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FINAL REPORT

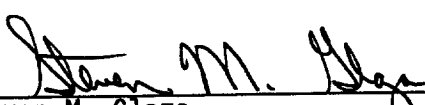
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Building 220-2E-02
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HWI Number: 40200469

Study Title:

Primary Dermal Irritation/Corrosion
Study of T-5898 in Rabbits
(OECD Guidelines)

Signed:


Steven M. Glaza
Study Director
Acute Toxicology

Date

3-23-94

RECEIVED

MAR 28 1994

3M
TOXICOLOGY

Sample: T-5898

KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report Supervisor

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

CONTENTS

	<u>Page</u>
Key Personnel	2
Objective	3
Test Material	3
Test System	3
Procedures	4
Summary of Results	6
Discussion	7
References	7
Appendix - Raw Data	8

Sample: T-5898

OBJECTIVE

The objective of this study was to assess the relative level of primary skin irritation/corrosion of a test material on rabbits under semioccluded conditions.¹

All procedures used in this study are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study did not unnecessarily duplicate any previous work.

TEST MATERIAL

Identification

The test material was identified as T-5898 and described as a clear, light-yellow liquid.

Purity and Stability

The 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 test material will be returned to the Sponsor after issuance of the final report according to Hazleton Wisconsin (HWI) Standard Operating Procedure (SOP).

Safety Precautions

The test material handling procedures were according to HWI SOPs and policies.

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were procured from HRP, Inc. and maintained at the Hazleton Wisconsin facility at 3802 Packers Avenue, Madison, Wisconsin. Animal husbandry and housing at HWI comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals".² The animals were individually housed in screen-bottom cages in temperature- and humidity-controlled quarters, provided access to water *ad libitum* and a measured amount of Laboratory Rabbit Diet HF® #5326, PMI Feeds, Inc., and held for an acclimation period of at least 7 days. The feed is routinely analyzed

Sample: T-5898

by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by HWI. There were no known contaminants in the feed or water that would have interfered with or affected the results of the study.

Three female acclimated animals, weighing from 2,961 to 3,203 g, were selected and maintained during the study in the same manner as for the acclimation period. If variations from the required temperature and humidity conditions existed, they were documented and considered to have had no adverse effect on the study outcome. Animals were identified by animal number and corresponding ear tag. On the day before treatment, the back and/or flanks of each animal were clipped free of hair to obtain an unblemished skin site.

Justification 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.

PROCEDURES

Preparation of Test Material

The test material was administered as received. The pH of the test material was determined to be 7.6.

Treatment

The test material was applied to the intact skin on each animal's back (approximate exposure area of 6.25 cm²) in the amount of 0.5 mL. The area of application was covered with a 2.5-cm x 2.5-cm gauze patch secured with paper tape, loosely overwrapped with Saran Wrap®, and secured with Elastoplast® tape to provide a semiocclusive dressing. Collars were not used to restrain the test animals during the 4-hour exposure period.

At the end of the 4-hour exposure period, the patches were removed and the test sites were washed using tap water and disposable paper towels. The test material was removed from the test sites as thoroughly as possible without irritating the skin.

Reason for Route of Administration

Historically, the dermal route has been the route of choice based on the method of Draize.³

Sample: T-5898

Observations

Approximately 30 minutes after removal of the test material, the degree of erythema and edema at each test site was read according to the Draize technique (recorded as the 4-hour score). Subsequent examinations were made at 24, 48, and 72 hours. The untreated skin of each animal was used for comparison.

Animals were weighed just before test material administration.

Termination

At termination of the experimental phase, all animals were designated to be euthanized and discarded.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and a copy of the final report will be retained in the archives of HWI in accordance with HWI SOP.

Sample: T-5898

SUMMARY OF RESULTS

Test Animal: Albino Rabbits - Hra:(NZW)SPF

Source: HRP, Inc., Kalamazoo, MI

Date Animals Received: 02/02/94

Experimental Start Date: 02/21/94 Experimental Termination Date: 02/24/94

Individual Dermal Irritation Scores

Animal Number	Sex	Hour							
		Erythema				Edema			
		<u>4</u>	<u>24</u>	<u>48</u>	<u>72</u>	<u>4</u>	<u>24</u>	<u>48</u>	<u>72</u>
F49385	F	0	0	0	0	0	0	0	0
F49364	F	0	0	0	0	0	0	0	0
F49398	F	0	0	0	0	0	0	0	0

Average Primary Dermal Irritation Scores*

<u>Observation Period (Hour)</u>	<u>Average Score</u>
4	0.0
24	0.0
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.

Sample: T-5898

DISCUSSION

Application of T-5898 to the skin of rabbits under 4-hour semioccluded conditions resulted in no dermal irritation.

REFERENCES

1. "Acute Dermal Irritation/Corrosion," *Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals*, Section 404 (adopted May 12, 1981).
2. NIH Publication No. 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 (1959).

HWI Number: 40200469

Page 8

Sample: T-5898

APPENDIX

Raw Data

HWI: 40200469

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Rose M. Bridge	Report Supervisor	<u>Rose M. Bridge</u>	<u>RB</u>
Anthony Cass	Lab Animal Technician	<u>Anthony Cass</u>	<u>AC</u>
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	<u>YC</u>
Donna J. Clemons, DVM, MS	Lab Animal Veterinarian	<u>Donna J. Clemons</u>	<u>DC</u>
John A. Disch	Lab Animal Caretaker	<u>John A. Disch</u>	<u>JD</u>
Charles W. Fritz	Lab Animal Technician	<u>Charles W. Fritz</u>	<u>CF</u>
Kari Garfoot	Lab Animal Technician	<u>Kari Garfoot</u>	<u>K7</u>
Steven M. Glaza	Manager	<u>Steven M. Glaza</u>	<u>SG</u>
Kevin Grossman	Lab Animal Caretaker	<u>Kevin Grossman</u>	<u>KG</u>
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	<u>JH</u>
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	<u>SH</u>
Wayne A. Madison	Supervisor	<u>Wayne A. Madison</u>	<u>WAM</u>
Doug McConnell	Lab Animal Technician	<u>Doug McConnell</u>	<u>DM</u>
Eileen McConnell	Staff Assistant	<u>Eileen McConnell</u>	<u>EM</u>
Bud McDonald	Study Coordinator	<u>Bud McDonald</u>	<u>BM</u>
Albert Oleson	Lab Animal Caretaker	<u>Albert Oleson</u>	<u>AO</u>
Patricia Padgham	In-life Supervisor	<u>Patricia Padgham</u>	<u>PP</u>
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	<u>SRS</u>
Annette R. Turner	Staff Assistant	<u>Annette R. Turner</u>	<u>AT</u>
Tamra L. Walker	Staff Assistant	<u>Tamra L. Walker</u>	<u>TW</u>
Lana M. Weeden	Staff Assistant	<u>Lana M. Weeden</u>	<u>LW</u>
Heather M. Weber	Lab Animal Caretaker	<u>Heather M. Weber</u>	<u>HW</u>
Janice Griffiths	Lab Animal Caretaker	<u>Janice Griffiths</u>	<u>JG</u>

HWI No.: 4020041A

DERMAL IRRITATION/BODY WEIGHT RECORD (4-HOUR EXPOSURE)

Test Material: T-5898 Physical Description: CLEAR LIGHT YELLOW LIQUID
 Dose: 0.5 mL Per Site NA Moistened with 0.9% Saline; Mfg/Lot No./Exp. Date: NA / NA / NA
 pH Result: 7.6 with Corning pH Meter No. 05510 Skin Preparation: ☒ Intact ☒ Abraded (with a clipper blade)
 Species/Source Strain/Location: Rabbit/Hra:(NZW)SPF/M1 Date Animals Received: 2-2-94 Initiated in Room No.: 103
 Technician/Date/Time Animals Clipped: K 12-20-94 / 10:32

Animal Number/Sex	⁹ <u>9385</u>	⁹ <u>9384</u>	⁹ <u>9388</u>				Technician	Recorded By	Date	Scale Used
Initial Body Weight (g)	<u>2961</u>	<u>3157</u>	<u>3203</u>				<u>K</u>	<u>K</u>	<u>2/21</u>	<u>CS604465</u>
Day 7 Body Weight (g)										

Observations

Irritation Score

4 Hour	Erythema	<u>0</u>	<u>0</u>	<u>0</u>				<u>K</u>	<u>K</u>	<u>2/21</u>	<u>✓ ac 2-24-94</u>
	Edema	<u>0</u>	<u>0</u>	<u>0</u>				<u>K</u>	<u>K</u>	<u>2/21</u>	<u>0.0 K 2-22-94</u>
24 Hour	Erythema	<u>0</u>	<u>0</u>	<u>0</u>				<u>K</u>	<u>K</u>	<u>2/22</u>	<u>✓ ac 2-24-94</u>
	Edema	<u>0</u>	<u>0</u>	<u>0</u>				<u>K</u>	<u>K</u>	<u>2/22</u>	<u>0.0 K 2-22-94</u>
48 Hour	Erythema	<u>0</u>	<u>0</u>	<u>0</u>				<u>K</u>	<u>K</u>	<u>2/23</u>	<u>✓ JH 2-27-94</u>
	Edema	<u>0</u>	<u>0</u>	<u>0</u>				<u>K</u>	<u>K</u>	<u>2/23</u>	<u>0.0 ac 2-24-94</u>
72 Hour	Erythema	<u>0</u>	<u>0</u>	<u>0</u>							<u>✓ JH 2-27-94</u>
	Edema	<u>0</u>	<u>0</u>	<u>0</u>				<u>ac</u>	<u>ac</u>	<u>2-24</u>	<u>0.0 ac 2-24-94</u>
96 Hour	Erythema										
	Edema										
Day 7	Erythema										
	Edema										

① INCORRECT DATE. K 2-21-94Storage conditions of test material: ROOM TEMPERATURE

NA Not applicable.
 B Blanching.

A Subcutaneous hemorrhage.
 N Possible necrotic area.

U Unable to determine pH.

* Animal(s) shaved prior to dermal observation by technician.

Animals were weighed and appeared normal before test material administration on the day of dosing. Technician/Date: K 12-21-94Surviving animals designated for sacrifice and discard. Technician/Date: ac 12-24-94

(S2/12-09-92)

Final data review by/Date: JH 12-27-94

HWI No.: 40200469

**Primary Dermal Irritation Scoring Scale
(Draize 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 are well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised approximately 1 mm and extending beyond area of exposure)	<u>4</u>
Highest possible edema score	4

(S5/01-07-91)