Corning Hazleton Inc.
P.O. Box 7545
Madison, WI 53707-7545
Deliveries: 3301 Kinsman Blvd., Madison, WI 53704
608.241.4471 608.241.7227 Fax

CORNING Hazleton

Sponsor:

3M
St. Paul, Minnesota

FINAL REPORT

Study Title:

Primary Dermal Irritation/Corrosion
Study of T-6684 in Rabbits
(OECD Guidelines)

Author:

Steven M. Glaza

Study Completion Date:

January 10, 1997

Performing Laboratory:

Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

CHW 61101150

RECEIVED
JAN 13 1997

COMPLIANCE STATEMENT

Primary Dermal Irritation/Corrosion
Study of T-6684 in Rabbits
(OECD Guidelines)

This study was conducted in accordance with the Organisation for Economic Cooperation and Development Principles of Good Laboratory Practice, C(81)30(Final).

Steven M. Glaza

Steven M. Glaza
Study Director
Acute Studies
Corning Hazleton Inc.

1-10-97
Date

QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Corning Hazleton Inc., in accordance with the Organisation for Ecomonic Cooperation and Development (OECD) Principles of Good Laboratory Practice, C(81)30(Final). The following inspections were conducted and findings reported to the Study Director and management.

Inspection Dates			Date Reported to	Date Reported to
From	To	Phase	Study Director	Management
11/25/96	11/25/96	Dose Preparation	11/25/96	11/25/96
01/08/97	01/08/97	Data/Report Review	01/08/97	01/08/97

Susan K. Swatch
Representative, Quality Assurance Unit

1-10-97
Date

STUDY IDENTIFICATION

Primary Dermal Irritation/Corrosion
Study of T-6684 in Rabbits
(OECD Guidelines)

Test Material	T-6684
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	Roger G. Perkins 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 736-7428
Study Director	Steven M. Glaza Corning Hazleton Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Corning Hazleton Inc. 3301 Kinsman Boulevard Madison, WI 53704
Study Timetable	
Study Initiation Date	November 22, 1996
Experimental (In-life) Start Date	November 25, 1996
In-life End Date	December 9, 1996
Experimental Termination Date	December 9, 1996
Study Completion Date	January 10, 1997

KEY PERSONNEL

Acute Studies

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Jeffrey B. Hicks
In-life Supervisor

Rose M. Bridge
Administrative Supervisor

Toxicology Support

Kathy Myers
Manager

Calvin L. Horton
Supervisor

Quality Assurance

Sherry R. W. Petsel
Manager

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

CONTENTS

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 were 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. All procedural times presented in this report fall within the acceptable ranges as specified in the Wisconsin facility of Corning Hazleton Inc. (CHW) Standard Operating Procedure (SOP).

TEST MATERIAL

Identification
The test material was identified as T-6684 and described as an off-white 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 CHW SOP.

Safety Precautions
The test material handling procedures were according to CHW SOPs and policies.

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were procured from HRP, Inc., Kalamazoo, Michigan on October 30, 1996.

Housing

After receipt, the animals were acclimated for a period of at least 7 days. During acclimation and throughout the study, the animals were individually housed in stainless steel cages. Environmental controls for the animal room were set to maintain a temperature of 19° to 23°C, a relative humidity of 50% ±20%, and a 12-hour light/ 12-hour dark lighting cycle. In cases where variations from these conditions existed, they were documented and considered to have had no adverse effect on the study outcome.

Animal Diet

The animals were provided access to water *ad libitum* and a measured amount of Laboratory Rabbit Diet HF #5326, PMI Feeds, Inc. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed. There were no known contaminants in the feed or water at levels that could be expected to interfere with or affect the results of the study.

Animal Selection and Preparation of Exposure Area

Two male and one female healthy, acclimated rabbits, weighing from 2,662 to 2,937 g and approximately 14 to 18 weeks of age, were selected at random and 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 one unblemished skin site. The animals were clipped as needed throughout the study.

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 not able to be determined.

Treatment

The undiluted test material was applied to the intact skin site 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 an 8-ply 2.5-cm x 2.5-cm gauze patch secured with paper tape, loosely overwrapped with Saran Wrap®, and secured with Elastoplast® to provide a semiocclusive dressing.

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.[2]

Observations

Thirty 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, 72, 96 hours and Days 7 and 14. The untreated skin of each animal was used for comparison.

Animals were weighed before test material administration and at weekly intervals throughout the study.

Termination

At termination of the in-life phase, all animals were 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 an original signed copy of the final report will be retained in the archives of CHW in accordance with CHW SOP.

RESULTS/DISCUSSION

Individual dermal irritation scores are presented in Table 1. Average primary dermal irritation scores and individual body weights are in Tables 2 and 3, respectively.

Application of T-6684 to the skin of rabbits under 4-hour semioccluded conditions resulted in well-defined erythema and slight to moderate edema reactions. Desquamation and fissuring were also observed. All irritation cleared by the Day 14 observation.

SIGNATURE

Steven M. Glaza
Study Director
Acute Studies

1-10-97
Date

REFERENCES

1. "Acute Dermal Irritation/Corrosion," *Organisation for Economic Cooperation and Development Guidelines for Testing of Chemicals,* Section 4, Health Effects, November 404, Paris Cedex (July 17, 1992).

2. 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).

Table 1

Individual Dermal Irritation Scores

Animal Number	Hour 4	24	48	72	96	Day 7	14
			Erythema				
F61197	2	1	1	1	2	1[d]	0
F61198	2	2	2	2	2	2[f]	0
F61199	2	2	2	2	2	1[d]	0
			Edema				
F61197	3	1	1	1	2	1	0
F61198	2	1	1	1	1	1	0
F61199	3	2	2	2	2	2	0

d Desquamation.
f Fissuring.

Table 2

Average Primary Dermal Irritation Scores

Observation Period	Average Score*
4 Hour	4.7
24 Hour	3.0
48 Hour	3.0
72 Hour	3.0
96 Hour	3.7
Day 7	2.7
Day 14	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.

Table 3

Individual Body Weights (g)

Animal Number	Sex	Predose	Day 7	Day 14
F61197	M	2,937	3,036	3,137
F61198	F	2,662	2,886	2,919
F61199	M	2,755	2,906	2,943

APPENDIX

Protocol TP2071
Protocol Amendment No. 1

Sample Submittal Form

This form is to be used when submitting samples for routine acute testing. Special testing needs can be easily arranged by contacting the Acute Studies Department at (608) 241-7292.

CHW Study No. 61101150
Enclose with samples and send to:
Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Submitted by: ROGER G. PERKINS
Date Sample Sent: 10/23/96
Company: _____
Number of Reports Required: 3

Full GLP Compliance: X Yes ___ No ___ FDA (21 CFR 58) ___ EPA (TSCA—40 CFR 792) ___ EPA (FIFRA—40 CFR 160) X OECD ___ MAFF ___ MOHW

Sample Name: T-6684, T-6685, T-6686
Physical Description: liquids
Special Handling Precautions: SEE MSDS 07-7444-8, 07-7587-4, 0
Test material purity and stability information (including under test conditions) on file with Sponsor: X Yes ___ No
Test mixture analysis for concentration/homogeneity/stability to be conducted: ___ Yes* ___ by Sponsor ___ by CHW X No

Sample Disposal: X Return to Sponsor at following address:
P. Wolf
3M SCD
Bld 23-35-02
St. Paul, Mn. 55144-100

___ Dispose of according to CHW SOPs

Sample Storage Requirements:
X Room temperature
___ Refrigerated
___ Other _____

* At additional cost to Sponsor (CHW will contact Sponsor as to these additional charges).

Tests

Acute Oral Toxicity in Rats

___TP8084 Up and down LD50 procedure
___TP3206 FHSA screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg
___TP3013 EPA screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg
X TP2069 OECD screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg

Special instructions: _____

Acute Dermal Toxicity in Rabbits

___TP3207 FHSA screen; 5M-5F at 2.0 g/kg
___TP3016 EPA screen; 5M-5F at 2.0 g/kg
___ Conduct defined study if death occurs at 2.0 g/kg
___TP2070 OECD screen; 5M-5F at 2.0 g/kg
___ Conduct defined study if death occurs at 2.0 g/kg

Special instructions: PK AND DERMAL ABSORB 5X for T-6684 only

Primary Skin Irritation

___TP3208 FHSA; 6 rabbits-1 abraded, 1 intact site/rabbit
___TP3014 EPA; 6 rabbits-1 intact site/rabbit
X TP2071 OECD; 3 rabbits-1 intact site/rabbit
___TP4206 DOT corrosivity; 6 rabbits-1 intact site/rabbit
___TP7145 Phototoxicity; 6 rabbits-2 intact sites/rabbit (one site with UVA exposure)

Special instructions: _____

Primary Eye Irritation

___TP6360 Low-volume procedure; 6 rabbits unwashed
___TP3209 FHSA; 6 rabbits unwashed
___TP2012 1978 EPA; 6 rabbits unwashed, 3 washed
___TP3015 1982 EPA; 6 rabbits unwashed
X TP2072 OECD; 3 rabbits unwashed
___ 3 rabbits washed at 4 seconds
___ 3 rabbits washed at 30 seconds

Special instructions: _____

Guinea Pig Sensitization

___TP2017 EPA Magnusson-Kligman maximization
___TP6164.EC OECD/EC Magnussun-Kligman maximization
___TP2008 Buehler sensitization
___TP6289 Photoallergenic contact dermatitis (Armstrong)

Special instructions: _____

For CHW Use Only

Protocol Issue Date: Steven M. Alles
Study Director: 11-22-96

White copy—CHW Yellow copy—Submitter

HAZLETON
WISCONSIN
POST OFFICE BOX 7545
MADISON, WISCONSIN 53707-7545

a CORNING Laboratory Services Company

Sponsor:

3M
St. Paul, Minnesota

PROTOCOL TP2071

Study Title:

Primary Dermal Irritation/Corrosion Study in Rabbits
(OECD Guidelines)

Date:

June 1, 1993

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 6110 1150

STUDY IDENTIFICATION

Primary Dermal Irritation/Corrosion Study in Rabbits
(OECD Guidelines)

HWI No.	6110150
Test Material	(See sample submittal form)
Sponsor	3M Toxicology Services 220-2E-02 3M Center St. Paul, MN 55144
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Services 220-2E-02 3M Center St. Paul, MN 55144 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. Building No. 3 3802 Packers Avenue Madison, WI 53704
Proposed Study Timetable	
Experimental Start Date	Week of 11-25-96
Experimental Termination Date	Week of 12-16-96
Final Report Date	Week of 1-27-97

1. Study
Primary Dermal Irritation/Corrosion Study in Rabbits (OECD Guidelines)

2. Purpose
To assess the relative level of primary skin irritation/corrosion of a test material on rabbits under semioccluded conditions

3. Regulatory Compliance
This study will be conducted in accordance with the following Good Laboratory Practice Regulations/Standards/Guidelines:

[ ] Conduct as a Nonregulated Study
[ ] 21 CFR 58 (FDA)
[ ] 40 CFR 160 (EPA-FIFRA)
[ ] 40 CFR 792 (EPA-TSCA)
[X] C(81)30 (Final) (OECD)
[ ] Notification No. 3850, August 10, 1984 (Japanese MAFF)
[ ] Notification No. 313, March 31, 1982, and as amended by Notification No. 870, October 5, 1988 (Japanese MOHW)

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

4. Quality Assurance
For regulated studies, the protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with Hazleton Wisconsin (HWI) Standard Operating Procedures (SOPs) and policies.

5. Test Material

A. Identification
(See sample submittal form)

B. Physical Description
(See sample submittal form)

C. Purity and Stability
The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Samples of test material/vehicle mixture(s) (if applicable) for concentration, solubility, homogeneity, and stability analyses will be taken before administration if requested by the Sponsor. These samples (if taken) will be sent to the Sponsor after experimental termination for possible analysis.

D. Storage
(See sample submittal form)

E. Reserve Samples
Studies of less than 4 weeks in experimental duration will not have reserve samples retained.

Reserve sample(s) of each batch/lot of test material will be taken if this study is more than 4 weeks in experimental duration.

The test material reserve sample will be stored at HWI in a freezer set to maintain a temperature of below 0°C for 10 years per HWI SOP. The Sponsor will be contacted after 10 years for disposition in accordance with the appropriate regulatory Good Laboratory Practices.

F. Retention
Any unused test material will be discarded after issuance of the final report, unless directed otherwise by the Sponsor.

G. Safety Precautions
As required by HWI SOPs and policies

6. Experimental Design

A. Animals

(1) Species
Rabbit

(2) Strain/Source
Hra:(NZW)SPF/Hazleton Research Products, Inc.

(3) Age at Initiation
Adult

(4) Weight at Initiation
2.0 to 3.5 kg

(5) Number and Sex
3 of any sex

(6) Identification
Individual numbered ear tag.

(7) Husbandry

(a) Housing
Individually, in screen-bottom stainless steel cages (heavy gauge).

(b) Food
A measured amount of High Fiber Rabbit Chow® #5326 (Purina Mills, Inc.). The food is routinely analyzed by the manufacturer for nutritional components and environmental contaminants.

(c) Water
Ad libitum from an automatic system. Samples of the water are analyzed by HWI for total dissolved solids, hardness, and specified microbiological content and for selected elements, heavy metals, organophosphates, and chlorinated hydrocarbons.

(d) Contaminants
There are no known contaminants in the food or water that would interfere with this study.

(e) Environment
Environmental controls for the animal room will be set to maintain a temperature of 19 to 23°C, a relative humidity of 50% ±20%, and a 12-hour light/12-hour dark cycle.

(f) Acclimation
At least 7 days

(8) Selection of Test Animals
Based on health and body weight according to HWI SOPs. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test.

(9) 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.

B. Dose Administration

(1) Preparation of Exposure Area
On the day before test material administration, the back and/or flanks of each animal will be clipped free of hair. The treatment sites will be inspected for interfering lesions, irritation, or defects that would preclude the use of any of the animals. The animals will be clipped as needed throughout the study.

(2) Dose Administration
Before administration of liquid test materials the pH of the material will be determined (if possible). The test material will be applied to the intact test area (approximately 6.25 cm^2) on each rabbit, in the amount of 0.5 mL in the case of liquids and 0.5 g in the case of solids. If a liquid, the test material will be applied undiluted. If a solid, the test material will be moistened with 0.9% saline. Aerosol materials will be discharged into a beaker and administered as a liquid. The area of application will be covered with a 2.5-cm x 2.5-cm gauze patch secured with paper tape and overwrapped with Saran Wrap® and Elastoplast® tape to provide a semiocclusive dressing. The rabbits will not be collared during the 4-hour application period.

(3) Reason for Route of Administration
Historically, the dermal route has been the route of choice based on the method of Draize.

(4) Removal of Test Material
After the 4 hours of exposure, the patches and test material will be removed as thoroughly as possible using water and/or an appropriate solvent without irritating the skin.

C. Observation of Animals

(1) Reading of Dermal Irritation
Approximately 30 minutes after removing patches, the degree of erythema and edema will be evaluated according to the Draize technique (Attachment 1) and recorded as the 4-hour score. The intact skin of each animal will serve as its own control. Subsequent readings will be taken at approximately 24, 48, and 72 hours after patch removal. If irritation is present at the 72-hour examination, additional observations will be made at approximately 96 hours and at Days 7, 14, and 21, or until all irritation

has cleared. Based on the level of irritation observed at any of these time points, the study may be terminated at the direction of the study director.

(2) Body Weights
Just before test material administration and weekly thereafter (when applicable).

D. Pathology
Any animals dying during the study will be subjected to an abbreviated gross necropsy examination and all abnormalities will be recorded. After necropsy, the animals will be discarded and no tissues will be saved. At termination of the experimental phase, surviving animals will be designated to be sacrificed and discarded.

E. Statistical Analyses
No statistical analyses are required.

7. Report
A final report including those items listed below will be submitted:

Description of the test material
Description of the test system
Procedures
Dates of experimental initiation and termination
Tabulation of irritation data
Description of any toxic effects other than dermal irritation

8. Location of Raw Data, Records, and Final Report
Original data, or copies thereof, will be available at HWI to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data, including those items listed below will be retained in the archives of HWI according to HWI SOP.

Protocol and protocol amendments
Dose preparation records
In-life records
  Body weights
  Dose administration
  Observations
Anatomical pathology records (if applicable)
Study correspondence
Final report (original signed copy)

The following supporting records will be retained at HWI but will not be archived with the study data.

Animal receipt/acclimation records
Water analysis records
Animal room temperature and humidity records
Refrigerator and freezer temperature records

PROTOCOL APPROVAL

John L. Butenhoff
John L. Butenhoff, PhD
Sponsor's Representative
3M

July 22, 1993
Date

Steven M. Glaza
Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

6-1-93
Date

Rebecca S. Nelson
Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

6/1/93
Date

(TP2071.3M)

Attachment 1

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

CHW No. 61101150

PROTOCOL AMENDMENTS

Amendment No. 1

Effective November 22, 1996

Portion of Protocol Being Modified: Applicable sections of the protocol.

Reason for Modification: To identify the location where the study will be conducted and to reflect a company name change from Hazleton Wisconsin, Inc. (HWI) to Corning Hazleton Inc. (CHW), replace wherever applicable the following changes

Modification: Corning Hazleton Inc. (CHW)
3301 Kinsman Boulevard.
Madison, WI 53704

Study Director Approval: Steven M. Hoy 11-22-96

(G21/01-07-91)