

Study Title

Skin Irritation Test with H-21953 in Rabbits

Laboratory Project ID

Haskell Laboratory Report No. 790-96

Author

Tracy A. Filliben

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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



GENERAL INFORMATION

Substance Tested:

[REDACTED]

Synonyms:

• H-21953

[REDACTED]

Physical Form:

Opaque tan to white liquid

Composition:

[REDACTED]

Contaminants:

[REDACTED]

Purity:

[REDACTED]

Submitter's Notebook No.:

[REDACTED]

CAS Registry No.:

[REDACTED]

Sponsor:

DuPont Specialty Chemicals
E. I. du Pont de Nemours and Company
Wilmington, Delaware

GENERAL INFORMATION (Continued)

Study Initiated - Completed: 6/21/96 - 8/30/96

In Life Phase
Initiated - Completed: 6/24/96 - 6/27/96

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours and Company, Newark, Delaware or in the DuPont Records Management Center, Wilmington, Delaware.

SUMMARY

H-21953 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 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.

H-21951 produced slight or mild erythema by 1 and 24 hours after test substance removal. By 48 and 72 hours, no or slight erythema was observed. In addition, 2 rabbits exhibited desquamation at 48 hours, and 4 rabbits exhibited desquamation at 72 hours. No edema or clinical signs of toxicity were observed during this study.

Under the conditions of this study, H-21953 was a mild skin irritant.

SIGNATURE PAGE

Report by: Tracy A. Filliben
Tracy A. Filliben
Toxicology Associate

Work by: Tracy A. Filliben
Tracy A. Filliben
Toxicology Associate

Reviewed and Approved for Issue: Tracy A. Filliben 8/30/96
Tracy A. Filliben
Study Director

TF/alw

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-21953 when applied to the shaved, intact 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, 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 Purina® Certified High Fiber Rabbit Chow® #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 assure 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 approximately 2 weeks. 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 2203 to 2403 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-21953 was applied directly on the test site beneath a 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. Two other test substances were tested concurrently on separate, localized test sites on these rabbits. In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration.

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 I). The adjacent areas of the untreated skin were used for comparison. In addition, the rabbits were observed for clinical signs of toxicity at each dermal evaluation.

RESULTS AND CONCLUSIONS

H-21953 produced slight erythema in 3 rabbits and mild erythema in 3 rabbits by 1 and 24 hours after test substance removal. By 48 hours, 1 rabbit was clear of all erythema, and 5 rabbits exhibited slight erythema. By 72 hours after the test substance was removed, 3 rabbits were clear of irritation, and 3 exhibited slight erythema. In addition, 2 rabbits exhibited desquamation at 48 hours, and 4 rabbits exhibited desquamation at 72 hours. No edema or clinical signs of toxicity were observed during the study. Individual skin irritation scores are presented in Table II. A summary of skin responses is presented in the following table.

Summary of Skin Responses to H-21953

Response	Erythema				Edema			
	1 hr	24 hr	48 hr	72 hr	1 hr	24 hr	48 hr	72 hr
No Response	0/6	0/6	1/6	3/6	6/6	6/6	6/6	6/6
Slight	3/6	3/6	5/6	3/6	0/6	0/6	0/6	0/6
Mild	3/6	3/6	0/6	0/6	0/6	0/6	0/6	0/6

Under the conditions of this study, H-21953 was a mild 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-21953 probably could be classified as "NON-IRRITANT" until further data is available.

TABLE I

DRAIZE¹ SCALE FOR SCORING PRIMARY SKIN IRRITATION

<u>Evaluation of Skin Reactions</u>	<u>Value</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:		
A = Abraded	F = Fissuring	L = Sloughing
I = Intact	N = Necrosis	R = Raw Areas
T = Thickening	G = Fissuring with	X = Compound Adhered
C = Eschar	Bleeding	to Skin
- = No Effect	S = Epidermal	SN = Superficial Necrosis
B = Blanching	Scaling	
D = Desquamation		

¹ 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 II**INDIVIDUAL SKIN IRRITATION SCORES****SKIN RESPONSES OBSERVED IN RABBITS**

Rabbit Number	Hours After Test Substance Removal							
	Erythema				Edema			
	1 hr	24 hr	48 hr	72 hr	1 hr	24 hr	48 hr	72 hr
31079	1	1	0	0	0	0	0	0
31083	2	2	1	0D	0	0	0	0
31080	1	1	1	1D	0	0	0	0
31081	2	2	1D	1D	0	0	0	0
31087	2	2	1	0	0	0	0	0
31091	1	1	1D	1D	0	0	0	0