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-6564 in Rabbits
(OECD Guidelines)

Author:

Steven M. Glaza

Study Completion Date:

September 5, 1996

Performing Laboratory:

Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

CHW 60504574

COMPLIANCE STATEMENT

Primary Eye Irritation/Corrosion
Study of T-6564 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.

9-5-96
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			Date Reported to Study	
From	To	Phase	Director	Date to Management
06/28/96	06/28/96	Dose Preparation	06/28/96	06/28/96
09/02/96	09/02/96	Data/Report Review	09/03/96	09/03/96

Randy Lentz
Representative, Quality Assurance Unit

9.5.96
Date

STUDY IDENTIFICATION

Primary Eye Irritation/Corrosion
Study of T-6564 in Rabbits
(OECD Guidelines)

Test Material	T-6564
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	June 20, 1996
Experimental (In-life) Start Date	June 28, 1996
In-life End Date	July 25, 1996
Experimental Termination Date	July 25, 1996
Study Completion Date	September 5, 1996

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

TABLE

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-6564 and described as a clear, colorless 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 May 29, 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 screen-bottom 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 female rabbits, weighing from 2,192 to 2,529 g and approximately 14 to 18 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 determined to be 8.4.

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, 14, and 21 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, 48, 72, and 96 hours and Days 7, 14, and 21.

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-6564, when evaluated for its primary eye irritation potential in rabbits, produced corneal and iridal involvement and severe conjunctival irritation. Ocular irritation was still present in two animals at Day 21 after treatment.

SIGNATURE

Steven M. Glaza
Study Director
Acute Studies

9-5-96
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	41.7
24 Hour	42.0
48 Hour	36.7
72 Hour	32.3
96 Hour	24.0
Day 7	16.3
Day 14	8.7
Day 21	6.7

* 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 A	Cornea B	Iris C	Conjunctivae D	Conjunctivae E	Conjunctivae F	Total Score*
			1 Hour				
F59541[u]	1	4	1[i]	2[b]	3	3[c]	41.0
F59542[u]	1	4	1[i]	2[b]	4	3[c]	43.0
F59543[u]	1	4	1[i]	2[b]	3	3[c]	41.0
						Mean	41.7
			24 Hours				
F59541	1[j]	4	1[i]	3[b]	3	3[d]	43.0
F59542	1[j]	3	1[i]	3[b]	3	3[d]	38.0
F59543	1[j]	4	1[i]	3[b]	4	3[d]	45.0
						Mean	42.0

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

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

b Blanching.

c Clear discharge.

d Purulent discharge.

i Injected.

j Corneal epithelial peeling.

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							
F59541	1[j]	4	1[i]	3[a,b]	3	3[d]	43.0
F59542	1[j]	2	1[i]	3[a,b]	3	2[d]	31.0
F59543	1[j]	3	1[i]	3[a,b]	2	3[c]	36.0
						Mean	36.7
72 Hours							
F59541	1[j]	4	1[i]	3[a,b]	3	2[d]	41.0
F59542	1[j]	2	1[i]	3[a,b]	2	1[c]	27.0
F59543	1[j]	2	1[i]	3[a,b]	2	2[d]	29.0
						Mean	32.3

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

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

a Petite hemorrhaging.

b Blanching

c Clear discharge.

d Purulent discharge.

i Injected.

j Corneal epithelial peeling.

Table 2 (Continued)

Individual Eye Irritation Scores

Animal Number	Cornea A	Cornea B	Iris C	Conjunctivae D	Conjunctivae E	Conjunctivae F	Total Score*
			96 Hours				
F59541	1[j]	3	1[i]	3[a,b]	2	1[d]	32.0
F59542	1[j]	2	0	2[b]	2	1[d]	20.0
F59543	1[j]	1	1[i]	2[b]	2	1[d]	20.0
						Mean	24.0
			Day 7				
F59541	1[p]	3	1[i]	2[b]	2	1[d]	30.0
F59542	1[j]	1	0	2[b]	1	1[d]	13.0
F59543	0	0	0	2	1	0	6.0
						Mean	16.3

Cornea

A - Degree of opacity
B - Area of involvement

Iris

C - Degree of iridal irritation

Conjunctivae

D - Redness
E - Chemosis
F - Discharge

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

a Petite hemorrhaging.
b Blanching
d Purulent discharge.
i Injected.
j Corneal epithelial peeling.
p Pannus.

Table 2 (Continued)

Individual Eye Irritation Scores

Animal Number	Cornea A	Cornea B	Iris C	Conjunctivae D	Conjunctivae E	Conjunctivae F	Total Score*
			Day 14				
F59541	1[j,n]	1	0	2	1	1[d]	13.0
F59542	1[j,n]	1	0	2	1	1[d]	13.0
F59543	0	0	0	0	0	0	0.0
						Mean	8.7
			Day 21				
F59541	1[j,n]	1	0	1	1	0	9.0
F59542	1[j,n]	1	0	2	1	0	11.0
F59543	0	0	0	0	0	0	0.0
						Mean	6.7

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

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

d Purulent discharge.

j Corneal epithelial peeling.

n Corneal neovascularization.

Table 3

Sodium Fluorescein Examinations

Animal Number	Observation Period			
	Preinitiation	24 Hour	48 Hour	72 Hour
F59541	NEG	POS (95%)	POS (90%)	POS (85%)
F59542	NEG	POS (55%)	POS (45%)	POS (20%)
F59543	NEG	POS (80%)	POS (60%)	POS (40%)

Animal Number	Observation Period			
	96 Hour	Day 7	Day 14	Day 21
F59541	POS (70%)	POS (55%)	POS (15%)	POS (5%)
F59542	POS (15%)	POS (10%)	POS (10%)	POS (10%)
F59543	POS (20%)	NEG	-	-

NEG Negative stain retention.
POS Positive stain retention (area of cornea involved).
- Sodium fluorescein examination not conducted.

Table 4

Individual Body Weights (g)

Animal Number	Sex	Initial	Day		
			7	14	21
F59541	F	2,470	2,575	2,608	2,733
F59542	F	2,529	2,671	2,706	2,872
F59543	F	2,192	2,274	2,335	2,483

APPENDIX

Protocol
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. 60504574

Enclose with samples and send to:
Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Submitted by: ROGER G. PERKINS
Date Sample Sent: _____
Company: 3M
Number of Reports Required: _____

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-6564
Physical Description: liquid
Special Handling Precautions: See MSDS 06-2846-1

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:
M. W L.J. Pickett
3M Specialty Chemical
Bldg 53-3S-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

___TP3084 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: _____

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: _____

and IV. PK and 5 x Dermal Absorption - Persistence.

For CHW Use Only

Protocol Issue Date: 6-20-96
Study Director: Steven M. Hoy

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 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 60504574

Phone 608 241 4471 Fax 608 241 7227
FOR EXPRESS MAIL DELIVERY 3301 KINSMAN BOULEVARD MADISON WISCONSIN 53704

STUDY IDENTIFICATION

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

HWI No.	60504574
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 6-24-96
Experimental Termination Date	Week of 7-15-96
Final Report Date	Week of 8-26-96

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)
[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 per group

(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. 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.

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.

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)

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, PhD
Sponsor's Representative
3M

July 22, 1993
Date

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

6-1-93
Date

Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

6/1/93
Date

(TP2072.3M)

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 5 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 5 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. (FHSA Interpretation)

CHW No. 60504574

PROTOCOL AMENDMENTS

Amendment No. 1

Effective June 20, 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. Hays 6/20/96

(G21/01-07-91)