HAZLETON LABORATORIES AMERICA, INC. Chemical & BioMedical Sciences Division
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SRPT T-4201

FINAL REPORT

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

SAMPLE NUMBER: 80600369
SAMPLE ENTERED: 06/02/88
REPORT PRINTED: 08/09/88

SAMPLE: T-4201

PURCHASE ORDER NUMBER: T514219-410 829

ENCLOSED: PRIMARY DERMAL IRRITATION/CORROSION STUDY IN RABBITS
(OECD GUIDELINES)

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

SIGNED: Steven M. Glaza ..... 8-10-88 .....
STEVEN M. GLAZA
STUDY DIRECTOR
ACUTE TOXICOLOGY
DATE

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SAMPLE: T-4201

KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director

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Report Coordinator

Quality Assurance

Debra Curley Arndt
Manager

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Cindy J. Cary, DVM
Diplomate, ACLAM

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OECD DERMAL IRRITATION

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

Regulatory Compliance: This is not a regulated study.

Test Material: T-4201

Physical Description:	White solid chunks
Purity and Stability:	Sponsor assumes responsibility for purity and stability determinations.
Storage and Retention:	The test material was stored at room temperature. Any unused material will be discarded according to HLA Standard Operating Procedure.
Safety Precautions:	Normal handling procedures were used according to HLA Standard Operating Procedure.

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 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 2334 to 2670 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 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.

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OECD DERMAL IRRITATION (CONTINUED)

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 and overwrapped with Saran Wrap and Elastoplast tape to provide a semi-occlusive dressing. Collars were applied to restrain the test animals for the 4-hour exposure period.

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

Observations: After the exposure period, the bandages were removed and 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, 72 and 96 hours and at 7 and 14 days after patch removal.

Individual body weights were taken just prior to study initiation and at Days 7 and 14.

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

Statistical Methods: Other than average dermal irritation scores, no other 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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OECD DERMAL IRRITATION (CONTINUED)

SUMMARY OF RESULTS

Test Animal: Albino Rabbits - New Zealand White
Source: Hazleton Research Products, Inc., Denver PA
Date Animals Received: 05/03/88

Start Date (In-life): 06/07/88 End Date (In-life): 06/21/88

Individual Dermal Irritation Scores

Animal		Erythema							Edema						
		Hours					Days		Hours					Days	
Number	Sex	4	24	48	72	96	7	14	4	24	48	72	96	7	14
F23191	M	3AB	3N	3N	3N	3N	3N	3N	4	2	2	2	2	2	2
F23195	M	3N	3N	3N	3N	3N	3N	4N	4	3	3	3	2	2	3
F23196	M	3AB	3N	3N	3N	4N	4N	4N	4	2	2	2	2	2	2
Mean		3.0	3.0	3.0	3.0	3.3	3.3	3.7	4.0	2.3	2.3	2.3	2.0	2.0	2.3

A - Subcutaneous hemorrhage
B - Blanching
N - Possible necrotic area

Primary Dermal Irritation Scores *

Observation Period	Three Rabbit Mean
4 Hours	7.0
24 Hours	5.3
48 Hours	5.3
72 Hours	5.3
96 Hours	5.3
7 Days	5.3
14 Days	6.0

* 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 (3) at each observation period.

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OECD DERMAL IRRITATION (CONTINUED)

References:

1. Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 404, Acute Dermal Irritation/ Corrosion, adopted May 12, 1981.

2. NIH Publication No. 86-23 (revised 1985).

3. 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).

4. OECD's Principles of Good Laboratory Practice, Annex 2, C(81)30 (Final).

HIA - 80600369

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

Name	Job Title	Signature	Initials
Becky Beckwith	Sr. Lab Animal Assistant	Becky Beckwith	BB
Ann Bursaw	Sr. Clerk	Ann M. Bursaw	AMB
Steven M. Glaza	Group Leader	Steven M. Glaza	SG
Ben Haley	Sr. Lab Animal Assistant	Ben Haley	BH
Jeff Hicks	Sr. Lab Animal Assistant	Jeff Hicks	JH
Sharen L. Howery	Administrative Assistant	Sharen L. Howery	SLH
Gregory Johnson	Lab Animal Technician	Gregory John	GJ
Wayne Madison	Senior Section Supervisor	Wayne A. Madison	WAM
Eileen McConnell	Administrative Clerk	Eileen McConnell	EMC
Albert Olson	Lab Animal Assistant	Albert Olson	AO
Patricia Padgham	Team Leader/ Lab Animal Technician	Patricia Padgham	PP
Michael Patzka	Lab Animal Assistant	Michael Patzka	MP
Jane Polnow	Lab Animal Technician	Jane Polnow	JP
Annette R. Turner	Sr. Clerk	Annette R. Turner	ART

(00261/ra)

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PRIMARY DERMAL IRRITATION SCORING SCALE (DRAIZE[1] 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)	4
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)	4
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).

(00261/vmt)

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DERMAL IRRITATION/BODY WEIGHT RECORD

(4-Hour Exposure)

Study Title: Primary Dermal Irritation
Test Material: T-4201
Physical Description: white solid chunks pH Result: NA with Hanna Meter No. 6890
Dose: 0.5g Per Site ____ Moistened with 0.9% Saline
Date Animals Received: 5-3-88 Source/Strain/Species: Hazleton Research Products/New Zealand White/Rabbit Room Number: 106
Technician/Date Animals Clipped: CS / 6-6-88 Initiated by: CS Date: 6-7-88
Skin Preparation: ✓ Intact NA Abraded (with a clipper blade) Reviewed by: M Date: 6-7-88

Animal Number/Sex F2-	3191 ♀	3195 ♂	3196 ♂				Technician	Recorded by	1988 Date	Scale used: KTRoll
Initial Body Weight (g)	2594	2334	2670				CS	CS	6-7	40021
7-Day Body Weight (g)	2666	2254	2814				CS	CS	6-14	40321
14 Day Body Weight (g)	2830	2354	3128				CS	CS	6-21	40021
21-Day Body Weight (g)										
Observation Period										Dermal Irritation Score
4 Hours Erythema	3AB	3N	3AB				CS	CS	6-7	✓ M 6-10-88 7.0 SG 6-8-88
4 Hours Edema	4	4	4							
24 Hours Erythema	3N	3N	3N				CS	CS	6-8	✓ M 6-10-88 5.3 SG 6-8-88
24 Hours Edema	2	3	2							
48 Hours Erythema	3N	3N	3N				CS	CS	6-9	✓ ~~M~~ 6-23-88 5.3 M 6-14-88
48 Hours Edema	2	3	2							
72 Hours Erythema	3N	3N	3N				BA	BA	6/10	✓ ~~M~~ 6-23-88 5.3 M 6-14-88
72 Hours Edema	2	3	2							
96 Hours Erythema	3N	3N	4N				BA	BA	6/11	✓ ~~M~~ 6-23-88 5.3 M 6-14-88
96 Hours Edema	2	2	2							
7 Days Erythema	3N	3N	4N				CS	CS	6/14	✓ ~~M~~ 6-23-88 5.3 M 6-14-88
7 Days Edema	2	2	2							
14 Days Erythema	3N	4N	4N				CS	CS	6/21	6.0 ~~M~~ 6-23-88
14 Days Edema	2	3	2							
21 Days Erythema										
21 Days Edema										

NA = Not applicable.
A - Subcutaneous hemorrhage.
B - Blanching.
N - Possible necrotic area.
U - Unable to determine pH.

All animals appeared normal just prior to dosing. Technician CS Date 6-7-88
Surviving animals designated for sacrifice and discard. Technician CS Date 6-22-88

Data reviewed by: M Date: 7-25-88