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AR226-0325

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

Steven M. Glaza
Study Director
Acute Toxicology

Date 3-23-94

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

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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

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 cm^2) 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]

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.

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			
		4	24	48	72	4	24	48	72
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*

Observation Period (Hour)	Average Score
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.

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).

APPENDIX

Raw Data

HWI: 402004469

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

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

HWI No.: 40200446

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 NA 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: KG 12-20-94 / 10:32

Animal Number/Sex	F4	9385 ♀	9304 ♀	9398 ♀				Technician	Recorded By	Date/94	Scale Used AID
Initial Body Weight (g)		2960	3157	3203				KG	KG	2/21	CS6044L05
Day 7 Body Weight (g)											

Observations — **Irritation Score**

4 Hour	Erythema	0	0	0				KG	KG	2/21 ①	✓ AC 2-24-94
	Edema	0	0	0							0.0 KG 2-22-94
24 Hour	Erythema	0	0	0				KG	KG	2/22	✓ AC 2-24-94
	Edema	0	0	0							0.0 KG 2-22-94
48 Hour	Erythema	0	0	0				KG	KG	2/23	✓ JH 2-27-94
	Edema	0	0	0							0.0 AC 2-24-94
72 Hour	Erythema	0	0	0				AC	AC	2-24	✓ JH 2-27-94
	Edema	0	0	0							0.0 AC 2-24-94
96 Hour	Erythema										
	Edema										
Day 7	Erythema										
	Edema										

① INCORRECT DATE. KG 2-21-94

Storage conditions of test material: ROOM TEMPERATURE

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

* 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: KG 12-21-94

Surviving 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

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HWI No.: 402004G9

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)	4
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)	4
Highest possible edema score	4

(S5/01-07-91)