TRADE SECRET

AR226-3085

Study Title

H-23004: SKIN IRRITATION TEST IN RABBITS

LABORATORY PROJECT ID: HL-1997-01294

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STUDY COMPLETED ON: December 30, 1997

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

WORK REQUEST NUMBER: [redacted]

CERTIFICATION

Study Director:

Issued by: Tracy A. Filliben 12/30/97

Tracy A. Filliben
Toxicology Associate

Date

STUDY INFORMATION

Substance Tested: [redacted]

Synonyms/Codes: • H-23004

Haskell Number: 23004

Submitter's Notebook Number(s): [redacted]

Composition: [redacted]

Known Impurities: [redacted]

Physical Characteristics: Off-white liquid

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.

Study Initiated/Completed: November 25, 1997 / (see report cover page)

In-Life Initiated/Completed: November 26, 1997 / November 29, 1997

STUDY PERSONNEL

Manager(s):	Judith C. Stadler, Ph.D.
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SUMMARY

H-23004 was evaluated for acute skin irritation potential in 6 New Zealand White rabbits. Approximately 0.5 mL of the test substance was applied 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 75 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.

One rabbit exhibited no dermal irritation during the study. The remaining 5 rabbits exhibited slight erythema at 1 hour and no or slight erythema at 24 and 48 hours. All dermal irritation had cleared in the treated rabbits by 75 hours after test substance removal. No edema or clinical signs of toxicity were observed in any of the rabbits during the study.

Under the conditions of this study, H-23004 was a slight skin irritant.

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-23004 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. 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 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 approximately 1 week. 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 1 male and 5 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 2625 to 3128 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-23004 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. Two 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 75 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

One rabbit exhibited no dermal irritation during the study. By 1 hour after test substance removal, the remaining 5 rabbits exhibited slight erythema. Three additional rabbits were clear of all dermal irritation by 24 hours. Slight erythema was observed in the remaining 2 rabbits at 24 and 48 hours and was clear by 75 hours. No edema or clinical signs of toxicity were observed during the study. Individual skin irritation scores are presented in Table 2. A summary of skin responses is presented in the following table.

SUMMARY OF SKIN RESPONSES TO H-23004

	ERYTHEMA				EDEMA			
RESPONSE	1 hour	24 hours	48 hours	75 hours	1 hour	24 hours	48 hours	75 hours
No Response	1/6	4/6	4/6	6/6	6/6	6/6	6/6	6/6
Slight	5/6	2/6	2/6	0/6	0/6	0/6	0/6	0/6

CONCLUSIONS

Under the conditions of this study, H-23004 was a slight 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-23004 probably should not be classified as an irritant unless further data proves otherwise.

RECORDS RETENTION

All study records, raw data, and the final report are retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain, 200 Todds Lane, Wilmington, Delaware 19802 (formerly known as the E. I. du Pont de Nemours and Company Records Management Center).

TABLE 1

DRAIZE[a] SCALE FOR SCORING SKIN IRRITATION

Evaluation of Skin Reactions	Score
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		
D = Desquamation		

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

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	75	1	24	48	75
32186	1	0	0	0	0	0	0	0
32402	0	0	0	0	0	0	0	0
32381	1	0	0	0	0	0	0	0
32406	1	1	1	0	0	0	0	0
32407	1	0	0	0	0	0	0	0
32410	1	1	1	0	0	0	0	0