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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

FEB 3 1987

SUBJECT: EPA File Symbol 241-EOI
Arsenal Herbicide Railroad Applicators Concentrate

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

mw 2/20/87
E 2/26/87

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

APPLICANT: American Cyanamid Company
Agricultural Research Division
P.O. Box 400
Princeton, NJ 08540

ACTIVE INGREDIENT:
Isopropylamine salt of Imazapyr (2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazole-2-yl]-3-pyridinecarboxylic acid) 53.1%
INERT INGREDIENTS: 46.9%

BACKGROUND:

The applicant has submitted an acute oral, acute dermal, acute inhalation, primary skin irritation, primary eye irritation, and dermal sensitization studies. The studies were conducted by Biosearch, Incorporated and Cyanamid Agricultural Research Division. The data Accession Number is 265948. The method of support was not indicated.

RECOMMENDATION:

FHB/TSS finds the data acceptable; however, the product(s) tested must be adequately identified. TSS requests that the registrant provide Confidential Statements of Formula (CSF) for

the product(s) tested (Arsenal 4 lb/gallon Aqueous Concentrate and Arsenal 4-AS). TSS also requests that the data along with the CSF's be returned to TSS so that it can be determined whether or not the data submitted can be used to support the product for which registration is sought.

The registrant should be informed that when conducting future primary skin irritation studies, the test site should be covered with occlusive wrap in order to avoid possible ingestion of the test material by the animals and to ensure that the test material remains on the test site for the full exposure period.

The registrant should also be informed that when conducting future primary eye irritation studies, individual scores should be provided for conjunctivae redness, chemosis and discharge.

The registrant should be informed that the acute inhalation toxicity report contains a typographical error on page 6. On page 6 the mean analytical concentration is listed as 4.26 mg/L and on page 12 it is listed as 4.62 mg/L.

LABELING:

Comments reserved until additional data are provided.

REVIEW:

(1) Acute Oral Toxicity Study: Cyanamid Agricultural Research Division; Report No. A84-52; October 8, 1984.

PROCEDURE:

Five male and five female Charles River rats received a single dose of 5000 mg/kg of 20% w/v aqueous dispersion of test material. Animals were observed for 14 days. Body weights were recorded weekly. Animals were necropsied at study conclusion.

RESULTS:

No deaths occurred and no toxic symptoms were observed. The LD_{50} was reported to be > 5000 mg/kg. Gross necropsy of one female revealed uterus filled with clear fluid. No other abnormalities were observed at gross necropsy.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: IV - CAUTION.

(2) Acute Dermal Toxicity Study: Cyanamid Agricultural Research Division; Report No. A84-52; October 8, 1984.

under occlusive wrap for 24 hours. Body weights were recorded on day of dosing and at 7 and 14 days. Animals were observed for 14 days and necropsied at study conclusion.

RESULTS:

One out of five females died. The LD_{50} was reported to be >.2000 mg/kg. No toxic symptoms were observed. No abnormalities were noted at necropsy. Gross necropsy of the one mortality revealed severe pneumonia evidenced by the pleural cavity filled with white exudate.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: III - CAUTION.

(3) Primary Skin Irritation Study: Cyanamid Agricultural Research Division; Report No. A84-52; October 8, 1984.

PROCEDURE:

Six New Zealand White rabbits were shaved and 24 hours later, each animal received 0.5 ml of test material per shaven test site (one abraded and one intact). After 24 hours of exposure, the test material was removed. Skin irritation was scored at 24 and 72 hours.

RESULTS:

No skin irritation was observed at the intact skin site at 24 or 72 hours. At 24 hours, 4/6 animals exhibited well-defined erythema, 2/6 animals exhibited very slight erythema, and 5/6 animals exhibited very slight edema at the abraded skin sites. All irritation had cleared by 72 hours.

STUDY CLASSIFICATION:

Core Minimum Data. See comments under Recommendation.

TOXICITY CATEGORY: IV - CAUTION.

(4) Primary Eye Irritation Study: Cyanamid Agricultural Research Division; Report No. A84-52; October 8, 1984.

PROCEDURE:

Six male New Zealand White rabbits each received 0.1 ml of test material which was instilled in the conjunctival sac of the right eye. The treated eye was held shut for 5 seconds after test material instillation. The left eye served as a

PROCEDURE:

Six male New Zealand White rabbits each received 0.1 ml of test material which was instilled in the conjunctival sac of the right eye. The treated eye was held shut for 5 seconds after test material instillation. The left eye served as a control. After 24 hours of exposure, the treated eyes were rinsed using tap water. Eye irritation was scored at 1 and 24 hours.

RESULTS:

At 24 hours, animals exhibited cumulative conjunctivae irritation scores of 1/6 = 6, 2/6 = 4, and 2/6 = 2. All irritation had subsided by 24 hours.

STUDY CLASSIFICATION:

Core Guideline Data. See comments under Recommendation.

TOXICITY CATEGORY: Category IV - CAUTION

(5) Acute Inhalation Toxicity Study: Biosearch, Incorporated; Project No. 86-4930A; May 13, 1986.

PROCEDURE:

Ten male and ten female Sprague-Dawley rats were exposed in a 230 L acrylic exposure chamber for 4 hours to an analytically measured mean concentration of 4.62 mg/L of test material. Animals were observed frequently on the day of exposure, twice per day on weekdays, and once per day on weekends for 14 days. Body weights were recorded on the day before exposure, the day of exposure, and at 7 and 14 days. All animals were necropsied at study conclusion.

RESULTS:

No deaths occurred. The LC_{50} was reported to be > 4.62 mg/L. No toxic symptoms were observed. Gross necropsy revealed hemorrhagic and congested lungs.

STUDY CLASSIFICATION:

Core Guideline Data. See comments under Recommendation.

TOXICITY CATEGORY: III - CAUTION.

(6) Dermal Sensitization Study: Biosearch, Incorporated; Project No. 86-4929A; April 28, 1986.

PROCEDURE:

Two groups of 12 guinea pigs were clipped free of fur from the back and at weekly intervals during the induction phase and prior to the challenge phase. Each group received nine induction treatments administered three times a week for 6 hours of exposure under occlusive wrap as follows: the test group received 0.4 ml of test material and the positive control group received 0.4 ml of 1-chloro-2,4-dinitrobenzene prepared as a 0.1% w/v suspension in a 50% ethanol:0.9% saline solution. A naive control group of 12 guinea pigs was maintained in the same manner; however, no induction treatments were administered. Two weeks after the last induction treatment, a challenge dose of test material was administered to the right flank of the test group and naive control group. The positive control group received a challenge dose identical to an induction dose. Skin irritation was scored 24 and 48 hours after each treatment. Animals were observed once daily for abnormal clinical signs.

RESULTS:

Test group exhibited no irritation during either induction or challenge phase. One animal in test group was found dead on day 32. No irritation was observed in the naive control group after challenge treatment. Positive control group exhibited erythema ranging from very slight to well-defined during induction phase. One animal found dead after first induction treatment. Twenty-four hours after ninth induction treatment 4/11 animals exhibited very slight erythema and 2/6 animals exhibited well-defined erythema. At 24 hours after challenge treatment, 7/11 animals exhibited well-defined erythema and 2/11 animals exhibited very slight erythema.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: NONSENSITIZER.