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

JANINE GLEASON
MINNESOTA MINING & MANUFACTURING COMPANY
TOXICOLOGY SERVICES
ST. PAUL, MN 55101

SAMPLE NUMBER: 50503500
SAMPLE ENTERED: 05/15/85
REPORT PRINTED: 06/21/85

SAMPLE: T-3752

PURCHASE ORDER NUMBER: T357842, REL. #513

ENCLOSED: PRIMARY DERMAL IRRITATION - METHOD, SUMMARY
QAU REPORT
RAW DATA APPENDIX

SIGNED: Steven M. Glaza ..... 6-24-85 .....
STEVEN M. GLAZA DATE
STUDY DIRECTOR
ACUTE TOXICOLOGY

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: 50503500

SAMPLE: T-3752

OECD SKIN IRRITATION

Objective: To determine the relative level of primary skin irritation of a test material on rabbits under semioccluded conditions according to the Organisation of Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 404, Acute Dermal Irritation/Corrosion, adopted May 12, 1981.

Test Material: T-3752
Physical Description: Brown granular solid
Purity and Stability: Sponsor has purity and stability determinations on file.

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand White strain were procured, maintained individually in screen-bottom cages in temperature- and humidity-controlled quarters, provided continuous access to Purina High Fiber Rabbit Chow and water, and held for an acclimation period of at least 7 days.

Three acclimated animals, weighing from 2212 to 2323 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.

Treatment: The test material was applied to the intact skin of each rabbit in the amount of 0.5 g per site and moistened with 0.9% saline. 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 semiocclusive dressing. Collars were applied to restrain the test animals for the 4-hour exposure period.

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SAMPLE: T-3752

OECD SKIN IRRITATION (CONTINUED)

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.

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

*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., Topeka, Kansas, pp. 46-59 (1959).

SAMPLE NUMBER: 50503500

SAMPLE: T-3752

OECD SKIN IRRITATION (CONTINUED)

SUMMARY

Test Animal: Albino Rabbits - New Zealand White
Source: Hazleton Research Products, Inc., Denver PA
Date Animals Received: 05/21/85

Temperature and Humidity of Animal Room: 21 - 23 Degrees C.;
46 - 64% Relative Humidity

Date Test Started: 05/29/85 Date Test Completed: 06/01/85

Vehicle: Moistened with 0.9% saline

Individual Dermal Irritation Scores
Test Material: T-3752

Animal Number	Erythema Score Hours 4	24	48	72	Edema Score Hours 4	24	48	72
F08693	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
F08704	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
F08690	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Primary Dermal Irritation Scores

Observation Period	3 Rabbit Mean
4 Hours:	0.0
24 Hours:	0.0
48 Hours:	0.0
72 Hours:	0.0

Results:

No dermal irritation was observed at any time during the study period.

Deviation from the protocol: The test material was moistened with 0.9% saline rather than deionized water as stated in the protocol. This deviation is not considered to have had an effect on the validity of the study.

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SAMPLE: T-3752

OECD SKIN 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. 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., Topeka, Kansas, pp. 46-59 (1959).

QUALITY ASSURANCE STATEMENT

Primary Dermal Irritation Study in Rabbits

Study No. 50503500

The report as herein attached for the above-mentioned study has been reviewed by the assigned Quality Assurance Unit of Hazleton Laboratories America, Inc. in accordance with the Good Laboratory Practice Regulations as set forth in 21 CFR 58.35 (b) (6) (7). It has been found to accurately identify and/or describe the authorized methods and standard operating procedures followed in the conduct of the study and that the reported data accurately reflect the raw data of the laboratory study. Furthermore, the Quality Assurance Unit has conducted the following inspections of the testing facilities utilized in the conduct of this study and has submitted written reports of said inspections to the study director and/or management.

Date of Inspection	Type of Inspection	Date Issued to Management
5/21-23/85	Process Audit	5/23/85
6/10/85	Report Review	6/10/85

Diana E. Skalitzky

Diana E. Skalitzky
Inspector, Quality Assurance Unit

6/12/85
Date

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)	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

PRIMARY DERMAL IRRITATION STUDY

Test Compound: T-3752 — HLA Number: 50503500

Dose: 0.5g/site — Vehicle: ① 0% moistened with 0.9% saline — pH Result: NA

Date Animals Received: 5-21-85 — Source: Hazleton Research Products — Room Number: 161-3

Date Animals Clipped: 5-28-85 — Tech: CK — Initiated by: CK — Date: 5/29/85

Skin Preparation: Intact — Reviewed by: pgr — Date: 5/29/85

Animal Number/Sex FO		86930♂	87040♂	86907♀				Technician	Recorded by	1985 Date	Ktron Scale used: 15019
Initial Body Weight (g)		2226	2323	2212				CK	CK	5-29	Dermal Irritation Score
Observation Period											
4 Hours	Erythema	0	0	0				CK	CK	5-29	0.0 SLH
	Edema	0	0	0							
24 Hours	Erythema	0	0	0				CK	CK	5-30	0.0 SLH
	Edema	0	0	0							
48 Hours	Erythema	0	0	0				Sam	Sam	5-31 ② ~~5-30~~	0.0 SLH
	Edema	0	0	0							
72 Hours	Erythema	0	0	0				Sam	Sam	6-1	0.0 SLH
	Edema	0	0	0							
96 Hours	Erythema										
	Edema										
7 Days	Erythema										
	Edema										
7 Day Body Weight (g)											Scale used:

NA - Not applicable.
A - Subcutaneous hemorrhage.
B - Blanching.
N - Possible necrotic area.

Reviewed by: SLH — Date: 6-3-85

(42-10)

① Entry Error CK 5-29-85
② Recording error Sam 5-31-85

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

PROTOCOL TP2071

Primary Dermal Irritation Study in Rabbits (OECD Guidelines)

Study No. 50503500

for

3M
St. Paul, Minnesota

by

Hazleton Laboratories America, Inc.
Life Sciences Division
3301 Kinsman Boulevard
Madison, Wisconsin 53704

May 21, 1985

PROTOCOL TP2071

Primary Dermal Irritation Study in Rabbits
(OECD Guidelines)

Study No.	50503500
Study Location	Hazleton Laboratories America, Inc. Life Sciences Division 3301 Kinsman Boulevard Madison, Wisconsin 53704
Test Material	T-3752
Sponsor's Representative	Janine Gleason
Study Director	Steven M. Glaza
Proposed Timetable	
Starting Date	Week of May 27, 1985
Completion Date	Week of May 27, 1985
Final Report Date	Week of June 24, 1985

OBJECTIVE

The objective of this study is to determine the relative level of primary skin irritation of a test material on rabbits under semioccluded conditions. All aspects of this study will conform to the Organisation for Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 404, Acute Dermal Irritation/Corrosion, Adopted May 12, 1981[1] and the Principles of Good Laboratory Practice.[2] All procedures will be done according to Hazleton Laboratories America, Inc. (HLA) Standard Operating Procedures (SOPs) referenced in this protocol.

TEST MATERIAL

Test Material:	T-3752.
Physical Description:	Brown granular solid.
Purity and Stability:	Sponsor has purity and stability determinations on file.
Storage Conditions:	Store at room temperature.
Test Material Retention:	Any unused test material will be returned to the Sponsor 30 days after issuance of the final report.
Safety Precautions:	Laboratory personnel will take the normal necessary precautions in handling a substance of unknown toxicity. Laboratory clothing, latex gloves, safety glasses, and a particle mask approved for toxic dusts must be worn.

TEST SYSTEM

Test Animal

Young adult albino rabbits of either sex of the New Zealand White strain, approximately 14 weeks of age, will be obtained from Hazleton Research

Products Inc., Denver, Pennsylvania. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. Historically, the New Zealand White albino rabbit has been the animal of choice for evaluating the effect of chemicals on the skin.

Acclimation

Upon receipt, the animals will be taken to a designated animal room where they will be acclimated for at least 1 week before being placed on test (OP-GENB 36). During acclimation, the animals will be examined for clinical abnormalities indicative of health problems (e.g., diarrhea, ectoparasites, rough hair coat, nasal or ocular discharge, evidence of injury, etc.). Any animals regarded as unsuitable for study purposes because of poor physical condition will not be released from acclimation and the reason(s) will be documented.

Identification

Each animal in the study will be assigned a permanent identification number and will be identified with a metal ear tag (OP-GENB 24). All data collected from an animal will be recorded and filed under its identification number.

Housing and Maintenance

The following environmental conditions will be maintained in the animal room used for this study (OP-TARC 230).

- Temperature: 21°C ±2°
- Relative humidity: 50% ±20%
- Air change: At least 10 changes an hour of filtered 100% outside air
- Light cycle: 12 hours light/12 hours dark

Temperature and humidity will be monitored throughout the study. Variations from prescribed environmental conditions will be documented.

Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals."[3] Care will be taken to ensure that the animals are not disturbed for reasons other than data collection and routine maintenance. The animals will be housed individually in screen-bottom stainless steel cages (heavy gauge) held on racks, with absorbent pan liners in the urine- and feces-collecting pans. Pan liners will be changed at least three times each week.

Feed and water will be provided ad libitum. The diet will be Purina High Fiber Rabbit Chow. No contaminants are expected to be present in the feed or water which would interfere and affect the results of the study.

Study Design

Three rabbits will be selected at random based upon health and a body weight of 2.0-3.5 kg. Each animal will serve as its own control.

PROCEDURES

Preparation and Administration of Test Material

Twenty-four hours prior to test material administration, the hair will be clipped from the back and flanks of each animal. The treatment sites will be inspected for interfering lesions, irritation, or defects that would preclude the use of any of the animals.

The test material will be applied to the test area (approximately 6 cm^2) on each rabbit, in the amount of 0.5 g and will be moistened with deionized water. The treated area will be covered with a 2.5-cm x 2.5-cm gauze patch

secured with paper tape and loosely overwrapped with Saran Wrap and Elastoplast tape to provide a semiocclusive dressing. Collars will be used to restrain the animals during the 4-hour exposure period.

Reason for Route of Administration

Historically, the route of choice based on the method of Draize.[4]

Observations

After the 4 hours of exposure the patches and the test material will be removed as thoroughly as possible using water or an appropriate solvent without irritating the skin. Thirty minutes after removing the patches, the degree of erythema and edema will be recorded according to the Draize Technique (Attachment 1). Subsequent readings will be taken at 24, 48, and 72 hours after patch removal. Further observations may be recorded, as necessary, to establish reversibility. If irritation is increasing in severity at the 72-hour examination period, observations will be repeated at 96 hours and at 7 and 14 days, if applicable.

Body weights will be taken just prior to test material administration and at weekly intervals during the study. Observations and body weights will be recorded in the study notebook.

Pathology

All animals, whether dying on test or sacrificed at study termination, will be discarded.

Report

The final report will present a description of the test material, a description of the test system, dates of study initiation and termination, a tabulation of irritation data, and a description of any toxic effects other than dermal irritation.

Maintenance of Raw Data and Records

Original data or copies thereof will be available at HLA to facilitate auditing the study during its progress and prior to acceptance of the final report. When the final report is completed, all original paper data, as well as the final report, will be retained in the archives of HLA, Madison, Wisconsin (OP-GEN 44).

REFERENCES

1. "Acute Dermal Irritation/Corrosion", OECD Guidelines for Testing Chemicals, Section 404, May 12, 1981.

2. Organisation for Economic Cooperation and Development's Principles of Good Laboratory Practice, Annex 2, 1981.

3. DHEW Publications No. (NIH) 78-23 (1978).

4. Draize, J. H., "Dermal Toxicity," Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Association of Food and Drug Officials of the U.S., Topeka, Kansas, pp. 46-59 (1959).

PROTOCOL APPROVAL

Janine Gleason — 5/24/85

Janine Gleason
Sponsor's Representative
3M

Date

Steven M. Glaza — 5-22-85

Steven M. Glaza
Study Director
Group Leader, Acute Toxicology
Hazleton Laboratories America, Inc.

Date

(1108S/tji)

ATTACHMENT I

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)	4
Highest possible erythema score	4

2. Edema Formation

No edema	0
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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