

US EPA ARCHIVE DOCUMENT



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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

April 5, 1999

MEMORANDUM

Subject: EPA Reg. No. 241-286: ARSENAL TECHNICAL HERBICIDE
DP Barcode: D252516
Case No: 050793
PC Code: 128829 Imazapyr, isopropylamine salt

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

Byron T. Backus
4/5/99

To: James Stone/Jim Tompkins, PM 25
Herbicide Branch
Registration Division (7505C)

Registrant: American Cyanamid Company

ACTION REQUESTED: "Third acute oral study. Can "Harmful if swallowed" be removed from label?"

COMMENTS AND RECOMMENDATIONS:

1. According to a letter dated January 13, 1999 from American Cyanamid it was found that dosing levels in a previously submitted acute oral toxicity study (in MRID 41551002) had been erroneously reported, and that the reported toxicity of ARSENAL technical should have been >2500 mg/kg rather than >5000 mg/kg. The registrant has now conducted a new oral LD50 study (MRID 44735301) in which rats were orally dosed with 5000 mg/kg of the test material.
2. TRB has reviewed the acute oral toxicity study in MRID 44735301, and has classified the study as acceptable. The test material is in toxicity category IV in terms of oral hazard potential. The registrant can either retain or remove the "harmful if swallowed" statement from the product label.

The following is the acute toxicity profile for this product, based on this and previous reviews:

Acute Oral LD50	IV	Acceptable
Acute Dermal LD50	III	Acceptable
Acute Inhalation LC50	III	Acceptable
Primary Eye Irritation	I	Acceptable
Primary Dermal Irritation	IV	Acceptable
Dermal Sensitization	No	Acceptable

The following is the precautionary labeling for this product based on the acute toxicity profile, as obtained from the Label Review System:

Date: 04/02/99 LABEL REVIEW SYSTEM

ID #: 000241-00286 ARSENAL TECHNICAL HERBICIDE

SIGNAL WORD: DANGER

PRECAUTIONARY STATEMENTS:

Corrosive. Causes irreversible eye damage. Harmful if absorbed through skin or inhaled. Do not get in eyes or on clothing. Avoid contact with skin. Avoid breathing dust. Wear goggles or face shield.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Do not induce vomiting. Drink promptly a large quantity of milk, egg whites, gelatin solution, or if these are not available, drink large quantities of water. If person is unconscious, do not give anything by mouth. Avoid alcohol.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

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

IF IN EYES: Hold eyelids open and flush with steady, gentle stream of water for 15 minutes. Get medical attention.

NOTE TO PHYSICIAN:

Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician." The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

The following "Note to Physician" statement is required for the subject product:

NOTE TO PHYSICIAN; Probable mucosal damage may contraindicate the use of gastric lavage.

The following statement should appear under the heading USER SAFETY RECOMMENDATIONS:

Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing and wash clothing before reuse.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1))

Product Manager: 25
MRID No.: 44735301
Report No.: A98-90

Reviewer: Byron T. Backus, Ph.D.
Study Completion Date: October 12, 1998
Study No.: T-1076

Testing Facility: American Cyanamid Company, Princeton, NJ 08543-0400
Author: Lowe, C.A.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: AC 243997; Lot No. AC 11574-27; 98.8% Imazapyr (consistent with the structure reported on p. 8 of MRID 44735301)

Species: Rat; Albino outbred, Sprague-Dawley-derived (CrI:CD®(SD)BR)

Age: 8 weeks (when dosed)

Weight (day 0): Males: 223-240 g; Females: 161-179 g

Source: Charles River Laboratories Inc., Raleigh, NC

Conclusion:

- LD₅₀ (mg/kg):**
Males: > 5000 mg/kg (1/5 died following dosage at this level)
Females: > 5000 mg/kg (no deaths in 5 rats following dosage at this level)
Combined: > 5000 mg/kg (1/10 died following dosage at this level)
- The estimated LD₅₀ is >5000 mg/kg**
- Tox. Category:** IV

Classification: Acceptable

Procedure (including deviations from 870.1100): "The test substance was ground to a fine powder with a mortar and pestle, [with?] 0.5% carboxymethyl cellulose (CMC) and then mixed with Scientific Products (SP) High Purity Water®... The test dispersion was prepared at a 25% nominal concentration to be dosed at a constant volume of 20 mL/kg of b.w. due to the viscosity of the test substance/diluent mixture. The test dispersion was prepared on the day of dosing and stirred continuously during dosing using a stir bar and stir plate..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	1/5	0/5	1/10

Observations: "Clinical signs appeared immediately after dosing in males only, immediately following dosing. Surviving males returned to normal by 2 hours postdosing." Symptoms included salivation in 4/5 males and writhing in 1 male (the one male which had writhing as a symptom - along with salivation - died within 1 hour of dosing). No symptoms were observed in any of the females. All surviving animals gained weight during the 14-day observation period.

Gross Necropsy: "There were no gross pathological findings observed in the one male that died or in the animals which were sacrificed at the termination of the study."

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D252516
2. **PC CODE:** 128829 Imazapyr, isopropylamine salt
3. **CURRENT DATE:** April 5, 1999
4. **TEST MATERIAL:** AC 243997; Lot No. AC 11574-27; 98.8% Imazapyr (consistent with the structure reported on p. 8 of MRID 44735301)

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/ American Cyanamid Co./ T-1076/10-12-1998	44735301	1/5 males and 0/5 females died after dosage at 5000 mg/kg; 4/5 males (including the one that died) had salivation; in addition, the male which died showed writhing in the hour after dosage. This male died within 1 hr of dosage. Other males no longer showed symptoms at 2 hrs; females did not exhibit symptoms. Necropsies were unremarkable.	IV	A

Core Grade Key: **A = Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**