JUN 24 1996

DPBarcode: D227235

Case: 046566

MEMORANDUM

Subject: EPA File Symbol/EPA Reg. No.: 241-GTT/**FOR USE IN IMI-CORN™ ONLY**; **AC 513,996** Resubmission

From: Carol E. Glasgow, Ph.D., Toxicologist carol
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division (7505C)

To: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (7505C)

Applicant: American Cyanamid Company
P.O. Box 400
Princeton, NJ 08543-0400

FORMULATION FROM LABEL:

Active Ingredient (s):	% by weight
Imazethapyr (±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid	52.5
Imazapyr 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid)	17.5
Inert ingredient(s)	30.0

BACKGROUND: American Cyanamid Company originally submitted a primary eye irritation study to support registration of its new product referenced above. Study performed by American Cyanamid Company Agricultural Research Division on MRID 438615-13. This product was discussed at the PRS Team meeting on April 1, 1996, as a candidate for bridging. The conclusion was that PRS could bridge the worst-case from most endpoints, but should review the primary eye irritation study for accuracy.

When Dr. Carol Glasgow initially reviewed this study, she gave it an **Acceptable** rating. However, she went on to say "PRS would appreciate more specific information about the acclimation period." She meant additional information would be appreciated in the future.

On 1 May, Project Manager Robert J. Taylor of EPA sent Desiree Little of American Cyanamid a copy of the review of the **Acceptable** primary eye irritation, with a request for more information on the rabbits' acclimation period. Ms. Little responded on 31 May with a Memorandum from Joel Fischer of Cyanamid's Toxicology Department, detailing the actual

time the rabbits were acclimated. Dr. Glasgow regrets the ambiguity concerning when the additional information would be "appreciated" in her initial review.

RECOMMENDATION: RSB/PRS findings are as follows:

The additional information from American Cyanamid reinforces the reasons an **Acceptable** review was given earlier.

TOXICITY PROFILES

Acute oral toxicity	IV	Acceptable
Acute dermal toxicity	III	Acceptable
Acute inhalation toxicity	III	Acceptable
Primary eye irritation	II	Acceptable
Primary dermal irritation	IV	Acceptable
Dermal sensitization	No	Acceptable

LABELING: The signal word for this product is "Warning" as the primary eye irritation study is category II. Language required for the label should include the following:

AGRICULTURAL USE REQUIREMENTS:

DIRECTIONS FOR USE:

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, wear: coveralls over long-sleeved shirt and long pants, socks and chemical resistant footwear, Wear goggles or face shield, and waterproof gloves.

SIGNAL WORD: WARNING AVISO

PRECAUTIONARY STATEMENTS:

Causes substantial but temprary eye injury. Harmful if absorbed through skin or inhaled. Do not get in eyes or on clothing. Avoid contact with skin. Avoid breathing vapor. Wear long-sleeved shirt and long pants, socks and shoes, goggles or face shield and waterproof gloves. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

2

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. 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.

Probable mucosal damage may contraindicate the use of gastric lavage.

DATA EVALUATION REVIEW FOR PRIMARY EYE IRRITATION (§81-4)

Product Manager: 25 **Reviewer**: Carol Glasgow, Ph.D.
MRID No.: 438615-13 **Report Date**: September 1, 1995
Testing Laboratory: American Cyanamid Company, Agricultural Research Division
Report No.: T-0792
Author(s): Lisa M. Boczon
Species: New Zealand White albino rabbit
Weight: not given
Age: 10 - 13 weeks
Sex: 6 males
Source: Skipjack farms, Skipjack, Pennsylvania
Test Material: AC 263,499/AC 243,997 70 DG Formulation, Lot Number AC 9786-68B; tan granules
Quality Assurance (40 CFR §160.12): Included, acceptable

Summary:

1. **Toxicity Category**: II

2. **Classification**: Acceptable

Procedure (Deviation from §81.4): Animals acclimated to laboratory conditions 11 days before testing. Animals' eyes examined two ways before treatment: 1) macroscopically with hand-held light source, and 2), with fluorescein and a UV light source. Animals with preexisting eye damage not used in study. Test substance ground into powder and 100 mg instilled into the conjunctival sac of the left eye. Contralateral eye used for control. Eyelids held shut for about 1 second to keep maximum contact. Eyes examined approximately 1 hour after treatment, at 24, 48, and 72 hours, and at days 4, 7, 10, 14, 17 and day 21. After first examination, fluorescein and the UV light source used for corneal examinations until no effect noted. Draize eye scale used for grading ocular irritation. Unusual ocular observations noted below.

Results: This product is a severe eye irritant, causing corneal damage and conjunctival irritation in all animals for up to 3 days. Corneal grade 2 in 2 animals. Corneas of all animals clear by day 21. Two rabbits exhibited corneal vascularization beginning at day 7. Iritis seen in 5/6 rabbits, but cleared in all animals within 72 hours. Conjunctivitis reaching grade 3 for redness in 3 rabbits as early as 24 hours. Chemosis and discharge were less severely affected, with up to grade 2 in 4/6 animals. Conjunctival irritation cleared by day 14 in all test subjects.