, 2/5 males and 2/5 females died. At 2400 mg/kg, 5/5 males and 5/5 females died. The $LD_{50}$ for males was reported to be 1362 (800-2400) mg/kg. The $LD_{50}$ for females was reported to be 1189 (749-3214) mg/kg.

Toxic symptoms observed were upward curvature of the spine, sides pinched in, stains around nose, signs of salivation, piloerection, increased breathing rate, chromodacryorrhea, signs of urinary incontinence, dehydration, and diarrhea. Gross necropsy revealed one male with congested lungs.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: Category III - CAUTION

(2) Acute Dermal Toxicity Study: Food & Drug Research Laboratories, Inc., FDRL Study no. 9469; MRID no. 404006-2; 7-28-87.

PROCEDURE:

Five groups of five male and five female New Zealand white rabbits were clipped free of fur on the back. Twenty-four hours later, each group received one of the following doses of test material as a topical application: 400, 557, 775, 1078, or 1500 mg/kg. The test site was covered with occlusive wrap for 24 hours of exposure. Animals were placed in collars during exposure. After exposure, the wrap and residual test material were removed. Animals were observed frequently on day of dosing and twice daily thereafter for 15 days. Animals were weighed prior to exposure and on days 8 and 15 or upon discovery of death. Animals were necropsied.

RESULTS:

No deaths occurred at 400 mg/kg. At 557 mg/kg, 1/5 females died. At 775 mg/kg, 2/5 males and 5/5 females died. At 1078 mg/kg, 4/5 males and 3/5 females died. At 1500 mg/kg, 3/5 males and 5/5 females died. The $LD_{50}$ for males was reported to be 1028 (677-1378) mg/kg. The $LD_{50}$ for females was reported to be 700 (467-933) mg/kg.

Toxic symptoms observed were anorexia, ataxia, decreased activity, nasal discharge, respiratory irregularity, salivation, diarrhea or soft stool, lacrimation and tremors. Gross necropsy revealed bladder filled with red fluid; enlarged kidneys; blanched, darkened or mottled liver; and reddened lungs.

STUDY CLASSIFICATION: Core Guideline Data

TY CATEGORY: Category II - WARNING