

TRADE SECRET

Study Title

H-23269: SKIN IRRITATION TEST IN RABBITS

LABORATORY PROJECT ID: DUPONT-1139

AUTHOR: Carol Finlay, B.A.

STUDY COMPLETED ON: July 21, 1998

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 19714-0050

[REDACTED]

~~Company Sanitized. Does not contain TSCA CBI~~

CERTIFICATION

I, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

Issued by: _____

Carol Finlay

Carol Finlay, B.A.
Toxicology Associate
Study Director

*7/21/98*_____
Date

Company Sanitized. Does not contain TSCA CBI

STUDY INFORMATION

Substance Tested:



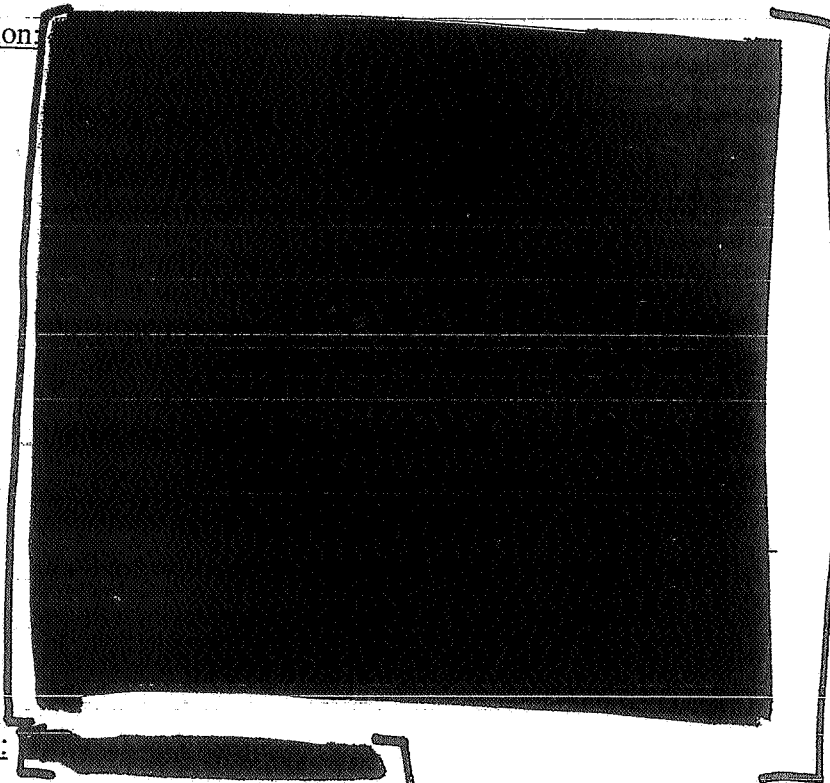
Synonyms/Codes: • H-23269

Haskell Number: 23269

Submitter's Notebook Number(s):



Composition:



Known Impurities:



Physical Characteristics: White fabric

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Company Sanitized. Does not contain TSCA CBI

STUDY INFORMATION (CONT.)

Study Initiated/Completed: June 8, 1998 / (see report cover page)

In-Life Initiated/Completed: June 9, 1998 / June 12, 1998

Company Sanitized. Does not contain TSCA CBI

STUDY PERSONNEL

Study Director: Carol Finlay, B.A.

Management: Judith C. Stadler, Ph.D.

Primary Technician: Carol Finlay, B.A.

Toxicology Report Preparation: Bonnie J. Bieber, B.S.

Laboratory Veterinarian: Charles E. Cover, V.M.D.

Company Sanitized. Does not contain TSCA CBI

SUMMARY

H-23269 was evaluated for acute skin irritation potential in 6 male New Zealand White rabbits. H-23269 was tested dry and wet on intact and abraded skin. An approximately 1-inch square of the test substance was applied directly on the skin beneath a 1-ply 1-inch gauze square that was held in place with non irritating tape 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.

No dermal irritation was observed on any test site during the study. No clinical signs of toxicity or body weight losses were observed during the study.

Under the conditions of this study, H-23269 was not a skin irritant.

Company Sanitized. Does not contain TSCA CBI

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-23269 when applied to the shaved, intact or abraded 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. 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 PMI Nutrition International, Inc. Certified High Fiber Rabbit LabDiet® 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 ensure 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 13 days. This exceeded the laboratory standard of approximately 1 week because the rabbits were not released from quarantine as early as they could have been. 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 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 2108 to 2296 grams on the day of treatment.

Company Sanitized. Does not contain TSCA CBI

H-23269 was tested dry and wet on intact and abraded skin. Deionized water was used to thoroughly moisten the samples that were tested wet.

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. The 2 test sites on one side of the rabbits were abraded by gently dragging the abrader across the skin. No bleeding was observed. The 2 test sites on the other side of the rabbits remained intact. An approximately 1-inch square of H-23269 was applied directly on the skin beneath a 1-ply 1-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. No other substances were tested 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. 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 1). The adjacent areas of the untreated skin were used for comparison. The rabbits were also examined for clinical signs of toxicity at every dermal evaluation.

RESULTS AND DISCUSSION

No dermal irritation was observed on any test site during the study. No clinical signs of toxicity or body weight losses were observed during the study.

Individual skin irritation scores are presented in Tables 2 through 5. A summary of skin responses is presented in the following table.

SUMMARY OF SKIN RESPONSES TO H-23269

RESPONSE	ERYTHEMA				EDEMA			
	1 hour	24 hours	48 hours	72 hours	1 hour	24 hours	48 hours	72 hours
No Response	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6

CONCLUSIONS

Under the conditions of this study, H-23269 was not a 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-23269 probably should not be classified as an irritant unless further data proves otherwise.

RECORDS AND SAMPLE STORAGE

Specimens (if applicable), raw data, and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware (formerly known as the E.I. du Pont de Nemours and Company Records Management Center).

~~Company Sanitized~~ Does not contain TSCA CB

TABLE 1

DRAIZE^a SCALE FOR SCORING SKIN IRRITATION

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

^a 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 2

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

INTACT SKIN/SAMPLE TESTED DRY

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
32921	0	0	0	0	0	0	0	0
32922	0	0	0	0	0	0	0	0
32923	0	0	0	0	0	0	0	0
32926	0	0	0	0	0	0	0	0
32927	0	0	0	0	0	0	0	0
32928	0	0	0	0	0	0	0	0

TABLE 3

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

INTACT SKIN/SAMPLE TESTED WET

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
32921	0	0	0	0	0	0	0	0
32922	0	0	0	0	0	0	0	0
32923	0	0	0	0	0	0	0	0
32926	0	0	0	0	0	0	0	0
32927	0	0	0	0	0	0	0	0
32928	0	0	0	0	0	0	0	0

Company Sanitized. Does not contain TSCA CB4

TABLE 4

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

ABRADED SKIN/SAMPLE TESTED DRY

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
32921	0	0	0	0	0	0	0	0
32922	0	0	0	0	0	0	0	0
32923	0	0	0	0	0	0	0	0
32926	0	0	0	0	0	0	0	0
32927	0	0	0	0	0	0	0	0
32928	0	0	0	0	0	0	0	0

TABLE 5

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

ABRADED SKIN/SAMPLE TESTED WET

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
32921	0	0	0	0	0	0	0	0
32922	0	0	0	0	0	0	0	0
32923	0	0	0	0	0	0	0	0
32926	0	0	0	0	0	0	0	0
32927	0	0	0	0	0	0	0	0
32928	0	0	0	0	0	0	0	0

Company Sanitized. Does not contain TSCA CB