

TRADE SECRET

Study Title

H-24256: Skin Irritation Test in Rabbits

Laboratory Project ID: DuPont-3606

AUTHOR: Deborah A. Vick, A.A.S.

STUDY COMPLETED ON: November 29, 1999

PERFORMING LABORATORY: E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, Delaware 19714-0050

WORK REQUEST NUMBER: [REDACTED]

SERVICE CODE NUMBER: [REDACTED]

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CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of the data obtained from this study.

Reviewed by:

Carol Finlay
Carol Finlay, B.A.
Associate Scientist

23-Nov-1999
Date

Issued by Study Director:

Deborah A. Vick
Deborah A. Vick, A.A.S.
Associate Scientist

29-Nov-1999
Date

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STUDY INFORMATION

9th Collective Nomenclature: [REDACTED]

Synonyms/Codes: [REDACTED]

• H-24256

Haskell Number: 24256

MSDS Reference Number: [REDACTED]

CAS Registry Number: [REDACTED]

Submitter's Notebook Number(s): [REDACTED]

Composition: [REDACTED]

Purity: [REDACTED]

Known Impurities: [REDACTED]

Physical Characteristics: [REDACTED]

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Study Initiated/Completed: October 19, 1999 / (see report cover page)

In-Life Initiated/Completed: November 9, 1999 / November 12, 1999

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STUDY PERSONNEL

Study Director: Deborah A. Vick, A.A.S.

Management: Nancy C. Chromey, Ph.D.

Primary Technician: Deborah A. Vick, A.A.S.

Toxicology Report Preparation: Bonnie J. Bieber, B.A.

Laboratory Veterinarian: Wanda L. West, D.V.M., A.C.L.A.M.

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SUMMARY

H-24256 was evaluated for acute skin irritation potential in 6 male New Zealand White rabbits. Approximately 0.5 mL of the test substance was applied to the shaved, intact skin of each rabbit and covered with a semi-occlusive dressing for a 4-hour exposure. Approximately 1, 24, 48, and 72 hours after removal of the test substance, the test sites were evaluated for erythema, edema, and other evidence of dermal effects and were scored according to the Draize Scale. The adjacent areas of untreated skin were used for comparison.

No dermal irritation was observed on the treated rabbits during the study. Three of the treated rabbits exhibited body weight losses of up to 3% of the initial body weight by study termination (72 hours). No clinical signs of toxicity were observed in the treated rabbits.

Under the conditions of this study, H-24256 was not a skin irritant.

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-24256 when applied to the shaved, intact skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Test Substance

The test substance, H-24256, was supplied by the sponsor as a [REDACTED] [REDACTED]. The test substance appeared to be stable under the conditions of the study. No evidence of instability, such as a change in color or physical state, was observed.

B. Animal Husbandry

Young adult HM:(NZW)fBR New Zealand White rabbits were received from Hare Marland, Hewitt, New Jersey. The rabbits were housed singly in suspended, stainless steel, wire-mesh cages. Each rabbit was assigned a unique identification number which was recorded on a card affixed to the cage. The last 3 digits of the identification number were written on the inside of each rabbit's ear with a water insoluble marker. The rabbits were offered approximately 125 grams of PMI Nutrition International, Inc. Certified High Fiber Rabbit LabDiet® 5325 daily during the study. Water was available *ad libitum* except during the exposure period while the animals were in stocks.

Haskell Laboratory has an animal health monitoring program. This program is monitored and administered by the Laboratory Veterinarian. Water samples are periodically analyzed for total bacterial counts and for the presence of coliforms, lead, and other contaminants. Additionally, samples from freshly washed cages and cage racks are periodically analyzed to ensure adequate sanitation by the cagewashers. Data from this program are maintained separately from study records. Animal feed is certified by the manufacturer to meet specified nutritional requirements and to be free of a list of specified contaminants. On the basis of these analyses, there is no evidence suggesting that contaminants were present in the feed or water in amounts which may have interfered with the results of this study.

Rabbits were quarantined, weighed, and observed for general health for 11 days. Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted for a temperature of $20^{\circ}\text{C} \pm 1^{\circ}\text{C}$ and relative humidity of $50\% \pm 10\%$. Excursions outside these ranges were judged to have been of insufficient magnitude and/or duration to have adversely affected the validity of the study.

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C. Protocol

On the day prior to treatment, the hair of 6 male New Zealand White rabbits was closely shaved to expose the skin from the scapular to the lumbar region of the back. The body weights of the rabbits ranged from 2140 to 2485 grams on the day of treatment.

Each rabbit was placed into a stock which had been fitted with a piece of rubber sheeting, approximately 8" x 18". The rabbits remained in the stocks throughout the exposure period and during that time did not have access to food or water. Approximately 0.5 mL of H-24256 was applied directly on the skin beneath a 1-inch, 2-ply gauze square that was held in place with non-irritating tape. The rubber sheeting was then wrapped around the animal and secured with clips to retard evaporation and to keep the test substance in contact with the skin without undue pressure. One other test substance was tested concurrently on a separate, localized test site on the backs of these rabbits.

Approximately 4 hours after application of the test substance, the rubber sheeting was loosened, and the skin at the corners of the gauze squares was marked with a waterproof pen; wrappings and gauze squares were then removed. The test sites were gently washed with warm water to remove excess test substance. The skin was gently patted dry, and the animals were returned to their cages.

Approximately 1, 24, 48, and 72 hours after removal of the test substance, the test sites were evaluated for erythema, edema, and other evidence of dermal effects and were scored according to the Draize Scale (Table 1). The adjacent areas of the untreated skin were used for comparison. The rabbits were also examined for clinical signs of toxicity at every dermal evaluation. The rabbits were weighed on the day of treatment and at the last dermal evaluation.

RESULTS AND DISCUSSION

No dermal irritation was observed on the treated rabbits during the study. Three of the treated rabbits exhibited body weight losses of up to 3% of the initial body weight by study termination (72 hours). No clinical signs of toxicity were observed in the treated rabbits. Individual skin irritation scores are presented in Table 2. A summary of skin responses is presented in the following table.

SUMMARY OF SKIN RESPONSES TO H-24256

RESPONSE	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
No Response	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6
Slight	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Mild	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Moderate	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6

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Severe	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
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CONCLUSIONS

Under the conditions of this study, H-24256 was not a skin irritant.

If these test scores are to be used for EEC/OECD classification, according to the guide to the labeling of dangerous substances published in the Official Journal of European Communities (EEC Directive 93/21, Annex VI), H-24256 probably should not be classified as an irritant unless additional data proves otherwise.

RECORDS AND SAMPLE STORAGE

Specimens (if applicable), raw data, and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware.

TABLES

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TABLE 1

DRAIZE^a SCALE FOR SCORING SKIN IRRITATION

<u>Evaluation of Skin Reactions</u>	<u>Score</u>
Erythema and eschar formation:	
No erythema	0
Very slight erythema (barely perceptible)	1 (Slight)
Well-defined erythema	2 (Mild)
Moderate to severe erythema	3 (Moderate)
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4 (Severe)
Edema formation:	
No edema	0
Very slight edema (barely perceptible)	1 (Slight)
Slight edema (edges of area well defined by definite raising)	2 (Mild)
Moderate edema (raised approximately 1.0 mm)	3 (Moderate)
Severe edema (raised more than 1.0 mm extending beyond the area of exposure)	4 (Severe)
Abbreviations of other dermal effects are:	
- = No Effect	I = Intact
A = Abraded	L = Sloughing
B = Blanching	N = Necrosis
C = Eschar	R = Raw Areas
D = Desquamation	S = Epidermal Scaling
F = Fissuring	T = Thickening
G = Fissuring with Bleeding	X = Compound Adhered to Skin
H = Hyperkeratosis	

a Draize, J. H., "Dermal Toxicity." Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. The Editorial Committee of the Association of Food and Drug Officials of the United States, Austin, Texas, 1959, pp. 46-59.

TABLE 2

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
34057	0	0	0	0	0	0	0	0
34058	0	0	0	0	0	0	0	0
34059	0	0	0	0	0	0	0	0
34060	0	0	0	0	0	0	0	0
34061	0	0	0	0	0	0	0	0
34062	0	0	0	0	0	0	0	0

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