TRADE SECRET

Study Title

H-23773 and H-23775: Skin Irritation Test in Rabbits

Laboratory Project ID: DuPont-2121

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STUDY COMPLETED ON: February 19, 1999

PERFORMING LABORATORY: E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
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[redacted]

CERTIFICATION

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

Reviewed by: Tracy A. Filliben 19-Feb-1999
Tracy A. Filliben
Toxicology Associate
Date

Issued by Study Director: Carol Finlay 19-Feb-1999
Carol Finlay, B.A.
Toxicology Associate
Date

STUDY INFORMATION

Substance Tested: [redacted]

Synonyms/Codes: • H-23773

Haskell Number: 23773

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

Composition: [redacted]

Known Impurities: [redacted]

Physical Characteristics: White fabric

Substance Tested: [redacted]

Synonyms/Codes: • H-23775

[redacted]

Haskell Number: 23775

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

Composition: [redacted]

Known Impurities: [redacted]

Physical Characteristics: White fabric

Stability: The test substances 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: January 11, 1999 / (see report cover page)

In-Life Initiated/Completed: January 12, 1999 / January 15, 1999

STUDY PERSONNEL

Study Director: Carol Finlay, B.A.
Management: Judith C. Stadler, Ph.D.
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Toxicology Report Preparation: Lisa G. Burchfield, A.A.

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SUMMARY

H-23773 was evaluated for acute skin irritation potential in 5 male New Zealand White rabbits. H-23775 was evaluated for acute skin irritation potential in 6 male New Zealand White rabbits. A 1-inch square of each test substance was applied directly on the skin on opposite sides of each rabbit beneath a 2-ply, 1-inch gauze square. The gauze square was held in place with non-irritating tape for a 4-hour exposure. Approximately 1, 24, 48, and 72 hours after test substance removal, 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-23773 produced no dermal irritation in 3 rabbits throughout the study. The remaining 2 rabbits exhibited no dermal irritation at 1 hour and slight or mild erythema 24 hours after test substance removal. At 48 hours, all dermal irritation had cleared in 1 rabbit; slight erythema was observed in the other rabbit. No dermal irritation was observed at 72 hours. No edema was observed.

H-23775 produced no dermal irritation in 5 rabbits throughout the study. The remaining rabbit exhibited no dermal irritation at 1 hour, mild erythema and mild edema at 24 and 48 hours, and no dermal irritation at 72 hours. Two rabbits exhibited a scratch on the test site during the study.

No significant weight loss or clinical signs of toxicity were observed.

Under the conditions of this study, H-23773 and H-23775 were both mild skin irritants.

INTRODUCTION

The purpose of this study was to evaluate the skin irritation potential of H-23773 and H-23775 when applied to separate, localized test sites on the shaved, intact skin of New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult 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 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 14 days. 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 2192 to 2512 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. Both test substances were thoroughly moistened with deionized water prior to treatment. A 1-inch square of H-23773 and a 1-inch square of H-23775 were applied directly to the skin on opposite sides of each rabbit beneath 2-ply, 1-inch gauze squares that were 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. One other substance was tested on a separate, localized test site on the backs of 2 of these rabbits.

Approximately 4 hours after application of the test substances, 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.

The gauze square and square of H-23773 became dislodged from the test site of 1 rabbit. This test site was not evaluated. 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

H-23773 produced no dermal irritation in 3 rabbits throughout the study. The remaining 2 rabbits exhibited no dermal irritation at 1 hour and slight or mild erythema at 24 hours after test substance removal. At 48 hours, all dermal irritation had cleared in 1 rabbit; slight erythema was observed in the other rabbit. No dermal irritation was observed at 72 hours. No edema was observed.

H-23775 produced no dermal irritation in 5 rabbits throughout the study. The remaining rabbit exhibited no dermal irritation at 1 hour, mild erythema and mild edema at 24 and 48 hours, and no dermal irritation at 72 hours. Two rabbits exhibited a scratch on the test site during the study.

No significant weight loss or clinical signs of toxicity were observed.

Individual skin irritation scores are presented in Tables 2 and 3. A summary of skin responses is presented in the following table.

SUMMARY OF SKIN RESPONSES TO H-23773

	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
RESPONSE	1	24	48	72	1	24	48	72
No Response	5/5	3/5	4/5	5/5	5/5	5/5	5/5	5/5
Slight	0/5	1/5	1/5	0/5	0/5	0/5	0/5	0/5
Mild	0/5	1/5	0/5	0/5	0/5	0/5	0/5	0/5

SUMMARY OF SKIN RESPONSES TO H-23775

	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
RESPONSE	1	24	48	72	1	24	48	72
No Response	6/6	5/6	5/6	6/6	6/6	5/6	5/6	6/6
Slight	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Mild	0/6	1/6	1/6	0/6	0/6	1/6	1/6	0/6

CONCLUSIONS

Under the conditions of this study, H-23773 and H-23775 were both mild skin irritants.

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-23773 or H-23775 probably should not be classified as irritants 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).

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:

- = No Effect		I = Intact	
A = Abraded		L = Sloughing	
B = Blanching		N = Necrosis	
C = Eschar		R = Raw Areas	
D = Desquamation		S = Epidermal Scaling	
F = Fissuring		T = Thickening	
G = Fissuring with Bleeding		X = Compound Adhered to Skin	
H = Hyperkeratosis			

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

H-23773

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
33354	a	a	a	a	a	a	a	a
33355	0	0	0	0	0	0	0	0
33358	0	0	0	0	0	0	0	0
33359	0	0	0	0	0	0	0	0
33360	0	1	0	0	0	0	0	0
33361	0	2	1	0	0	0	0	0

a The patch became dislodged during the exposure period.

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL			
	OTHER DERMAL EFFECTS			
	1	24	48	72
33354	-	-	-	-
33355	-	-	-	-
33358	-	-	-	-
33359	-	-	-	-
33360	-	-	-	-
33361	-	-	-	-

Symbol is defined on page 10.

TABLE 3

INDIVIDUAL SKIN IRRITATION SCORES AND
SKIN RESPONSES OBSERVED IN RABBITS

H-23775

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL							
	ERYTHEMA				EDEMA			
	1	24	48	72	1	24	48	72
33354	0	0	0	0	0	0	0	0
33355	0	0	0	0	0	0	0	0
33358	0	0	0	0	0	0	0	0
33359	0	2	2	0	0	2	2	0
33360	0	0	0	0	0	0	0	0
33361	0	0	0	0	0	0	0	0

RABBIT NUMBER	HOURS AFTER TEST SUBSTANCE REMOVAL			
	OTHER DERMAL EFFECTS			
	1	24	48	72
33354	-	-	-	-
33355	-	-	-	-
33358	-	-	-	-
33359	-	-	-	-
33360	-	a	a	a
33361	-	a	a	a

a Scratch on test site.
Symbol is defined on page 10.