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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

APR 11 1988

SUBJECT: EPA Registration Number 5481-144
Technical Isopropyl Ester of 2,4-D

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

TO: Richard F. Mountfort, PM 23
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: Amvac Corporation
4100 E. Washington Blvd.
Los Angeles, CA 90023

ACTIVE INGREDIENT:
Isopropyl ester of 2,4-dichlorophenoxy-acetic acid 93.0%
INERT INGREDIENTS: 7.0%

BACKGROUND:

The registrant has submitted an acute oral, acute dermal, acute inhalation, primary skin irritation, primary eye irritation and dermal sensitization study. The acute oral and acute dermal toxicity studies were conducted by Northview Pacific Laboratories, Inc. The data accession number is 253099. The remainder of the studies were conducted by Stillmeadow, Inc. The MRID Numbers are 403527-01 through -04. The method of support was not indicated.

RECOMMENDATION:

FHB/TSS finds the studies acceptable to support registration of 5481-144. The signal word is "WARNING" based on the acute oral toxicity study.

When conducting future acute oral and acute dermal toxicity studies, the registrant should be sure to submit the test methods specific for the study and not the test protocols.

LABELING:

1. Change the signal word on the front and side panel to "WARNING."

2. Add the following to the Statement of Practical Treatment:

   IF INHALED: Removed victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

3. Revise Precautionary Statements as follows:

   May be fatal if swallowed. Harmful if absorbed through skin or inhaled. Causes eye irritation. Avoid contact with skin, eyes, or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling and before eating or smoking. Remove contaminated clothing and wash before reuse.

REVIEW:

(1) Acute Oral Toxicity Study: Northview Pacific Laboratories, Inc.; NVP No. X2J033; accession number 253099; 2-3-83.

PROCEDURE:

Six groups of 5 male and 5 female Sprague-Dawley rats were administered by gavage either 250, 350, 420, 500, 630 or 700 mg/kg of test material. Animals were observed for 14 days. Animals were necropsied.

RESULTS:

No deaths occurred at 250 mg/kg. At 350 mg/kg, 1/5 males and 1/5 females died. At 420 mg/kg, 2/5 males and 3/5 females died. At 500 mg/kg, 2/5 males and 4/5 females died. At 630 mg/kg, 1/5 males and 4/5 females died. At 700 mg/kg, 3/5 males and 4/5 females died. The LD_{50} for males was reported to be 640 (500-819) mg/kg. The LD_{50} for females was reported to be 440 (275-704) mg/kg.

Toxic symptoms observed were impaired motor responses, hemorhagging from nose and eyes, weight loss, scruffy coat. Gross necropsy revealed hepatotoxicity, discoloration of the kidneys and pulmonary edema.

STUDY CLASSIFICATION:

Core Minimum Data - See comments under Recommendation.

TOXICITY CATEGORY: Category II - WARNING

(2) Acute Dermal Toxicity Study: Northview Pacific Laboratories, Inc.; NVP No. X2J033; accession number 253099; 2-3-83.

PROCEDURE:

Five male and five female New Zealand white rabbits were administered a topical application of 2000 mg/kg of test material to a previously shaven test site. The test sites were covered with occlusive wrap for 24 hours of exposure. Animals were observed for 14 days. Animals were necropsied.

RESULTS:

No deaths occurred. No toxic symptoms were observed. Gross necropsy revealed discolored kidneys and respiratory congestion. Since no deaths occurred during the study, it can be assumed that the LD_{50} is >2000 mg/kg.

STUDY CLASSIFICATION:

Core Minimum Data - See comments under Recommendation.

TOXICITY CATEGORY: Category III - CAUTION

(3) Acute Inhalation Toxicity Study: Stillmeadow, Inc.; Project No. 4377-86; MRID No. 403527-01; 10-15-86.

PROCEDURE:

Five male and five female albino rats were exposed for 4 hours in a 200 L stainless steel dynamic flow inhalation chamber to a mean analytically determined concentration of 4.97 mg/L of test material. Animals were observed frequently on day of dosing and once daily thereafter for 14 days. Body weights were recorded prior to exposure and on days 7 and 14 or upon discovery of death. Animals were necropsied.

RESULTS:

1/5 females died. The LC_{50} was reported to be > 4.97 mg/L. Toxic symptoms observed were decreased activity, ataxia,

constricted pupils, exophthalmos, lacrimation, nasal discharge, piloerection, polyuria, ptosis, salivation and sensitive to touch. Gross necropsy revealed discoloration of the contents of the gastrointestinal tract, and discoloration of the liver.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: Category III - CAUTION

(4) Primary Eye Irritation Study: Stillmeadow, Inc.; Project No. 4374-86; MRID Number 403527-02; 10-9-86.

PROCEDURE:

Nine New Zealand white rabbits were each administered 0.1 ml of test material which was placed in the conjunctival sac of the right eye of each animal. The treated eye was held shut for one second. The treated eyes of 3/9 animals were washed with deionized water for one minute beginning 30 seconds after treatment. The untreated eye served as a control. Eye irritation was scored at 1, 24, 48, and 72 hours and at 4 and 7 days.

RESULTS:

Eye irritation in the unwashed group was scored as follows: at 24 hours, conjunctivae redness (4/6=1), chemosis (4/6=1), and discharge (1/6=1); and at 4 days, all irritation had cleared.

Eye irritation in the washed group was scored as follows: at 24 hours, conjunctivae redness (2/3=2, 1/3=1), chemosis (3/3=1) and discharge (2/3=1); and at 72 hours, all irritation had cleared.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: Category III - CAUTION

(5) Primary Skin Irritation Study: Stillmeadow, Inc.; Project No. 4375-86; MRID No. 403527-03; 10-10-86.

PROCEDURE:

Six New Zealand white rabbits were clipped free of fur on the dorsal area of the trunk. Approximately 24 hours later, each animal was administered a topical application of 0.5 ml of test material to the previously shaven test site which was covered with occlusive wrap for 4 hours. After exposure, the wrap and residual test material were removed. Skin irritation was scored at 1, 24, 48 and 72 hours.

RESULTS:

At 24 hours, 2/6 animals exhibited very slight erythema and 1/6 animals exhibited very slight edema. No irritation was observed at 72 hours.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: Category IV - CAUTION

(6) Dermal Sensitization Study: Stillmeadow, Inc.; Project No. 4376-86; MRID No. 403527-04; 11-12-86.

PROCEDURE:

Two groups of 10 albino guinea pigs were each administered induction treatments on days 1, 3, 6, 8, 10, 13, 15, 17, 20, and 22. Each induction treatment consisted of 0.5 ml of material injected beneath a gauze positioned on the previously shaven back of each animal. The test group was induced with 100% test material and the positive control group was induced with 0.05% w/v solution of 2,4-dinitrochlorobenzene (DNCB) in ethanol. Animals were restrained during each treatment which lasted six hours. Two weeks after the last induction treatment, each group was challenged in an identical manner at the original test site and additionally at a second test site. Skin irritation was scored at 24 hours after each treatment and at 48 hours after the first and last induction treatment and challenge treatment.

RESULTS:

After the third induction treatment, five positive control animals exhibited very slight erythema and 2/10 exhibited very slight edema. Irritation increased in severity and number of animals involved with each subsequent treatment. By day 22, 9/10 positive control group animals exhibited moderate to severe erythema, 1/10 exhibited well-defined erythema, 5/10 exhibited severe edema with eschar formation and 5/10 exhibited moderate edema. After challenge, irritation at both test sites (previously induced and virgin site) ranged from well-defined erythema to moderate to severe erythema and very slight edema to slight edema.

After the third induction treatment, 2/10 animals in the test group exhibited very slight erythema and 1/10 exhibited very slight edema. Irritation observed during induction phase ranged from very slight erythema to well-defined erythema and very slight edema with some sloughing of skin. At challenge, no irritation was observed at the previously treated site or at the virgin site.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: NONSENSITIZER