

TRADE SECRET

Study Title

H-23271: SKIN IRRITATION TEST IN RABBITS

LABORATORY PROJECT ID: DUPONT-1161

AUTHOR: Carol Finlay, B.A.

STUDY COMPLETED ON: July 21, 1998

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

[REDACTED]

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CERTIFICATION

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

Issued by:

Carol Finlay

Carol Finlay, B.A.
Toxicology Associate
Study Director

7/21/98

Date

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STUDY INFORMATION

Substance Tested: [REDACTED]

Synonyms/Codes: • H-23271
[REDACTED]

Haskell Number: 23271

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

Composition: [REDACTED]

Known Impurities: Not supplied by the sponsor

Physical Characteristics: Yellow to tan liquid

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: June 16, 1998 / (see report cover page)

In-Life Initiated/Completed: June 18, 1998 / June 21, 1998

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STUDY PERSONNEL

Study Director: Carol Finlay, B.A.

Management: Judith C. Stadler, Ph.D.

Primary Technician: Carol Finlay, B.A.

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

Laboratory Veterinarian: Charles E. Cover, V.M.D.

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SUMMARY

H-23271 was evaluated for acute skin irritation potential in 6 female New Zealand White rabbits. Approximately 0.5 mL of the test substance was applied to the shaved, intact or abraded 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.

Mild or moderate erythema was observed on the intact test sites 1 hour after test substance removal. At 24 hours, no dermal irritation was observed in 2 rabbits, and slight or mild erythema was observed in 4 rabbits. At 48 hours, no dermal irritation was observed in 4 rabbits, and slight or mild erythema was observed in 2 rabbits. At 72 hours, no dermal irritation was observed in 5 rabbits, and mild erythema and epidermal scaling were observed in 1 rabbit. No edema was observed on the intact test sites.

Mild or moderate erythema was observed on the abraded test sites 1 hour after test substance removal. At 24 hours, slight to moderate erythema was observed in the rabbits. At 48 hours, no dermal irritation was observed in 3 rabbits, and slight to moderate erythema was observed in 3 rabbits. Two rabbits also exhibited epidermal scaling. At 72 hours, no dermal irritation was observed in 3 rabbits, mild or moderate erythema was observed in 2 rabbits, and epidermal scaling was observed in 3 rabbits. No edema was observed on the abraded test sites.

No clinical signs of toxicity were observed, and no body weight loss occurred during the study.

Under the conditions of this study, H-23271 was a moderate skin irritant on both intact and abraded skin.

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INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-23271 when applied to the shaved, intact or abraded skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult female HM:(NZW)fBR New Zealand White rabbits were received from Hare Marland. 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 20 days. This exceeded the laboratory standard of approximately 1 week because the rabbits were not released from quarantine as early as they could have been. 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.

B. Protocol

On the day prior to treatment, the hair of 6 female 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 2687 to 2976 grams on the day of treatment.

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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. H-23271 was tested on intact and abraded skin. The test site on one side of the rabbits was abraded by gently dragging the abrader across the skin. No bleeding was observed. The test site on the other side of the rabbits remained intact. Approximately 0.5 mL of H-23271 was applied directly on the skin beneath a 2-ply 2-inch 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. No other substances were tested 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.

RESULTS AND DISCUSSION

On the intact test sites, H-23271 produced mild erythema in 4 rabbits and moderate erythema in 2 rabbits by 1 hour after test substance removal. At 24 hours, no dermal irritation was observed in 2 rabbits, slight erythema was observed in 2 rabbits, and mild erythema was observed in 2 rabbits. At 48 hours, no dermal irritation was observed in 4 rabbits, slight erythema was observed in 1 rabbit, and mild erythema was observed in 1 rabbit. At 72 hours, no dermal irritation was observed in 5 rabbits, and mild erythema and epidermal scaling were observed in 1 rabbit. No edema was observed on the intact test sites.

On the abraded test sites, H-23271 produced mild erythema in 5 rabbits and moderate erythema in 1 rabbit by 1 hour after test substance removal. At 24 hours, slight erythema was observed in 3 rabbits, mild erythema was observed in 2 rabbits, and moderate erythema was observed in 1 rabbit. At 48 hours, no dermal irritation was observed in 3 rabbits, slight erythema was observed in 1 rabbit, mild erythema was observed in 1 rabbit, moderate erythema was observed in 1 rabbit, and epidermal scaling was observed in 2 rabbits. At 72 hours, no dermal irritation was observed in 3 rabbits, mild erythema was observed in 1 rabbit, moderate erythema was observed in 1 rabbit, and epidermal scaling was observed in 3 rabbits.

No clinical signs of toxicity were observed, and no body weight loss occurred during the study.

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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-23271

RESPONSE	INTACT							
	ERYTHEMA				EDEMA			
	1 hour	24 hours	48 hours	72 hours	1 hour	24 hours	48 hours	72 hours
No Response	0/6	2/6	4/6	5/6	6/6	6/6	6/6	6/6
Slight	0/6	2/6	1/6	0/6	0/6	0/6	0/6	0/6
Mild	4/6	2/6	1/6	1/6	0/6	0/6	0/6	0/6
Moderate	2/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
RESPONSE	ABRADED							
	ERYTHEMA				EDEMA			
	1 hour	24 hours	48 hours	72 hours	1 hour	24 hours	48 hours	72 hours
No Response	0/6	0/6	3/6	4/6	6/6	6/6	6/6	6/6
Slight	0/6	3/6	1/6	0/6	0/6	0/6	0/6	0/6
Mild	5/6	2/6	1/6	1/6	0/6	0/6	0/6	0/6
Moderate	1/6	1/6	1/6	1/6	0/6	0/6	0/6	0/6

CONCLUSIONS

Under the conditions of this study, H-23271 was a moderate 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-23271 probably should not be classified as an irritant unless further 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 (formerly known as the E.I. du Pont de Nemours and Company Records Management Center).

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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	L = Sloughing
A = Abraded	N = Necrosis
B = Blanching	R = Raw Areas
C = Eschar	S = Epidermal Scaling
D = Desquamation	SN = Superficial Necrosis
F = Fissuring	T = Thickening
G = Fissuring with Bleeding	X = Compound Adhered to Skin
I = Intact	

- 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.

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TABLE 2

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	INTACT							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
32896	3	1	0	0	0	0	0	0
32897	2	2	1	0	0	0	0	0
32899	3	2	2	2S	0	0	0	0
32900	2	1	0	0	0	0	0	0
32901	2	0	0	0	0	0	0	0
32902	2	0	0	0	0	0	0	0

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ABRADED							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
32896	2	1	0	0	0	0	0	0
32897	2	2	1	0	0	0	0	0
32899	3	3	2S	2S	0	0	0	0
32900	2	1	0	0S	0	0	0	0
32901	2	1	0	0	0	0	0	0
32902	2	2	3S	3S	0	0	0	0

Symbols are defined on page 9.

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