

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

Author:

Steven M. Glaza

Study Completion Date:

January 28, 1997

Performing Laboratory:

Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

CHW 61101151

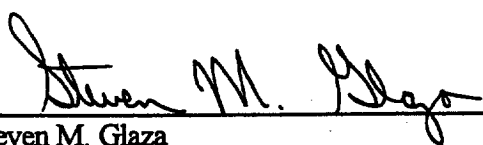
Page 1 of 31

FEB - 3 1997

COMPLIANCE STATEMENT

Primary Eye 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
Study Director
Acute Studies
Corning Hazleton Inc.

1-28-97

Date

QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Corning Hazleton Inc., in accordance with the Organisation for Economic 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		Phase	Date Reported to Study Director	Date Reported to Management
From	To			
12/03/96	12/03/96	Dose Preparation	12/03/96	12/03/96
01/23/97	01/23/97	Data/Report Review	01/23/97	01/23/97

Rebecca J. Innes
Representative, Quality Assurance Unit

1.28.97
Date

STUDY IDENTIFICATION**Primary Eye 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, PhD 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-3222
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 27, 1996
Experimental (In-life) Start Date	December 3, 1996
In-life End Date	December 17, 1996
Experimental Termination Date	December 17, 1996
Study Completion Date	January 28, 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

Quality Assurance

Sherry R. W. Petsel
Manager

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

Toxicology Support

Kathy Myers
Manager

Calvin L. Horton
Supervisor

CONTENTS

COMPLIANCE STATEMENT	2
QUALITY ASSURANCE STATEMENT	3
STUDY IDENTIFICATION	4
KEY PERSONNEL	5
OBJECTIVE	8
TEST MATERIAL	8
Identification	8
Purity and Stability	8
Storage and Retention	8
Safety Precautions	8
TEST SYSTEM	9
Test Animal	9
Housing	9
Animal Diet	9
Animal Selection	9
Justification for Species Selection	9
PROCEDURES	10
Preparation of Test Material	10
Treatment	10
Reason for Route of Administration	10
Observations	10
Termination	10
Statistical Analyses	11
Location of Raw Data, Records, and Final Report	11
RESULTS/DISCUSSION	11
SIGNATURE	11
REFERENCES	12

TABLE

1	Average Primary Eye Irritation Scores	13
2	Individual Eye Irritation Scores.....	14
3	Sodium Fluorescein Examinations.....	18
4	Individual Body Weights (g)	18

APPENDIX.....	19
Protocol TP2072	20
Protocol Amendment No. 1	31

OBJECTIVE

The objective of this study was to assess the relative level of irritation/corrosion produced following a single exposure of a test material to one eye of albino rabbits.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

Three healthy, acclimated male rabbits, weighing from 2,526 to 2,685 g and approximately 17 weeks of age, were selected at random and identified by animal number and corresponding ear tag. The animals' eyes were examined on the day before test material administration using sodium fluorescein dye procedures. Only those animals with no sign of ocular injury or irritation were used.

Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice based on its large orbit and nonpigmented iris.

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

Each rabbit received 0.1 mL of the undiluted test material placed into the everted lower lid of the right eye, with the left eye serving as the untreated control. The upper and lower lids were gently held together for 1 second to prevent loss of material and then released. The eyes of the rabbits remained unflushed immediately after treatment.

Reason for Route of Administration

Historically, the ocular route has been the route of choice based on the method of Draize.²

Observations

The treated eyes were observed for ocular irritation at 1, 24, 48, 72, and 96 hours and Days 7 and 14 after treatment. Irritation was graded and scored according to the Draize technique using a penlight as the source of illumination. Sodium fluorescein examinations were used to aid in revealing possible corneal injury at the observations conducted at 24 hours.

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.

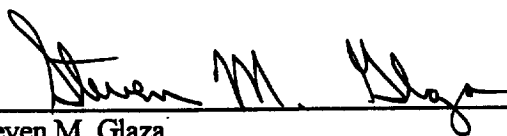
Location of Raw Data, Records, and Final Report

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

Average primary eye irritation scores are in Table 1, with individual eye irritation scores in Table 2. Sodium fluorescein examinations and the individual body weights are in Tables 3 and 4, respectively.

The test material, T-6684, when evaluated for its primary eye irritation potential in rabbits, produced a corneal opacity in one animal, iridal involvement in two animals, and slight to moderate conjunctival irritation in all three animals. All treated eyes had returned to a normal appearance by Day 14 after treatment.

SIGNATURE

Steven M. Glaza

Study Director

Acute Studies

1-28-97

Date

REFERENCES

1. "Acute Eye Irritation/Corrosion," Organisation for Economic Cooperation and Development Guidelines for Testing of Chemicals, Section 405 (adopted May 12, 1981).
2. Draize, J. H., "Eye Mucosa," 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. 49-50 (1959).

Table 1**Average Primary Eye Irritation Scores**

Observation Period	Average Score*
1 Hour	12.3
24 Hour	6.7
48 Hour	6.7
72 Hour	5.3
96 Hour	4.0
Day 7	0.7
Day 14	0.0

* The average primary eye irritation score is the total eye irritation score for all the animals divided by the number of animals (3) at each observation period.

Table 2

Individual Eye Irritation Scores

Animal Number	Cornea		Iris	Conjunctivae			Total Score*
	A	B	C	D	E	F	
1 Hour							
F61209 ^t	1	1	1 ⁱ	2	1	1 ^d	18.0
F61210 ^u	0	0	1 ⁱ	2	1	1 ^d	13.0
F61211 ^t	0	0	0	2	1	0	6.0
						Mean	12.3
24 Hours							
F61209	0	0	0	2 ^b	1	1 ^d	8.0
F61210	0	0	0	2 ^b	1	0	6.0
F61211	0	0	0	2	1	0	6.0
						Mean	6.7
Cornea			Iris		Conjunctivae		
A - Degree of opacity			C - Degree of iridal		D - Redness		
B - Area of involvement			irritation		E - Chemosis		
					F - Discharge		

* Total score = (A x B x 5) + (C x 5) + [(D + E + F) x 2].

b Blanching.

d Purulent discharge.

i Injected.

t No pain response after test material instillation.

u Excessive pawing at the treated eye after test material instillation.

Table 2 (Continued)

Individual Eye Irritation Scores

Animal Number	Cornea		Iris	Conjunctivae			Total Score*
	A	B	C	D	E	F	
48 Hours							
F61209	0	0	0	2 ^b	1	1 ^d	8.0
F61210	0	0	0	2	1	0	6.0
F61211	0	0	0	2	1	0	6.0
						Mean	6.7
72 Hours							
F61209	0	0	0	2	1	1 ^d	8.0
F61210	0	0	0	1	1	0	4.0
F61211	0	0	0	1	1	0	4.0
						Mean	5.3
Cornea			Iris		Conjunctivae		
A - Degree of opacity			C - Degree of iridal		D - Redness		
B - Area of involvement			irritation		E - Chemosis		
					F - Discharge		

* Total score = (A x B x 5) + (C x 5) + [(D + E + F) x 2].

b Blanching.

d Purulent discharge.

Table 2 (Continued)
Individual Eye Irritation Scores

Animal Number	Cornea		Iris	Conjunctivae			Total Score*
	A	B	C	D	E	F	
96 Hours							
F61209	0	0	0	1	1	0	4.0
F61210	0	0	0	1	1	0	4.0
F61211	0	0	0	1	1	0	4.0
						Mean	4.0
Day 7							
F61209	0	0	0	1	0	0	2.0
F61210	0	0	0	0	0	0	0.0
F61211	0	0	0	0	0	0	0.0
						Mean	0.7
Cornea			Iris		Conjunctivae		
A - Degree of opacity			C - Degree of iridal		D - Redness		
B - Area of involvement			irritation		E - Chemosis		
					F - Discharge		

* Total score = (A x B x 5) + (C x 5) + [(D + E + F) x 2].

Table 2 (Continued)**Individual Eye Irritation Scores**

Animal Number	Cornea		Iris	Conjunctivae			Total Score*
	A	B	C	D	E	F	
Day 14							
F61209	0	0	0	0	0	0	0.0
F61210	0	0	0	0	0	0	0.0
F61211	0	0	0	0	0	0	0.0
Mean							0.0

Cornea	Iris	Conjunctivae
A - Degree of opacity	C - Degree of iridal	D - Redness
B - Area of involvement	irritation	E - Chemosis
		F - Discharge

* Total score = (A x B x 5) + (C x 5) + [(D + E + F) x 2].

Table 3**Sodium Fluorescein Examinations**

Animal Number	Observation Period	
	Preinitiation	24 Hour
F61209	NEG	NEG
F61210	NEG	NEG
F61211	NEG	NEG
NEG Negative stain retention.		

Table 4**Individual Body Weights (g)**

Animal Number	Sex	Initial	Day	
			7	14
F61209	M	2,685	2,802	2,900
F61210	M	2,526	2,684	2,796
F61211	M	2,632	2,814	2,992

APPENDIX

Protocol TP2072
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. 61101151

Enclose with samples and send to:
Coming 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: ☒ Yes ☐ No FDA (21 CFR 58) ☐ EPA (FIFRA-40 CFR 160) ☐ MAFF
☐ EPA (TSCA-40 CFR 792) ☒ OECD ☐ 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: ☒ Yes ☐ No
 Test mixture analysis for concentration/homogeneity/stability to be conducted: ☐ Yes* ☐ by Sponsor ☐ by CHW
 Sample Disposal: ☒ Return to Sponsor at following address: ☒ No
P. Wolf
3m SCD
Box 23-35-02
St. Paul, Mn 55144-700
 _____ Dispose of according to CHW SOPs

Sample Storage Requirements:

- ☒ 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
☒ 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

For CHW Use Only

Protocol Issue Date: 11-27-96
 Study Director: Steve M. Alga

White copy—CHW Yellow copy—Submitter

Primary Skin Irritation

- ☐ TP3208 FHSA; 6 rabbits-1 abraded, 1 intact site/rabbit
☒ TP3014 EPA; 6 rabbits-1 intact site/rabbit
☒ 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
☒ 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 Magnusson-Kligman maximization
☐ TP2008 Buehler sensitization
☐ TP6289 Photoallergic contact dermatitis (Armstrong)

Special instructions: _____



• CORNING Laboratory Services Company

Sponsor:

3M
St. Paul, Minnesota

PROTOCOL TP2072

Study Title:

Primary Eye 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 61101151

TP2072
Page 2

STUDY IDENTIFICATION

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

HWI No.	61101151
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 12-2-96
Experimental Termination Date	Week of 12-23-96
Final Report Date	Week of 2-3-97

TP2072
Page 3

1. Study
Primary Eye Irritation/Corrosion Study in Rabbits (OECD Guidelines)
2. Purpose
To assess the relative level of irritation/corrosion produced following a single exposure of a test material to one eye of albino rabbits
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)
 - ☒ 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.

TP2072

Page 4

- 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 per group
- (6) Identification
Individual numbered ear tag

TP2072
Page 5(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% $\pm$ 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. The rabbits' eyes will be examined using sodium fluorescein dye procedures on the day before test material administration. Only animals with no sign of corneal injury or eye abnormalities will be used.

(9) Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice based upon its large orbit and nonpigmented iris.

TP2072

Page 6

B. Dose Administration**(1) Dose Administration**

Before administration of liquid test materials, the pH of the material will be determined (if possible). Each rabbit will receive 0.1 mL of undiluted liquid test material or the weight equivalent of 0.1 mL of solid test material (not to exceed 0.1 g). If necessary, solid test materials will be finely ground into a dust or powder. The test material will be placed into the everted lower lid of the rabbit's eye. The upper and lower lids will then be gently held together for 1 second before releasing to prevent loss of material. If the test material is an aerosol, the test eye will be held open and the test material administered in a single burst of about 1 second from a distance of approximately 10 cm directly in front of the eye. The eyes of the Group 1 rabbits will remain unflushed for approximately 24 hours following instillation of the test material. After 24 hours, a washout may be used if considered appropriate. If specified by the Sponsor, the treated eyes of two other groups of animals (three animals/group) will be washed with lukewarm tap water for approximately 30 seconds beginning approximately 4 and 30 seconds, respectively, after instillation of the test material. The volume and velocity of the flow should not cause injury. The right eye of each animal will be treated with the test material and the left eye will serve as the untreated control.

(2) Reason for Route of Administration

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

C. Observation of Animals**(1) Reading of Ocular Irritation**

The treated eyes of all animals will be examined for ocular irritation at approximately 1, 24, 48, and 72 hours after treatment. If no irritation or injury is present at 72 hours, the group will be terminated. If irritation is present at 72 hours, additional observations may be made at 96 hours and at 7, 14, and 21 days. If at any of these time points there is no irritation, the group will be terminated.

If injury is still present at 21 days, additional observations may be requested by the Sponsor. After recording the 24-hour observations, sodium fluorescein may be used to aid in revealing possible corneal injury.

TP2072

Page 7

Irritation will be graded and scored using the Draize technique (Attachment 1). All eye abnormalities will be recorded. All animals that have a damaged eye producing undue stress or discomfort will be brought to the attention of the study director or designee according to HWI policy.

(2) Body Weights

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

Summary table showing the irritation data at each observation period

Any special observations that were recorded

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)

TP2072
Page 8

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
Instrument calibration and maintenance records

TP2072
Page 9

PROTOCOL APPROVAL

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

July 12, 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.
(TP2072.3M)

6/1/93
Date

TP2072
Page 10

Attachment 1

SCALE FOR SCORING OCULAR LESIONS (DRAIZE TECHNIQUE)

(1) Cornea

- (A) Opacity - Degree of density (area most dense taken for reading)
- No opacity.....0
 - Scattered or diffuse area, details of iris clearly visible.....1*
 - Easily discernible translucent areas, details of iris slightly obscured.....2*
 - Opalescent areas, no details of iris visible, size of pupil barely discernible.....3*
 - Opaque, iris invisible.....4*
- (B) Area of Cornea Involved
- One-quarter (or less), but not zero.....1
 - Greater than one-quarter, but less than half.....2
 - Greater than half, but less than three-quarters.....3
 - Greater than three-quarters up to whole area.....4
- A x B x C Total Maximum = 80

(2) Iris

- (A) Values
- Normal.....0
 - Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris is still reacting to light (sluggish reaction is positive).....1*
 - No reaction to light, hemorrhage, gross destruction (any or all of these).....2*
- A x B Total Maximum = 10

(3) Conjunctivae

- (A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)
- Vessels normal.....0
 - Vessels definitely injected above normal.....1
 - More diffuse, deeper crimson red, individual vessels not easily discernible.....2*
 - Diffuse beefy red.....3*
- (B) Chemosis
- No swelling.....0
 - Any swelling above normal (includes nictitating membrane).....1
 - Obvious swelling with partial eversion of the lids.....2*
 - Swelling with lids about half closed.....3*
 - Swelling with lids about half closed to completely closed.....4*
- (C) Discharge
- No discharge.....0
 - Any amount different from normal (does not include small amounts observed in inner canthus of normal animals).....1
 - Discharge with moistening of the lids and hairs just adjacent to the lids.....2
 - Discharge with moistening of the lids and hairs, and considerable area around the eye.....3
- Score (A + B + C) x 2 Total Maximum = 20

The total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctivae.

* Indicates a positive effect. (FKSA Interpretation)

CHW No. 61101151

PROTOCOL AMENDMENTS

Amendment No. <u>1</u>
Effective <u>NOVEMBER 27, 1996</u>
Portion of Protocol Being Modified: <u>Applicable sections of the protocol.</u>
Reason for Modification: <u>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</u>
Modification: <u>Corning Hazleton Inc. (CHW)</u> <u>3301 Kinsman Boulevard.</u> <u>Madison, WI 53704</u>
Study Director Approval: <u>Steven M. Papp 11-27-96</u>

(G21/01-07-91)