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

006022

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

APR 30 1986

SUBJECT: EPA File Symbol 464-ANA
Turflon II Amine Herbicide

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

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

APPLICANT: Dow Chemical U.S.A.
P.O. Box 1706
Midland, MI 48640

ACTIVE INGREDIENTS:

315 2,4-D (2,4-dichlorophenoxyacetic acid) as the dimethylamine salt 34.2%

Triclopyr (3,5,6-trichloro-2-pyridinyloxyacetic acid) as the triethylamine salt 15.2%

INERT INGREDIENTS: 50.6%

BACKGROUND:

The applicant has submitted acute oral, acute dermal, acute inhalation, primary eye irritation, primary skin irritation, and dermal sensitization studies. The studies were conducted by Dow Chemical U.S.A., Mammalian and Environmental Toxicology Research Laboratory. The data Accession Number is 260747. The method of support is owner submission.

RECOMMENDATION:

FHB/TSS finds the data acceptable to support registration provided Turflon Superamine (product tested) and Turflon II Amine Herbicide (product to be registered) are the same. If any difference exists between the two products, the data must

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be returned to FHB/TSS in order that a determination can be made as to whether or not the data are acceptable to support registration of 464-ANA. The signal word is "DANGER" based on the eye study.

The Product Manager should inform the registrant that when conducting future acute inhalation toxicity studies, gross necropsy findings should be specified in detail.

LABELING:

Revise Statements of Practical Treatment as follows:

1. Delete sentence "Remove and wash contaminated clothes before reuse."

2. Add "NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage."

Revise Precautionary Statement as follows:

1. Expand sentence to read "Harmful if swallowed or inhaled."

2. Add "Avoid breathing vapors."

REVIEW:

(1) Acute Oral Toxicity Study: Mammalian and Environmental Toxicology Research Laboratory; October 23, 1985.

PROCEDURE:

Three groups of six male and six female Fischer 344 rats were administered a single oral dose of test material as follows: 500, 1000, or 2000 mg/kg. Animals were weighed prior to dosing, the day after dosing, and weekly thereafter for 2 weeks. Animals were observed closely the day of dosing and once daily thereafter for 14 days. All animals were submitted to gross necropsy at study conclusion.

RESULTS:

No deaths occurred at 500 and 1000 mg/kg. At 2000 mg/kg, 5/6 males and 4/6 females died. The LD_{50} for males was reported to be 1576 mg/kg (1266-2222 mg/kg, 95% confidence interval). The LD_{50} for females was reported to be 1743 mg/kg (1347-3700 mg/kg, 95% confidence interval).

Toxic symptoms observed were loss of motor coordination, lethargy, labored respiration, palpebral closure, excessive

lacrimation, semiconsciousness, and unconsciousness. Gross necropsy revealed congested and pale liver, multifocal erosion of the glandular mucosa of the stomach, hemolyzed blood in the small intestine, watery substance in the gastrointestinal tract, intraocular hemorrhaging, and cloudy corneas.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICOLOGY CATEGORY: Category III - CAUTION.

(2). Acute Dermal Toxicity Study: Mammalian and Environmental Toxicology Research Laboratory; October 29, 1985.

PROCEDURE:

Three groups of five male and five female New Zealand White rabbits were shaved. Twenty-four hours later, each animal received a single topical application of 630, 1300, or 2000 mg/kg of test material applied to a test site located on the animals' backs. The test sites were kept under occlusive wrap for 24 hours, and afterwards all wrap was removed and the test sites were washed with soap and water. Animals were restrained for 72 hours after removal of wrap. Animals were observed for 14 days to note toxic symptoms and mortality. All animals were submitted for gross necropsy.

RESULTS:

No deaths occurred at 630 and 1300 mg/kg. At 2000 mg/kg, 4/5 males and 3/5 females died. The LD_{50} for males was reported to be 1744 mg/kg (1484-2889 mg/kg, 95% confidence interval). The LD_{50} for females was reported to be 1892 mg/kg (1556-8372 mg/kg, 95% confidence interval).

Toxic symptoms included loss of motor coordination, loss of appetite, lethargy, shallow respiration, and unconsciousness. Gross necropsy revealed congested and pale liver, cortical surface of kidneys depressed, congested and edematous lungs, multifocal hemorrhaging of the thymus, decreased amount of fat in abdominal cavity, distended bladder, multifocal erosion of the stomach, hyperemia and necrosis of skin at test site.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category II - WARNING.

(3) Acute Inhalation Toxicity Study: Mammalian and Environmental Toxicology Research Laboratory; XRM-4814; October 7, 1985.

PROCEDURE:

Six male and six female Fischer 344 rats were exposed in a 112 L glass and stainless steel Rochester type chamber for 4 hours to an aerosol generated from the test material having a gravimetrically measured concentration of 2.0 mg/L (highest concentration attainable). Chamber concentrations were measured four times during exposure. All animals were weighed on days 2, 4, 8, 11, and 15. Animals were observed during exposure and at least once daily for 14 days. All animals were submitted for gross necropsy.

RESULTS:

One out of six females died. Since less than 50 percent of the test animals died at 2.0 mg/L, it can be assumed that the LC_{50} for both males and females is > 2.0 mg/L.

Toxic symptoms during exposure included tearing, salivation, urination, and animals wet with test material. Toxic symptoms after exposure included labored breathing, slight encrustations around mouth and nose, urine-stained perineum, and weight loss during first week. Gross necropsy of one mortality revealed observations compatible with stress.

STUDY CLASSIFICATION:

Core Guideline Data. See comments under Recommendation.

TOXICITY CATEGORY: Category III - CAUTION.

(4) Primary Eye Irritation Study: Mammalian and Environmental Toxicology Research Laboratory; October 24, 1985.

PROCEDURE:

Six New Zealand White rabbits were examined using 5 percent fluorescein stain and found free of defects. Twenty-four hours later, each animal received a dose of 0.1 ml of test material instilled into the conjunctival sac of the right eye. The left eye served as a control. Eyes were examined and scored for irritation at 1, 24, 48, and 72 hours and at 7, 14, and 21 days.

RESULTS:

Eye irritation was scored as follows: at 24 hours, corneal opacity (6/6 = 20), iris irritation (6/6 = 5), conjunctivae redness (6/6 = 2), chemosis (1/6 = 3, 5/6 = 2) and discharge (3/6 = 3, 2/6 = 2); at 7 days, corneal opacity (1/6 = 60, 3/6 = 40, 2/6 = 20), iris irritation (6/6 = 5),

conjunctivae redness (3/6 = 2, 3/6 = 1), chemosis (6/6 = 1) and discharge (2/6 = 2, 2/6 = 1); at 14 days, corneal opacity (1/6 = 60, 1/6 = 40, 3/6 = 20), iris irritation (1/6 = 10, 1/6 = 5), conjunctivae redness (5/6 = 2), chemosis (5/6 = 1), and discharge (1/6 = 2, 2/6 = 2); and at 21 days, corneal opacity (1/6 = 60, 1/6 = 40, 2/6 = 20), iris irritation (1/6 = 10, 1/6 = 5), conjunctivae redness (2/6 = 2, 2/6 = 1), chemosis (2/6 = 1), and discharge (2/6 = 1). Other toxic symptoms included vascularization over cornea and dry appearance of corneal surface.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category I - DANGER.

(5) Primary Dermal Irritation Study: Mammalian and Environmental Toxicology Research Laboratory; October 25, 1985.

PROCEDURE:

Two male and four female New Zealand White rabbits were clipped, and 24 hours later, each animal received 0.5 ml of test material applied to the test site under occlusive wrap. After 4 hours of exposure, the wrap was removed and residual test material washed from the test site using water. Skin irritation was scored within 30 minutes after removal of wrap and at 24, 48, and 72 hours later.

RESULTS:

No skin irritation occurred. The primary irritation score was 0.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category IV - CAUTION.

(6) Dermal Sensitization Study: Mammalian and Environmental Toxicology Research Laboratory; October 25, 1985.

PROCEDURE:

Two groups of 10 guinea pigs were clipped free of hair on the back region, and the next day the clipped areas on each animal were depilated. Twenty-four hours later, the animals in each group received the first of four topical applications to be given over a 10-day period. Each insult treatment consisted of 0.1 ml of test material or 0.1 ml of 10 percent DER 331 epoxy resin (known sensitizer) in DOWANOL DPM/TWEEN 80 applied to a patch which was placed on the

animals' backs under occlusive wrap for 48 hours. In addition to the third insult treatment, each animal received a total of 0.2 m of Freund's Complete Adjuvant injected intradermally at multiple points adjacent to the test site. The fourth insult treatment was removed after 24 hours. After 2 weeks, both flanks of each animal were clipped and challenged with test material or positive control and solvent. Skin irritation was scored after each insult treatment and challenge treatment.

RESULTS:

The test material caused no irritation during the insult phase and after challenge treatment. The positive control caused no irritation during the insult phase; however, after challenge treatment the positive control caused moderate to marked erythema. The solvent caused no irritation.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: NONSENSITIZER.