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E. I. du Pont de Nemours and Company Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50
Newark, Delaware 19714

HASKELL LABORATORY REPORT NO. HLO-388-84 [redacted]

Material tested* [redacted]

Haskell No. 15,388

Other Codes [redacted]

Study Initiated/Completed
6/12/84 - 6/15/84

Material Submitted by
[redacted]
Polymer Products Department
Washington Works

SKIN IRRITATION TEST ON RABBITS

Haskell Evaluation: Haskell Standard Operating Procedure for skin irritation testing was followed [redacted] Details are given in the appendix. [redacted] was applied to the occluded skin of six rabbits for 24 hours and produced moderate erythema in five of six rabbits and mild erythema in the sixth. Effects appeared reversible. When tested by this procedure, [redacted] is a moderate skin irritant.

*Purity: [redacted]

*Composition: [redacted]

*Synonyms: [redacted]

Report by:

Carol S. Auletta/Ira W. Daly
Bio/dynamics Inc.

Reviewed by:

George W. Lovett, M.D.
Skin and Eye Studies Coordinator

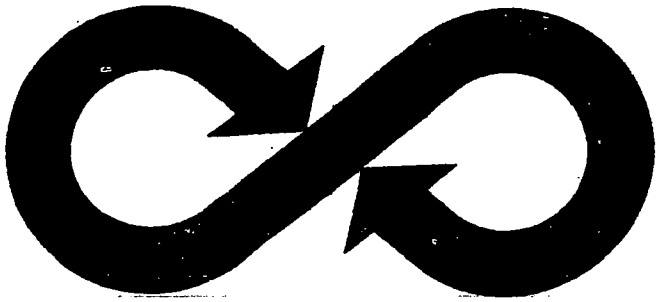
Gerald L. Kennedy Jr.
Section Supervisor
Acute Investigations

Approved by:

Frank A. Bower
Associate Director

GWL/egg

Date Issued: August 30, 1984
Haskell Lab. Report No. HLO-388-84
Appendix attached: 8 pp, Bio/dynamics Project No. 5228-84
Total pages in this report: 10



Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO.: 5228-84

PRIMARY DERMAL IRRITATION STUDY IN RABBITS
(HASKELL SKIN IRRITATION TEST)

TEST MATERIAL: HL 15,388

Submitted to: E.I. duPont de Nemours & Co.
Haskell Laboratory for Toxicology
and Industrial Medicine
P.O. Box 50, Elkton Road
Newark, Delaware 19711

Attn: [redacted]

Date: August 13, 1984

I. INTRODUCTION

This study was conducted for E.I. duPont de Nemours & Co. to evaluate the primary dermal irritation produced by HL 15,388 in rabbits. The study was performed at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and raw data. All raw data, the original study protocol and final report will be retained on file in the Bio/dynamics Archives.

II. DATES OF STUDY

Animal Receipt:	May 7, 1984
Initiation (Dosing):	June 12, 1984
Termination (Last Observation):	June 15, 1984

III. STUDY PERSONNEL

Study Director:	Carol S. Auletta, B.A., D.A.B.T.
Laboratory Supervisor:	Donna L. Blaszcak, B.S., AALAS L.A.Tg.
Technician-in-Charge:	Dawn Areia, B.A., AALAS L.A.T.
Study Monitor (Report Preparation):	Donna L. Blaszcak, B.S., AALAS L.A.Tg.

IV. MATERIALS

A. Test Animals:	Albino Rabbits
Breed:	New Zealand White
Reason for Selection:	Standard laboratory animal for dermal irritation studies. The New Zealand White breed was used because of its availability and because of the existing historical data base for comparative evaluation.
Supplier:	Hazleton-Dutchland, Inc. Denver, Pennsylvania

IV. MATERIALS (cont.)

Number:	Six (2 males, 4 females)
Age:	Young adults
Weight: (Pretest)	3.0 to 3.2 kilograms
Equilibration Period:	36 days
Husbandry:	Currently acceptable practices of good animal husbandry were followed, e.g., Guide for the Care and Use of Laboratory Animals; DHEW Publication No. (NIH) 78-23 Revised 1978.
Housing:	Individually housed
Cages:	Suspended, stainless steel.
Environmental Conditions:	Temperature: 60-70°F is considered an acceptable temperature range for rabbits; room temperature was monitored and recorded twice daily and maintained within this range to the maximum extent possible. Humidity: 30-70% is considered an acceptable humidity range for rabbits; room humidity was monitored and recorded daily and maintained within this range to the maximum extent possible. Light Cycle: 12 hours light, 12 hours dark (controlled by an automatic timer).
Food:	Lab Rabbit Chow HF (Purina #5326), ad libitum.
Water:	Automatic watering system, ad libitum. Municipal water supply (Elizabethtown Water Co.)
Identification:	Each animal was identified with a monel ear tag bearing a unique number prior to testing.

IV. MATERIALS (cont.)

Selection:	Animals were randomly placed in cages upon receipt and were placed on study as available at the time of study initiation. Animals considered unsuitable for study because of poor health, unacceptable skin, or outlying body weights were excluded from selection.
B. Test Material:	HL 15,388
Description:	White powder
Date of Receipt:	May 21, 1984
Received from:	E.I. duPont de Nemours & Co.
Storage:	Room temperature

V. METHODS

A. Preparation of Test Material:

The test material was mixed with 0.9% saline to form a slurry.

B. Preparation of Animals:

On the day before dosing, the hair of each rabbit was closely clipped from the back with an electric clipper, so as to expose the back from the scapular to the lumbar region. The skin remained intact, i.e., no abrasions were made.

C. Administration of Test Material:

There was one test site on the back of each animal. 0.5 ml of the test material (as a slurry) was applied to each site beneath a surgical gauze square, 1"x1", placed directly on the test site and held in place with tape. Plastic sheeting was then wrapped around the animal and secured with tape to retard evaporation and keep the test substance in contact with the skin without undue pressure. Elizabethan collars were then placed on the animals to prevent disruption of the wrappings and ingestion of the test material.

Following approximately 24 hours of exposure, the wrappings and gauze squares were removed and the test sites gently wiped free of excess test material with gauze and water and dried with gauze.

VI. EXPERIMENTAL EVALUATION (In-Life)

Viability Check: Twice Daily

Evaluation of Skin Irritation:

1. Intervals:

Approximately 24.5 (30 minutes after removal of wrappings), 48 and 72 hours after administration.

2. Methods:

At each interval all sites were evaluated for erythema and edema or other evidence of dermal irritation according to the Draize scoring system (presented in Appendix A). Adjacent areas of untreated skin was used for comparison. Special notation was made of necrosis, eschar, or other evidence of irreversible alteration of tissue structure. Any abnormal pharmacologic or toxic signs were also noted.

VII. RESULTS AND DISCUSSION

Dermal observations are presented in Table I; the scoring system used is presented in Appendix A.

HL 15,388 produced moderate to severe but reversible dermal irritation. Most of the animals had moderate to severe erythema with slight edema at 24.5 hours and very slight or well-defined erythema and edema at 48 hours. By the termination of the study (72 hours) most animals exhibited only slight erythema, with little or no edema.

Carol S. Auletta, B.A., D.A.B.T.
Study Director
Manager, Acute Toxicology

4/13/84
Date

Ira W. Daly, Ph.D., D.A.B.T.
Director of Toxicology

4/15/84
Date

TABLE I

PRIMARY DERMAL IRRITATION STUDY IN RABBITS

TEST MATERIAL: HL 15,388

INDIVIDUAL DERMAL IRRITATION SCORES[a] - 24.5, 48 AND 72 HOURS

Time Interval	Patch Sites & Observations		Animal Number and Sex					
			3924F	3925M	3238F	3941M	3944F	3928F
24.5 Hours	Left Front	ER	3	3	3	2	3	3
	Right Back	ED	2	1	2	2	2	2
48 Hours	Left Front	ER	2	2	2	1	1	1
	Right Back	ED	1	1	2	1	0	1
72 Hours	Left Front	ER	1	1	2	1	0	1
	Right Back	ED	0	1	1	1	0	0

[a]Scored using scale presented in Appendix A.
M-Male
F-Female
ER-Erythema
ED-Edema

APPENDIX A

DRAIZE[1] EVALUATION OF DERMAL IRRITATION

Dermal Observations

Erythema and Eschar Formation (Most severely affected area graded):

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness)	4
Eschar formation	4E
Necrosis	4N

Edema Formation (Most severely affected area graded):

No edema	0
Very slignt edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

[1]Draize, J.H. 1959. The Appraisal of Chemicals in Foods, Drugs, and Cosmetics, p. 48. Association of Food and Drug Officials of the United States, Austin, Texas.