



HAZLETON
LABORATORIES AMERICA, INC.
3301 KINSMAN BLVD., P.O. BOX 7545
MADISON, WI 53707 USA

FINAL REPORT

Karen Armstrong
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Toxicology Services
Building 220-2E-02
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HLA Number: 91201740

Sample: T-4416

Enclosed: Primary Dermal Irritation/Corrosion Study in Rabbits
(OECD Guidelines)

- o Key Personnel
- o Methodology
- o Summary of Results
- o References
- o Raw Data Appendix

Signed:



Steven M. Glaza
Study Director
Acute Toxicology

Date

2-14-90



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KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Section Supervisor

Steven R. Sorenson
Study Coordinator

Patricia Padgham
Group Leader

Sharen L. Howery
Report Coordinator

Quality Assurance

Deborah L. Keller
Manager

Laboratory Animal Veterinarian

Cindy J. Cary, DVM
Diplomate, ACLAM



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METHODOLOGY

Objective: To determine the relative level of primary skin irritation/corrosion of a test material on rabbits under semioccluded conditions according to the Organization for Economic Cooperation and Development's Guidelines for Testing Chemicals.¹

Test Material: T-4416

Physical Description: Clear colorless liquid

Purity and Stability: Sponsor assumes responsibility for purity and stability determinations (including under test conditions).

Storage and Retention: The test material was stored at room temperature. Any unused material will be returned to the Sponsor according to HLA Standard Operating Procedure.

Safety Precautions: Normal handling procedures were used according to HLA Standard Operating Procedure.

Test Animal: Young adult albino rabbits, Hra:(NZW)SPF, were procured, maintained individually in screen-bottom cages in temperature- and humidity-controlled quarters, provided access to water ad libitum and a measured amount of High Fiber Rabbit Chow® 5326, Purina Mills, Inc., and held for an acclimation period of at least 7 days. Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals".² If variations from the prescribed environmental conditions existed, they were documented and considered to have no effect on the study outcome. No contaminants were expected to have been present in the feed or water which would have interfered with or affected the results of the study.

Three acclimated animals, weighing from 2040 to 2247 g, were chosen at random for the test, treated, and maintained during the observation period as specified for the acclimation period. Test animals were identified by animal number and corresponding ear tag. Within 24 hours prior to treatment the hair was clipped from the back and flanks of each animal.

Reason for Species Selection: Historically, the New Zealand White albino rabbit has been the animal of choice for evaluating the effect of chemicals on the skin.

Preparation of Test Material: The sample was dosed as received. The pH was determined to be 9.9.



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Treatment: The test material was applied to the intact skin of each rabbit in the amount of 0.5 mL. The treated area was covered with a 2.5- x 2.5-cm gauze patch secured with paper tape, loosely overwrapped with Saran Wrap® and secured with Elastoplast® tape to provide a semioclusive dressing. Collars were applied to restrain the test animals for the 4-hour exposure period.

Reason for Route of Administration: Historically, this is the route of choice based on the method of Draize.³

Observations: After the exposure period, the patches were removed. The test sites were washed using lukewarm tap water and disposable paper towels. The test material was removed from the test sites as thoroughly as possible without irritating the skin. Thirty minutes following removal of the test material, the degree of erythema and edema was read according to the Draize technique. Subsequent examinations were made at 24, 48, and 72 hours after patch removal.

Individual body weights were taken just prior to study initiation.

Termination: At termination of the experimental phase, all animals were euthanatized and discarded.

Statistical Methods: No statistical method was performed.

Location of Raw Data and Final Report: The raw data and a copy of the final report will be retained in the archives of HLA.



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SUMMARY OF RESULTS

Test Animal: Albino Rabbits - Hra:(NZW)SPF
Source: Hazleton Research Products, Inc., Denver PA
Date Animals Received: 12/19/89

Start Date (In-life): 01/09/90

End Date (In-Life): 01/12/90

Individual Dermal Irritation Scores

Animal Number	Sex	Erythema (Hour)				Edema (Hour)			
		4	24	48	72	4	24	48	72
F31148	M	1	1	0	0	0	0	0	0
F31141	F	0	0	0	0	0	0	0	0
F31147	F	0	0	0	0	0	0	0	0

Average Primary Dermal Irritation Scores*

Observation Period (Hour)	Average Score
4	0.3
24	0.3
48	0.0
72	0.0

- * The average primary dermal irritation score is the total dermal irritation score for all the animals (erythema and edema) divided by the number of test sites (3) at each observation period.



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REFERENCES

1. "Acute Dermal Irritation/Corrosion," *Organization for Economic Cooperation and Development's Guidelines for Testing of Chemicals*, Section 404 (adopted May 12, 1981).
2. NIH Publication 86-23 (revised 1985).
3. Draize, J. H., "Primary Irritation of the Skin," In: *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity*, Association of Food and Drug Officials of the U.S., pp. 46-47 (1975).

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PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Becky Beckwith	Lab Animal Technician	<u>Becky Beckwith</u>	<u>BB</u>
Ann Bursaw	Sr. Clerk	<u>Ann Bursaw</u>	<u>AB</u>
Anthony Cass	Lab Animal Assistant	<u>Anthony Cass</u>	<u>AC</u>
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	<u>CJ</u>
Kari Gassen	Sr. Lab Animal Assistant	<u>Kari Gassen</u>	<u>KG</u>
Steven M. Glaza	Section Supervisor	<u>Steven M. Glaza</u>	<u>SG</u>
Ben Haley	Sr. Lab Animal Assistant	<u>Ben Haley</u>	<u>BH</u>
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	<u>JH</u>
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	<u>SLH</u>
Jim Jirschele	Lab Animal Assistant	<u>Jim Jirschele</u>	<u>JJ</u>
Wayne Madison	Senior Section Supervisor	<u>Wayne R. Madison</u>	<u>WM</u>
Bud McDonald	Sr. Lab Animal Assistant	<u>Bud McDonald</u>	<u>BM</u>
Eileen McConnell	Administrative Clerk	<u>Eileen McConnell</u>	<u>EM</u>
Henry Mikula	Lab Animal Assistant	<u>Henry Mikula</u>	<u>HM</u>
Albert Oleson	Sr. Lab Animal Assistant	<u>Albert Oleson</u>	<u>AO</u>
Patricia Padgham	Group Leader	<u>Patricia Padgham</u>	<u>PP</u>
Jane Polnow	Lab Animal Technician	<u>Jane Polnow</u>	<u>JP</u>
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	<u>SRS</u>
Dawn Thieding	Clerk	<u>Dawn Thieding</u>	<u>DT</u>
Annette R. Turner	Sr. Clerk	<u>Annette R. Turner</u>	<u>AT</u>
<u>KEVIN BRIDGES</u>	<u>Sr. Lab Animal Asst.</u>	<u>Kevin Bridges</u>	<u>KB</u>

(09/11/89)

DERMAL IRRITATION/BODY WEIGHT RECORD

(1-Hour Exposure)

Study Title: Primary Dermal Irritation

Test Material: T-4416

Physical Description: Clear Colorless Liquid

Dose: 0.5 ml Per Site NA Moistened with 0.5% Saline

Date Animals Received: 12/9/89 Source/Strain/Species: Marleton Research Products/New Zealand White/Habibit Room Number: 104

Technician/Date Animals Clipped: AB / 1/8/90 Initiated by: AB Date: 1/9/90

Skin Preparation: ✓ Intact NA Anesthetized (with a clipper blade) Reviewed by: SAS Date: 1-9-90

pH Result: 9.9 with COPPING OH METER NO. 05510

Animal Number/Sex	F3	1148	♂	1141	♀	1147	♀	Technician	Recorded by	1990 Date	KTRON Scale used:
Initial Body Weight (g)		2178		2040		2247		DB	DB	1/9	40021
7-Day Body Weight (g)											
14-Day Body Weight (g)											
21-Day Body Weight (g)											
Observation Period											
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PRIMARY DERMAL IRRITATION SCORING SCALE
(DRAIZE¹ TECHNIQUE)

(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	<u>4</u>
Highest possible erythema score	4

(2) Edema Formation

No edema	0
Very slight 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)	<u>4</u>
Highest possible edema score	4

¹ Draize, J. H., "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics - Dermal-Toxicity." Association of Food and Drug and Drug Officials of the U.S., pp. 46-59 (1975).