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:

Acute Oral Toxicity Study of T-6684 in Rats
(OECD Guidelines)

Author:

Steven M. Glaza

Study Completion Date:

January 31, 1997

Performing Laboratory:

Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

CHW 61101149

COMPLIANCE STATEMENT

Acute Oral Toxicity Study of T-6684 in Rats
(OECD Guidelines)

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

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

1-31-97
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
12/19/96	12/19/96	Necropsy	12/19/96	12/19/96
01/23/97	01/24/97	Data/Report Review	01/24/97	01/24/97

Susan K. Swatch
Representative, Quality Assurance Unit

1-31-97
Date

STUDY IDENTIFICATION

Acute Oral Toxicity Study of T-6684 in Rats
(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 5, 1996
In-life End Date	December 19, 1996
Experimental Termination Date	January 31, 1997
Study Completion Date	January 31, 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

Anatomical Pathology

Thomas E. Palmer, PhD
Anatomical Pathologist

Deborah L. Pirkel/
Jack Serfort
Supervisors
Necropsy

CONTENTS

OBJECTIVE

The objective of this study was to assess the acute oral toxicity produced when the test material is administered by the oral route (gavage) to rats.[1]

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

Young adult albino rats of the Crl:CD (SD)BR strain were procured from Charles River Laboratories, Inc. on November 4, 1996 (Portage, Michigan facility) and November 12, 1996 (Raleigh, North Carolina facility).

Housing

After receipt, the animals were acclimated for a period of at least 7 days. During acclimation and throughout the study, the animals were separated by sex and group housed in screen-bottom stainless steel cages. Environmental controls for the animal room were set to maintain a temperature of 19° to 25°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 continuous access to Laboratory Rodent Diet #5001, PMI Feeds, Inc., and water except for approximately 17 to 20 hours before test material administration when food, but not water, was withheld. 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 Grouping

Five male and five female healthy, acclimated rats, weighing from 255 to 299 g and approximately 10 to 13 weeks of age, were used for a single dose level of 5,000 mg/kg of body weight. The animals were identified by animal number and corresponding ear tag throughout the study.

Justification for Species Selection

Historically, rats have been used as a representative of a rodent species and are preferred by various regulatory agencies.

PROCEDURES

Preparation and Administration of Test Material

An individual dose of the test material was calculated for each animal based on its fasted body weight and administered as a single dose by gavage. The test material was administered at a volume of 5.05 mL/kg of body weight based on an average bulk density of 0.99 g/mL.

Reason for Route of Administration

Historically, the oral route has been the route of choice for administering a known amount of test material.

Observations

Clinical observations were conducted at 1, 2.5, and 4 hours after test material administration and daily thereafter for 14 days. Mortality checks were conducted twice a day (morning and afternoon) for 13 days after test material administration and again the morning of Day 14.

Body weights were determined before test material administration (Day 0), at Day 7, and at termination of the in-life phase (Day 14).

Pathology

At termination of the in-life phase, all surviving animals were euthanized. All animals, whether found dead during the study or euthanized, were subjected to an abbreviated gross necropsy examination and any abnormalities were recorded. After necropsy, the animals were discarded and no tissues were saved.

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

Mortality

A summary of the survival rate is in Table 1. One female was found dead on Day 7. No other mortality was observed. The estimated oral LD_{50} values for male and female rats were determined to be greater than 5,000 mg/kg of body weight.

Body Weights

Individual and mean body weights and body weight gains are in Table 2. All surviving animals exhibited body weight gain with the exception of 3 females which exhibited body weight losses of 1 to 22 g during the first week of the study and one male which exhibited a weight loss of 66 g during the second week.

Clinical Signs

Individual clinical signs are in Table 3. All animals appeared normal with the exception of the one female which died during the study which exhibited red-stained face, wet/yellow-stained urogenital area, hunched posture, tremors, hypersensitivity to touch, and tonic convulsions. In addition, one male was noted to have a missing front tooth on Day 11. This animal subsequently appeared thin on Days 12 through 14. This animal's weight loss noted above is probably due to the missing tooth and is not considered to be test material related.

Pathology

Individual gross necropsy findings are in Table 4. A summary report by the study pathologist is on Page 13. There were no test material related lesions in any of the animals.

DISCUSSION

The acute oral toxicity of T-6684 was evaluated in male and female rats at a dose level of 5,000 mg/kg. The estimated LD_{50} value for male and female rats was determined to be greater than 5,000 mg/kg. The only mortality was the death of one female on Day 7. The only test material related clinical signs of toxicity were in one male which included a missing upper right front tooth and thin appearance and the female which died during the study and included red-stained face, wet/yellow-stained urogenital area, hunched posture, tremors, hypersensitivity to touch, and tonic convulsions. All surviving animals exhibited body weight gain with the exception of three females which exhibited body weight losses of 1 to 22 g during the first week of the study and one male which exhibited a weight loss of 66 g during the second week. The weight loss in the male animal was due to a non-test material related condition. There were no test material related lesions observed at necropsy.

SIGNATURE

Steven M. Glaza
Study Director
Acute Studies

1-31-97
Date

REFERENCE

1. "Acute Oral Toxicity," *Organisation for Economic Cooperation and Development Guidelines for Testing of Chemicals*, Section 4, Health Effects, Number 401, Paris Cedex (February 24, 1987).

PATHOLOGY REPORT

There were 10 rats (five males, five females) necropsied. One female died on Test Day 7 and the remaining animals were euthanized and necropsied at the termination of the study. The dose level, day of death, and gross observations recorded for each animal are in the Individual Pathology Comments that follow this report.

At necropsy, the only lesions observed were in the female that died on test. The ventral haircoat was stained and the glandular portion of the stomach had multiple, dark red, pinpoint foci. These changes were considered incidental findings and unrelated to the test material. There were no visible lesions in any of the animals that survived to study termination..

Thomas E. Palmer 1-31-97

Thomas E. Palmer, PhD
Pathologist

Date

(61101149.fin)
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Table 1

Mortality Summary

Dose Level (mg/kg)	Sex	Mortality Results No. Died/ No. Dosed*
5,000	M	0/5
5,000	F	1/5, Day 7[1]

* Superscript number indicates number of animals found dead on the indicated day.

Table 2

**Individual and Mean Body Weights/
Body Weight Gains (g)**

Animal Number	Day 0 Weight	Day 7 Weight	Day 7 Gain*	Day 14 Weight	Day 14 Gain*
		Males (5,000 mg/kg)			
C15368	264	310	46	334	70
C15363	270	305	35	339	69
C15374	299	352	53	382	83
C15367	298	324	26	372	74
C15337	298	346	48	280	-18
Mean	286	327	42	341	56
		Females (5,000 mg/kg)			
C12896	284	213	-71	(209)[7]	-
C12898	270	270	0	303	33
C12905	273	251	-22	294	21
C12903	286	285	-1	301	15
C12908	255	247	-8	271	16
Mean	274	253	- 20	292	21

* Gain from Day 0 body weight.
( ) Value in parantheses is a dead body weight. Superscript number indicates the day the animal was found dead.

Table 3

Individual Clinical Signs

Animal Number	Observation	Hour 1.0	2.5	4.0	Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Males (5,000 mg/kg)													
C15368	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C15363	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C15374	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C15367	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C15337	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	-	-
	Missing upper right front tooth	-	-	-	-	-	-	-	-	-	-	-	-	-	✓	✓	✓	✓
	Thin appearance	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✓	✓	✓
					Females (5,000 mg/kg)													
C12896	Appeared normal	✓	✓	✓	-	-	-	-	-	-	-							
	Yellow-stained urogenital area	-	-	-	✓	✓	✓	-	✓	✓	✓							
	Red-stained face	-	-	-	-	-	✓	✓	✓	-	✓							
	Wet urogenital area	-	-	-	-	-	-	✓	✓	✓	✓							
	Tremors	-	-	-	-	-	-	✓	-	-	-							
	Hypersensitive to touch	-	-	-	-	-	-	-	-	✓	✓							
	Tonic convulsions	-	-	-	-	-	-	-	-	✓	-							
	Hunched posture	-	-	-	-	-	-	-	-	-	✓							
	Found dead (after clinical observation)	-	-	-	-	-	-	-	-	-	✓							
C12898	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12905	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12903	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12908	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

✓ Condition existed.
- Condition not evident.

Table 4

Individual Pathology Comments

Dose Level: 5,000 mg/kg of Body Weight

Animal Number	Sex	Test Day		Necropsy Observation
		Died	Sacrificed	
C15368	M	-	14	No visible lesions.
C15363	M	-	14	No visible lesions.
C15374	M	-	14	No visible lesions.
C15367	M	-	14	No visible lesions.
C15337	M	-	14	No visible lesions.
C12896	F	7	-	The haircoat of the entire ventral surface is stained with dark red and dry material. The mucosal surface of the glandular portion of the stomach has multiple, dark red, pinpoint foci.
C12898	F	-	14	No visible lesions.
C12905	F	-	14	No visible lesions.
C12903	F	-	14	No visible lesions.
C12908	F	-	14	No visible lesions.

- Not applicable.

APPENDIX

Protocol TP2069
Protocol Amendment No. 1
Protocol Amendment No. 2

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. 61101149
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 MSDSs 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
Bg 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: 11-27-96
Study Director: Steven M. Illig

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 TP2069

Study Title:

Acute Oral Toxicity Study in Rats
(OECD Guidelines)

Date:

June 1, 1993

Performing Laboratory:

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

Laboratory Project Identification:

HWI 6110149

STUDY IDENTIFICATION

Acute Oral Toxicity Study in Rats (OECD Guidelines)

HWI No.	61101149
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 1-27-97
Final Report Date	Week of 1-27-97

1. Study
   Acute Oral Toxicity Study in Rats (OECD Guidelines)

2. Purpose
   To assess the acute oral toxicity produced when the test material is administered by the oral route (gavage) to rats

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
Rat

(2) Strain/Source
[X] Crl:CD®BR/Charles River Laboratories, Inc.
[ ] Hsd:Sprague Dawley SD®/Harlan Sprague Dawley, Inc.

(3) Age at Initiation
Young adult

(4) Weight at Initiation
200 to 300 g

(5) Number and Sex
5 males and 5 females for the initial dose level
5 males and/or 5 females for any additional dose levels (if required)

(6) Identification
Individual numbered ear tag

(7) Husbandry

(a) Housing
Separated by sex and group housed in screen-bottom stainless steel cages (heavy gauge)

(b) Food
Rodent Chow® #5001 (Purina Mills, Inc.) *ad libitum* except for overnight before test material administration. 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 25°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, rats have been used as representative of a rodent species and are preferred by various regulatory agencies.

B. Dose Administration

(1) Dose Level
A single dose of 5,000 mg/kg of body weight will be administered to five males and five females. If no test material-related mortality is produced at this level, no

further testing will be required. If any mortality occurs at the 5,000 mg/kg dose level, additional dose levels may be added at the direction of the study director in order to meet the objectives of the study.

(2) Dose Preparation and Administration
All animals will receive the same concentration of test mixture per dose level. If a solid, the test material will be suspended in an appropriate vehicle. If a liquid, the test material will be dosed undiluted, using the bulk density to determine the dose volume. If the material is an aerosol, it will be discharged into a beaker and administered as a liquid. Individual doses will be based upon the animal's body weight taken just before test material administration, and administered by gavage. The animals will have food withheld for 17 to 20 hours before test material administration. The prepared test mixtures will be stored at room temperature until administration. After administration, any remaining test mixtures will be discarded.

(3) Reason for Route of Administration
Historically, the oral route has been the route of choice for administering a known amount of test material.

C. Observation of Animals

(1) Clinical Observations
At approximately 1, 2.5, and 4 hours after test material administration and daily thereafter for at least 14 days for clinical signs and twice daily (a.m. and p.m.) for mortality. Observations may be extended when directed by the study director.

(2) Body Weights
Before experimental initiation, at 7 and 14 days after test material administration, and at death (when survival exceeds 1 day)

D. Pathology
At termination of the experimental phase, surviving animals will be euthanized. All animals, whether dying during the study or euthanized, 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.

E. Statistical Analyses
Other than LD_{50} calculations (when applicable) 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 mortality data by sex and dose level
Description of any toxic effects
Tabulation of mean body weights by sex and dose level
LD_{50} calculations for each sex with 95% confidence intervals (when applicable)
Gross pathology findings/gross pathology report (when applicable)

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
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

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

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

6/1/93
Date

(TP2069.3M)

CHW No. 61101149

PROTOCOL AMENDMENTS

Amendment No. 1

Effective NOVEMBER 27, 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. Klaja 11-27-96

(G21/01-07-91)

CHW No. 61101149

PROTOCOL AMENDMENTS

Amendment No. 2

Effective November 27, 1996

Portion of Protocol Being Modified: Page 4, 6. Experimental Design: A. Animals (2) Strain/Source

Reason for Modification: To correctly identify the nomenclature used for animals received from Charles River Laboratories, Inc.

Modification: Replace this section with the following change:

(2) Strain/Source

☒ Crl:CD®(SD)BR/Charles River Laboratories, Inc.
Hsd:Sprague Dawley SD®/Harlan Sprague Dawley, Inc.

Study Director Approval: Steven M. Hoge 11-27-96

(G21/01-07-91)