

Study Title

Skin Irritation Test with H-21460 in Rabbits

Laboratory Project ID

Haskell Laboratory Report No. 83-96

Author

Tracy A. Filliben

Study Completed On

February 26, 1996

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

[REDACTED]

GENERAL INFORMATION

Substance Tested:

[REDACTED]

Synonyms:

• H-21460
[REDACTED]

Physical Form:

Yellow 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:

1/15/96 - 2/26/96

In Life Phase

Initiated - Completed:

1/16/96 - 1/18/96

Skin Irritation Test with H-21460 in Rabbits

SUMMARY

H-21460 was evaluated for acute skin irritation potential in 2 male and 4 female 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, and 48 hours after application 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-21460 produced slight or mild erythema by 1 hour after test substance removal. By 24 hours, no or slight erythema was observed. All dermal irritation had cleared in the treated rabbits by 48 hours after the test substance was removed. No edema and no clinical signs of toxicity were observed during the study.

Under the conditions of this study, H-21460 was a mild skin irritant.

SIGNATURE PAGE

Report by: Amy L. Williamson
Amy L. Williamson
Secretary

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

Reviewed and Approved for Issue: Tracy A. Filliben 2/26/96
Tracy A. Filliben
Study Director

TF/alw

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-21460 when applied to the shaved, intact skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male and 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 2 male and 4 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 2833 to 3263 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-21460 was applied directly on the skin 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. Three other 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, and 48 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

H-21460 produced slight erythema in 3 rabbits and mild erythema in 3 rabbits by 1 hour after test substance removal. By 24 hours, 4 rabbits were clear of dermal irritation; 2 rabbits exhibited slight erythema. All dermal irritation had cleared in the treated rabbits by 48 hours after the test substance was removed. No edema and no 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-21460

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

Under the conditions of this study, H-21460 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-21460 probably could be classified as "NON-IRRITANT" until further data is available.

SKIN IRRITATION TEST WITH H-21460

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-21460

TABLE II
INDIVIDUAL SKIN IRRITATION SCORES

SKIN RESPONSES OBSERVED IN RABBITS

Rabbit Number	Erythema			Edema		
	1 hr	24 hr	48 hr	1 hr	24 hr	48 hr
30562	1	0	0	0	0	0
30646	1	0	0	0	0	0
30650	1	0	0	0	0	0
30621	2	1	0	0	0	0
30654	2	0	0	0	0	0
30655	2	1	0	0	0	0