



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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

February 28, 1997

MEMORANDUM

EPA File Symbol: 400-398

DP Barcode: D232085

Chemical: 118901 Dimethipin

Test Material: Harvade®-25F, a brown liquid

From: Wallace Powell, Biologist
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division *Wallace Powell*

To: Product Manager, Team 22
James Stone, Team Reviewer, Team 22

Applicant: Uniroyal Chemical Co., Inc.

Performing Lab: MB Research Laboratories, Inc.
P.O. Box 178
Steinsburg and Wentz Roads
Spinnerstown, PA 18968

FORMULATION FROM LABEL

<u>Ingredient(s)</u>	<u>% by wt.</u>
Dimethipin (2,3-dihydro-5,6-dimethyl- 1,4-dithiin-1,1,4,4-tetraoxide)	22.4
Inerts	77.6
Total	100.0

BACKGROUND

Uniroyal Chemical Co., Inc. has submitted a primary eye irritation study and an acute skin irritation study, in support of a change in the signal word, first aid statements, and personal protective equipment instructions on the label for Harvade®-25F, EPA Registration No. 400-398. (The PM team reviewer has pointed out that there is no previous review of acute studies in the registration file for this product.)

The 1983 dermal irritation study (MRID No. 001324-15) submitted previously for this product was considered to have indicated a toxicity category I response. However, the exposure period was 24 hours rather than the current guidelines standard of 4 hours. This may account for the discrepancy between the category I rating indicated by the 1983 study and the category III indicated by the newer study reviewed below.

The results of the 1983 eye irritation study (MRID No. 001324-16) submitted previously for this product would suggest a category III rating, the same rating indicated by the newer eye irritation study reviewed below.

RECOMMENDATION

This review evaluates only the proposed precautionary labeling changes and the two studies submitted in support of those changes. Other acute toxicity studies which were submitted in the past (but appear not to have been formally reviewed) will be reviewed as part of the final stage of the reregistration process if submitted for that purpose.

81-4. Eye Irritation: Category III. The submitted study is acceptable.

81-5. Skin Irritation: Category III. The submitted study is acceptable.

LABELING RECOMMENDATIONS (Based on the Label Review Manual)

All label changes on the first page of the draft label, and in the "AGRICULTURAL USE REQUIREMENTS" box in the second page of the draft label, are acceptable based on the Label Review Manual and the two studies reviewed below.

The proposed deletion of the label statements pertaining to acute inhalation hazard are acceptable based on the observation that the 1983 acute inhalation study (MRID No. 001324-14), submitted previously for this product but apparently not formally reviewed, would suggest a category IV rating for acute inhalation.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 22
 MRID No.: 441615-01
 Author: Daniel R. Cerven, M.S.

Reviewer: W. Powell
 Report No.: MB 94-4177 D
 Report Date: July 19, 1995

Conclusion:

Toxicity Category: III
 Classification: Acceptable
 Quality Assurance (40 CFR §160.12): Included

Deviations from §81-4: None

Testing Facility: MB Research Laboratories, Inc.
 P.O. Box 178
 Steinsburg and Wentz Roads
 Spinnerstown, PA 18968

Test Material: Harvade®-25F, a brown liquid

Test Animal:

Rabbit; Rabbit, New Zealand Albino, 6 females
 Age: 2 to 2½ months
 Weight: 2.4 to 3.1 kg
 Source: Ace Animals, Boyertown, PA

Test Conditions: 0.1 gram of the undiluted test substance was instilled into one eye of each of six rabbits. The other eye was untreated and served as a control. Eyelids were held together for about 1 second; this was followed by a 24 hour exposure period during which the eyes were not rinsed. Ocular irritation was evaluated by the Draize method at 1 hour and 1, 2, 3, and 7 days post-dosing.

Results:

Observations	Number positive/tested at				
	1 Hr	24 Hrs	48 Hrs	72 Hrs	7 Days
Cornea Opacity	0/6	0/6	0/6	0/6	0/6
Iris	1/6	0/6	0/6	0/6	0/6
Conjunctivae: Redness	6/6	6/6	5/6	4/6	0/6
Chemosis	6/6	6/6	5/6	3/6	0/6

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: 22
MRID No.: 441615-02
Authors: Lori Kieffer, B.A.

Reviewer: W. Powell
Report No.: MB 94-4177 C
Report Date: October 6, 1995
(as amended)

Conclusion:

Toxicity Category: III
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included

Procedure Deviations from §81-5: None

Testing Facility: MB Research Laboratories, Inc.
P.O. Box 178
Steinsburg and Wentz Roads
Spinnerstown, PA 18968

Test Material: Harvade®-25F, a brown liquid

Test Animal:

Rabbit, New Zealand Albino
Age: 2 to 3 months
Weight: 2.5 to 2.7 kg
Source: Ace Animals, Boyertown, PA

Test Conditions: A 0.5 ml dose of the test substance was applied to each rabbit's skin on a 10 cm² site which had been clipped free of hair the previous day. This site was then covered with a 6 cm² gauze pad and occluded with a dressing. At the end of a four hour exposure period, the dressings were removed and the test sites gently washed with distilled water. The sites were then observed for dermal effects at ½ to 1 hour after removal of the dressings and again at hours 24, 48, and 72 and on days 7 and 10. Severity of erythema and edema was scored using the Draize scale.

Results: Erythema and/or eschar at hour 72 was well-defined (grade 2) in 1 animal and slight (grade 1) in the other 5 animals. Slight edema in 1 animal at hour 72. All irritation cleared by day 10. Irritation generally persisted longer in one animal than in the other five.

ACUTE TOX ONE-LINER

ID No.: 400-398
 DP Barcode: D232085
 Chemical: 118901 Dimethipin
 Applicant: Uniroyal Chemical Co., Inc.
 Test Material: Harvade®-25F, a brown liquid

Date: February 28, 1997

Study, Animal, Test Laboratory, Study #, Date	MRID No.	Results	Tox. Cat.	Core Grade
Eye Irritation, Rabbit, MB Research Laboratories, MB 94-4177 D, 7/19/95	441615-01	No 'positive' corneal effect. Iridial effect cleared by hour 24, conjuncti- val by day 7	III	A
Skin Irritation, Rabbit, MB Research Laboratories, MB 94-4177 C, 10/6/95 (as amended)	441615-02	Slight to well- defined irritation at hour 72	III	A

A = Acceptable