

**HAZLETON**

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

FINAL REPORT

ROGER G. PERKINS
MINNESOTA MINING & MANUFACTURING COMPANY
TOXICOLOGY SERVICES
ST. PAUL, MN 55101

SAMPLE NUMBER: 70100354

SAMPLE ENTERED: 01/07/87

REPORT PRINTED: 02/26/87

SAMPLE: T-4016

PURCHASE ORDER NUMBER: T837389-410 712

ENCLOSED: PRIMARY DERMAL IRRITATION STUDY IN RABBITS - METHOD, SUMMARY
RAW DATA APPENDIX

SIGNED:

STEVEN M. GLAZA
STUDY DIRECTOR
ACUTE TOXICOLOGY

DATE

.....~~2-27-86~~ 2-27-87.
50 2-27-87

BY AND FOR HAZLETON LABORATORIES AMERICA, INC.

RAW DATA FOR THIS STUDY ARE KEPT ON FILE AT HAZLETON LABORATORIES
AMERICA, INC., MADISON, WISCONSIN.



SAMPLE NUMBER: 70100354

PAGE 2

SAMPLE: T-4016

PRIMARY DERMAL IRRITATION

Objective: To determine the relative level of primary skin irritation of a test material on rabbits under occluded conditions according to the Federal Hazardous Substances Act Regulations.

Test Material: T-4016

Physical Description: Thick brown liquid

Purity and Stability: Sponsor assumes responsibility for purity and stability determinations.

Test Animal: Young adult rabbits of the New Zealand White strain 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 Purina High Fiber Rabbit Chow, and held for an acclimation period of at least 7 days.

Three male and three female acclimated animals, weighing from 2414 g to 2738 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. Approximately twenty-four hours before 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 and Administration of Test Material: The sample was dosed as received. The pH was not determined.

Treatment: Just before the test material was applied, crisscross epidermal abrasions were made on one exposed area of each rabbit to provide one abraded and one intact test site. (The abrasions were sufficiently deep to penetrate the stratum corneum, but not deep enough to penetrate to the dermal layer and cause bleeding.)

The test material was applied to the two test sites on each rabbit in the amount of 0.5 ml per site. Each treated area was covered with a 5.0 x 5.0-cm gauze patch secured with paper tape and overwrapped with Saran Wrap and Elastoplast tape to maintain the test material in contact with the skin and decrease the rate of evaporation. Collars were used to restrain the test animals during the 24-hour exposure period.

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

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SAMPLE NUMBER: 70100354

PAGE 3

SAMPLE: T-4016

PRIMARY DERMAL IRRITATION

(CONTINUED)

Observations: After the exposure period, the patches were removed. The test material was removed with acetone and then the test sites were washed using lukewarm tap water and disposable paper towels. Care was taken to remove the test material 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. A second reading was taken at 72 hours to determine the primary dermal irritation index for the sample. Additional observations were conducted at 96 hours, and at 7 and 14 days.

Individual body weights were taken just prior to study initiation and at weekly intervals throughout the study period.

Pathology: At study termination all animals were euthanatized and discarded.

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SAMPLE NUMBER: 70100354

PAGE 4

SAMPLE: T-4016

PRIMARY DERMAL IRRITATION

(CONTINUED)

SUMMARY

Test Animal: Albino Rabbits - New Zealand White
Source: Hazleton Research Products, Inc., Denver PA
Date Animals Received: 12/16/86

Date Test Started: 01/08/87 Date Test Completed: 01/22/87

Primary Dermal Irritation Scores *

Observation Period	6 Rabbit Mean
24 Hours:	2.0
72 Hours:	1.8
96 Hours:	1.4
7 Days:	0.7
14 Days:	0.0

Primary Dermal Irritation Index**: 1.9

* The Primary Dermal Irritation Score is the total dermal irritation score for all the animals (erythema and edema) divided by the number of test sites (12) at each observation period.

**The Primary Dermal Irritation Index is the sum of the 24 and 72-hour primary dermal irritation scores, divided by two and rounded to the nearest tenth.

Comments:

Tape or mechanical irritation was observed on the test sites of two animals. One animal exhibited subcutaneous hemorrhaging within both test sites at 24 hours and within the abraded test site at 72 and 96 hours. Slight scab formation was observed within the abraded test site of this animal at Day 7.

Conclusion: According to FHSA regulations, this test material is not a primary skin irritant.

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SAMPLE NUMBER: 70100354

PAGE 5

SAMPLE: T-4016

PRIMARY DERMAL IRRITATION

(CONTINUED)

References:

1. Code of Federal Regulations, Title 16, Section 1500.3: Federal Hazardous Substances Act Regulations, pp. 325-342, (January 1, 1985).
2. Draize, J.H., "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics - Dermal Toxicity", Association of Food and Drug Officials of the U.S., pp. 46-59 (1975).
3. 21 CFR 58 (United States Food and Drug Administration's Good Laboratory Practices Regulations for Nonclinical Laboratory Studies).
4. DHHS Publication No. (NIH 85-23 1985) Guide for the Care and Use of Laboratory Animals.

PRIMARY SKIN IRRITATION SCORING SCALE

(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

PRIMARY DERMAL IRRITATION STUDY
(24 Hour Exposure)

HLA Number: 70100354
pH Result: 7.0 with Fisher Accumul
pH Meter No. NA
Room Number: 161 Date: 1-8-87
Initiated by: BB Date: 1-8-87
Reviewed by: MA Date: 1-8-87

Test Material: I-4016
Physical Description: Thick Brown Liquid
Dose: 0.5ml Per Site
Date Animals Received: 12-16-86 Source: HRP
Date Animals Clipped: 1-7-87 Technician: LMC Initiated by: BB
Skin Preparation: Site A Intact and Site B Abraded (with a clipper blade) Reviewed by: BB

Strain/Species: New Zealand White/Rabbit

Animal Number/Seg	Fl	60263 ♀	60284 ♂	60285 ♂	60283 ♀	6018 ♂	60211 ♀	Technician	Recorded by	1987 Date	Scale used: <u>Kram</u>
Initial Body Weight (g)	2463	2414	2673	2426	2738	2551	2551	BB	BB	1-8	15019
7-Day Body Weight (g)	2447	2485	2703	2488	2791	2589	2589	BB	BB	1-15	15019
14-Day Body Weight (g)	2523	2594	2892	2628	2953	2717	2717	BB	BB	1-22	15019
Observation Period											Thermal Irritation score
24 hours	Erythema	2	1	1	2	1	2	3	NP	1-9	2.0 <u>sh</u> 1-9-87
	Edema	0	0	0	1	0	0	0	NP	1-10	2.0 <u>sh</u> 1-9-87
72 hours	Erythema	2	0	0	1	2	3	3	NP	1-12	1.8 <u>sh</u> 1-11-87
	Edema	1	0	0	0	1	1	1	NP	1-12	2.0 <u>sh</u> 1-11-87
96 hours	Erythema	2	0	0	1	1	2	2	BB	1-15	2.0 <u>sh</u> 1-15-87
	Edema	1	0	0	0	1	1	1	BB	1-15	2.0 <u>sh</u> 1-15-87
7 days	Erythema	0	0	0	0	0	0	0	BB	1-22	2.0 <u>sh</u> 1-22-87
	Edema	0	0	0	0	0	0	0	BB	1-22	2.0 <u>sh</u> 1-22-87
14 days	Erythema	0	0	0	0	0	0	0	BB	1-22	2.0 <u>sh</u> 1-22-87
	Edema	0	0	0	0	0	0	0	BB	1-22	2.0 <u>sh</u> 1-22-87

All animals appeared normal just prior to dosing.

Reviewed by: BB Date: 1-18-87

Head Intact A B

Neck Intact A B

Tail Intact A B

HA - Not applicable.

A - Subcutaneous hemorrhage.

B - Blanching.

n - Possible necrotic area.

u - Unable to determine pH.

2 - Significant 1-15-87

3 - Significant 1-15-87

4 - Tape irritation

5 - Tape irritation

6 - Tape irritation

7 - Tape irritation

8 - Tape irritation

9 - Tape irritation

10 - Tape irritation

11 - Tape irritation

12 - Tape irritation

13 - Tape irritation

14 - Tape irritation

15 - Tape irritation

16 - Tape irritation

17 - Tape irritation

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94 - Tape irritation

95 - Tape irritation

96 - Tape irritation

97 - Tape irritation

98 - Tape irritation

99 - Tape irritation

100 - Tape irritation

(4253A)

④ Entry errors BB 1-15-87

③ Possibly mechanical irritation due to difficulty in removing test material.

③ entry error NP 1-11-87