Study Title

Skin Irritation Test with H-21665 in Rabbits

Laboratory Project ID

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Author

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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
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[redacted]

GENERAL INFORMATION

Substance Tested: [redacted]

Synonyms/Other Codes:
- H-21665
- [redacted]

Physical Form: Yellowish 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

Study Initiated - Completed: 2/19/96 - 3/28/96

In Life Phase
Initiated - Completed: 2/20/96 - 2/23/96

SUMMARY

H-21665 was evaluated for acute skin irritation potential in 6 male New Zealand White rabbits. Approximately 0.5 mL of the test substance was applied directly 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.

The test sites felt sticky to the touch and therefore it was concluded that part of the test substance remained on the skin. H-21665 produced mild or moderate erythema and slight or mild edema by 1 hour after test substance removal. By 24 hours, moderate erythema and moderate edema were observed. By 48 and 72 hours after test substance removal, mild or moderate erythema and slight to moderate edema were observed. In addition, all rabbits exhibited desquamation at 72 hours. No clinical signs of toxicity were observed during the study.

Under the conditions of this study, H-21665 was a moderate skin irritant.

SIGNATURE PAGE

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INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-21665 when applied to the shaved, intact skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male 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°C ± 1°C and relative humidity of 50% ± 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 2220 to 2369 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-21665 was applied directly to the skin beneath a 2-inch, 4-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. In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration. Three 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 Ivory® soap and 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.

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 sites felt sticky to the touch and therefore it was concluded that part of the test substance remained on the skin. H-21665 produced mild erythema and slight edema in 3 rabbits, mild erythema and mild edema in 2 rabbits, and moderate erythema and mild edema in 1 rabbit by 1 hour after test substance removal. By 24 hours, 6 rabbits exhibited moderate erythema and moderate edema. By 48 hours, mild erythema and slight or mild edema were observed in 3 rabbits, and moderate erythema and mild or moderate edema were observed in 3 rabbits. By 72 hours after test substance removal, 5 rabbits exhibited mild erythema and slight or mild edema, and 1 rabbit exhibited moderate erythema and moderate edema; all rabbits exhibited desquamation. No clinical signs of toxicity were observed throughout 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-21665

	Erythema				Edema			
Response	1 hr	24 hr	48 hr	72 hr	1 hr	24 hr	48 hr	72 hr
No Response	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Slight	0/6	0/6	0/6	0/6	3/6	0/6	1/6	2/6
Mild	5/6	0/6	3/6	5/6	3/6	0/6	4/6	3/6
Moderate	1/6	6/6	3/6	1/6	0/6	6/6	1/6	1/6

Under the conditions of this study, H-21665 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-21665 probably should be classified as "IRRITANT" until further data is available.

TABLE I

DRAIZE[1] SCALE FOR SCORING PRIMARY SKIN IRRITATION

Evaluation of Skin Reactions	Value
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		D = Desquamation
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.

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
30732	2X	3X	2X	2XD	2	3	2	1
30737	3X	3X	2X	2XD	2	3	1	1
30742	2X	3X	3X	2XD	1	3	2	2
30743	2X	3X	3X	2XD	1	3	2	2
30746	2X	3X	2X	2XD	1	3	2	2
30747	2X	3X	3X	3XD	2	3	3	3

X = Test site felt sticky as though the test substance was still there.