

Study Title

Skin Irritation Test with H-21095 in Rabbits

Laboratory Project ID

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Author

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Performing Laboratory

E. I. du Pont de Nemours and Company
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Medical Research No. [REDACTED]

Company Sanitized. Does not contain TSCA CBI

GENERAL INFORMATION

<u>Substance Tested:</u>	[REDACTED]
<u>Synonyms/Codes:</u>	• H-21095 [REDACTED]
<u>Physical Form:</u>	Transparent tan liquid
<u>Composition:</u>	H-21095 contains: [REDACTED]
<u>Contaminants:</u>	None
<u>Purity:</u>	30%
<u>CAS Registry No.:</u>	None available
<u>Sponsor:</u>	DuPont Specialty Chemicals E. I. du Pont de Nemours and Company Wilmington, Delaware
<u>Study Initiated - Completed:</u>	3/20/95 - 4/26/95
<u>In Life Phase Initiated - Completed:</u>	3/21/95 - 3/24/95

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Skin Irritation Test with H-21095 in Rabbits

SUMMARY

H-21095 was evaluated for acute skin irritation potential in 6 male New Zealand White rabbits. A 0.5 mL aliquot of the test substance was applied to the shaved, intact skin of each rabbit and covered with a semi-occlusive dressing. The rabbits were exposed for 4 hours after which the test substance was removed. 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.

The test substance adhered to the skin of the rabbits; however, the test sites could still be evaluated. Slight to moderate erythema and no edema were observed in the rabbits by 1 hour after removal of the test substance. By 24 hours, slight or mild erythema and no to mild edema were observed. By 48 and 72 hours, the rabbits exhibited no or slight erythema and no edema. No clinical signs of toxicity were observed during this study.

Under the conditions of this study, H-21095 was a moderate skin irritant.

Work by:

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Reviewed and
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Acknowledgments: Bryan W. Crossley also participated in the conduct of this study.

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INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-21095 when applied to the shaved, intact skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male NM:(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 throughout the period while the animals were in cages.

Haske's Laboratory has an animal health monitoring program. This program is initiated and administered by the Laboratory Veterinarian. Animal samples are periodically analyzed for total bacterial counts and for the presence of coliforms, fungi, 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 quarterly weighed, and observed for general health for approximately 2 months. 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 $20^{\circ}\text{C} \pm 1^{\circ}$ 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 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 1930 to 2174 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. A 0.5 mL aliquot of H-21095 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. In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration. Up to 3 other test substances were tested concurrently on separate, localized test sites 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 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 observation.

C. Records Retention

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.

RESULTS AND CONCLUSIONS

The test substance adhered to the skin of the rabbits; however, the test sites could still be evaluated. H-21095 produced slight erythema in 4 rabbits, mild erythema in 1 rabbit, and moderate erythema in 1 rabbit by 1 hour after removal of the test substance. No edema was observed at 1 hour.

By 24 hours, 3 rabbits exhibited slight erythema but no edema, and 3 exhibited mild erythema and no to mild edema. By 48 hours, 2 rabbits exhibited no dermal irritation, and 4 exhibited slight erythema but no edema. By 72 hours, 3 rabbits exhibited no dermal irritation, and 3 exhibited slight erythema but no edema. No clinical signs of toxicity were observed during this 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-21095

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	2/6	3/6	6/6	4/6	6/6	6/6
Slight	4/6	3/6	4/6	3/6	0/6	1/6	0/6	0/6
Mild	1/6	3/6	0/6	0/6	0/6	1/6	0/6	0/6
Moderate	1/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6

Under the conditions of this study, H-21095 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-21095 probably could be classified as a "NON-IRRITANT" until further data is available.

SKIN IRRITATION TEST WITH H-21095

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 Bleeding	X = Compound Adhered to Skin
C = Eschar	S = Epidermal Scaling	SN = Superficial Necrosis
- = No Effect		
B = Blanching		

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.

SKIN IRRITATION TEST WITH H-21095

TABLE IIINDIVIDUAL SKIN IRRITATION SCORESSKIN RESPONSES OBSERVED IN RABBITS

Rabbit Number	Erythema				Edema			
	1 hr	24 hr	48 hr	72 hr	1 hr	24 hr	48 hr	72 hr
29985	2X ^a	2X ^a	1X ^a	1X ^a	0	0	0	0
29986	1X ^a	1X ^a	1X ^a	0X ^a	0	0	0	0
29987	1X ^a	1X ^a	0X ^a	0X ^a	0	0	0	0
29994	3X ^a	2X ^a	1X ^a	1X ^a	0	2	0	0
29995	1X ^a	2X ^a	1X ^a	1X ^a	0	1	0	0
29996	1X ^a	1X ^a	0X ^a	0X ^a	0	0	0	0

^a Although the test substance adhered to the skin of the rabbits, the test sites could be evaluated.