DP Barcode: D225224 OCT 3 1996 Case: 287674

MEMORANDUM

Subject: EPA File Symbol/EPA Reg. No.: 352-439/Du Pont **Escort®** Herbicide Adverse Action Additional Response

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: E.I. du Pont de Nemours & Company
P.O. Box 80038
Wilmington, DE 19880-0038

FORMULATION FROM LETTER:

Active Ingredient (s):	% by weight
Metasulfuron methyl	60
Inert ingredient(s)	40

BACKGROUND: No label or CSF sent with package. Information on formulation found in letter to P.M. E.I. du Pont de Nemours & Company submitted an adverse action study on primary dermal irritation with modern techniques under GLP. This indicated a more severe finding and will alter the label. The original study was performed in 1984 and classified as IV. The present study was completed by Haskell Laboratory on MRID 439454-01.

On August 1, 1996, James W. Denny of du Pont sent a letter to Ms. Vicki Walters of PM Team 25 requesting a meeting with several OPP personnel to discuss a re-evaluation of the study review which was sent on to PRS. Dr. Tina Levine and Dr. Carol Glasgow discussed the review and du Pont's comments and decided the study review could be reduced to II, but not to the III that was originally requested by du Pont.

RECOMMENDATION: RSB/PRS findings are as follows:

This study is **Acceptable**. However, although the letter sent with the study labeled this as III, it will be labeled as II. A rating of II is defined as "Severe irritation at 72 hours (severe erythema or edema)." The decision by PRS on labeling is not an average of all the rabbits in the study at any one point, but the most severe result at that point. EPA has established 72 hours as

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the time for review and to make preliminary judgements. At 72 hours in this study, 2 rabbits had grade 4 erythema, and 1 rabbit, grade 3. Also, at the same time, 2 rabbits exhibited desquamation, 2 had eschar and 2 rabbits were sloughing skin. However, the results were reversible with complete clearing by day 13 and no permanent scarring, although sloughing and scaling were apparent through day 10.

TOXICITY PROFILES

Primary dermal irritation	II	Acceptable

LABELING: The signal word for this product is "Warning" as the primary dermal irritation study is category II. Language required for the label based on this study can be found in the LRS and below:

SIGNAL WORD: WARNING

PRECAUTIONARY STATEMENTS:

Causes skin irritation. Do not get on skin or on clothing. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

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.

Probable mucosal damage may contraindicate the use of gastric lavage.

DATA EVALUATION REVIEW FOR PRIMARY DERMAL IRRITATION (§81-5)

Product Manager: 25
MRID No.: 439454-01
Testing Laboratory: Haskell Laboratory
Report No.: 3-96
Author(s): Carol Finlay
Species: HM:(NZW)fBR New Zealand White rabbit
Weight: males, 2,190 - 2,448 g
Age: young adult
Sex: 6 males
Source: Hare Marland, Hewitt, New Jersey
Test Material: Escort® Herbicide; beige solid -- no batch or lot number given
Quality Assurance (40 CFR §160.12): Included, acceptable

Reviewer: Carol Glasgow, Ph.D.
Report Date: February 6, 1996

Summary:

1. **Toxicity Category:** II

2. **Classification:** Acceptable

Procedure (Deviation from §81-5): Rabbits quarantined ~2 weeks and weighed before testing. Animals shaved from scapular to lumbar region of back on day before dosing and placed in stocks with rubber sheeting (~ 8 x 18"). Test material (0.5 g) mixed with 0.2 ml deionized water to form a thick paste spread evenly on 6 square cm. of skin, and covered with a 1" 4-ply gauze square secured with non-irritating tape. Animals then placed in stocks and rubber sheeting wrapped around for 4 hours without food or water. At this point, wrappings removed and test site cleaned off by washing with Ivory® soap and warm water and gently patted dry. Observations made for dermal irritation at ~ 1, 24, 48, and 72 hours, and on subsequent days till end of study, day 13. Draize scale used for scoring dermal effects.

Results: Test material produced mild to severe erythema and slight to moderate edema after wrappings removed. One of the rabbits had a very slight response, with the first four readings grade 1 erythema and no edema. All the others had both erythema up to grade 4 and edema up to grade 3. All erythema and edema had resolved in treated animals 10 days after application, but other dermal responses in one rabbit (sloughing and epidermal scaling) were still seen on day 10. Other signs noted in 5/6 animals were eschar and desquamation. One rabbit demonstrated a lowered weight gain over the period of observation.