

Study Title

Skin Irritation Test with E-10913 in Rabbits

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Performing Laboratory

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[REDACTED]

Laboratory Project ID

Haskell Laboratory Report No. 28-93

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted according to EPA TSCA Good Laboratory Practice Standards (40 CFR 792). Any areas of noncompliance are documented in the study records. No deviations existed that affected the validity of the study.

Submitter: E. I. du Pont de Nemours and Company

**Sponsor: Du Pont Chemicals
E. I. du Pont de Nemours and Company**

Study Director:

John W. Sarver

John V. Sarver
Toxicologist

2 / 2 / 93

GENERAL INFORMATION

Substance Tested:

[REDACTED]

Synonyms/Codes:

• H-19913

[REDACTED]

Physical Form:

[REDACTED]

Composition:

[REDACTED]

Purity:

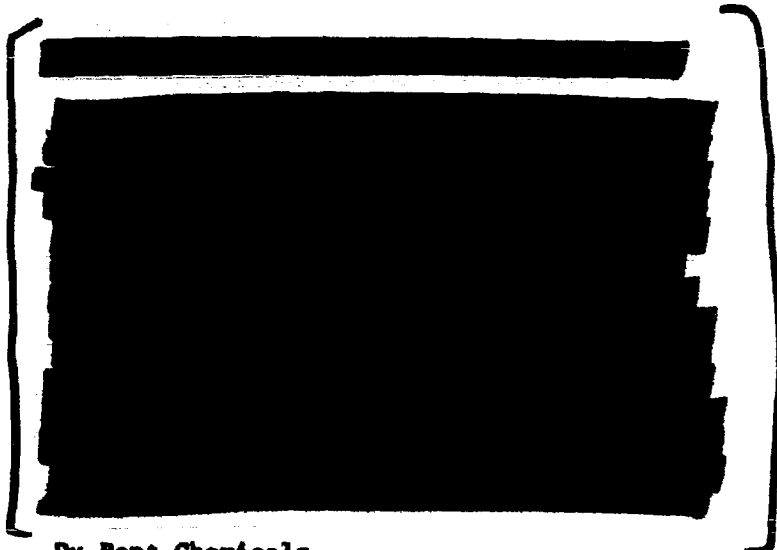
[REDACTED]

Submitter's Notebook No.:

[REDACTED]

GENERAL INFORMATION (CONT.)

CAS Registry No.:



Sponsor:

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

Study Initiated - Completed:

12/7/92 - 2/2/93

In Life Phase

Initiated - Completed:

12/8/92 - 12/11/92

Skin Irritation Test with H-19913 in Rabbits

SUMMARY

H-19913 was evaluated for acute skin irritation potential in 6 female rabbits. The test substance produced mild or moderate erythema and no or slight edema by 24 hours following application. By 48 hours slight to moderate erythema and no to mild edema were observed. By 72 hours the rabbits exhibited slight or mild erythema and no or mild edema.

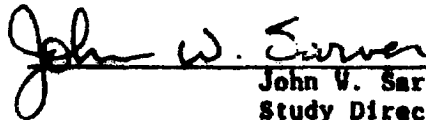
Under the conditions of this study, H-19913 was a moderate skin irritant.

Work by:



H. Scott Karr
Toxicology Technician

Reviewed and
Approved for Issue:



John W. Sarver
Study Director

2/2/93

Acknowledgements: Tracy Filliben and Bryan Crossley also participated in the conduct of this study.

JWS/alv

QUALITY ASSURANCE DOCUMENTATION
(H-19913)

Dates of Inspection:

Conduct - 12/8/92

Records, Report(s) - 1/26/93

Date(s) Findings Reported to:

Study Director - 1/26/93

Management - 2/1/93

Reported by: Donna R. Holt
Donna R. Holt
Quality Assurance Auditor

2/1/93
Date

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-19913 when applied to the shaved, intact skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult female New Zealand White rabbits were received from Hare Marland, Hewitt, New Jersey or Harleton Research Products, Denver, Pennsylvania. 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 rabbits were offered approximately 125 grams of Purina Certified High Fiber Rabbit Chow® #5325 daily during the study and water was available ad libitum except as noted under Protocol. 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 $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and relative humidity of $50\% \pm 10\%$. Any excursions outside these ranges were of small magnitude and/or brief duration and did not adversely affect 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 2947 to 3320 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. In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration. Approximately 0.5 mL of H-19913 was applied directly to a 2-inch gauze square that was then placed on the test site. The patch 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.

Approximately 24 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 24, 48, and 72 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 (Table I). The adjacent areas of the untreated skin were used for comparison. No other test substances were tested on these rabbits.

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 Du Pont Records Management Center, Wilmington, Delaware.

RESULTS AND CONCLUSIONS

H-19913 produced mild erythema with no edema in 5 rabbits and moderate erythema with slight edema in 1 rabbit by 24 hours following application. By 48 hours slight erythema with no edema was observed in 1 rabbit, mild erythema with no or slight edema was observed in 3 rabbits, and moderate erythema with slight or mild edema was observed in 2 rabbits. By 72 hours 2 rabbits exhibited slight erythema with no edema and 4 rabbits exhibited mild erythema with no or mild edema. 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-19913

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

Under the conditions of this study, H-19913 was a moderate skin irritant.

If these test scores are to be used for EEC/OSCD classification, according to the guide to the labeling of dangerous substances published in the Official Journal of European Communities (EEC Directive 83/467, Annex VI), H-19913 probably should be classified as an "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
B = Blanching	Scaling	Necrosis

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 TEST
RABBITS FOLLOWING TOPICAL EXPOSURE TO H-19913

<u>Rabbit Number</u>	<u>Erythema</u>			<u>Edema</u>		
	<u>24 hr</u>	<u>48 hr</u>	<u>72 hr</u>	<u>24 hr</u>	<u>48 hr</u>	<u>72 hr</u>
27558	2	3	2	0	2	0
27659	2	3	2	0	1	0
27662	2	2	2	0	0	0
27663	3	2	2	1	1	2
27664	2	2	1	0	0	0
27665	2	1	1	0	0	0