

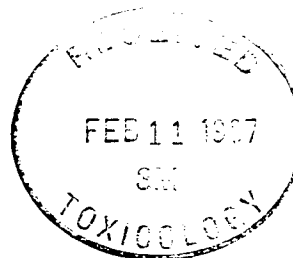
**HAZLETON**

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

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

FINAL REPORT



ROGER PERKINS
MINNESOTA MINING & MANUFACTURING COMPANY
TOXICOLOGY SERVICES
ST. PAUL, MN 55101

SAMPLE NUMBER: 70100353

SAMPLE ENTERED: 01/07/87

REPORT PRINTED: 02/05/87

SAMPLE: T-4016

PURCHASE ORDER NUMBER: T837389-410 712

ENCLOSED: ACUTE ORAL TOXICITY STUDY IN RATS - METHOD, SUMMARY, PATHOLOGY
RAW DATA APPENDIX

SIGNED:

Steven M. Glaza
.....
STEVEN M. GLAZA
STUDY DIRECTOR
ACUTE TOXICOLOGY

DATE

.....29-87.....

BY AND FOR HAZLETON LABORATORIES AMERICA, INC.

RAW DATA FOR THIS STUDY ARE KEPT ON FILE AT HAZLETON LABORATORIES
AMERICA, INC., MADISON, WISCONSIN.



SAMPLE NUMBER: 70100353

PAGE 2

SAMPLE: T-4016

ACUTE ORAL TOXICITY

Objective: To determine the acute oral toxicity produced when a test material is administered by the oral route (gavage) to rats according to the U.S. Environmental Protection Agency's Guidelines for Testing Pesticides and Toxic Substances.

Test Material: T-4016

Physical Description: Thick brown liquid

Purity and Stability: Sponsor assumes responsibility for purity and stability determinations.

Test Animal: Young adult male and female albino rats of the Sprague-Dawley strain were procured, maintained by sex in group cages in temperature- and humidity-controlled quarters, provided continuous access to Purina Rodent Chow and water, and held for an acclimation period of at least 7 days.

Acclimated animals were chosen at random for the study. Test animals were housed by sex in groups of five and identified by animal number and corresponding ear tag. Food and water were available ad libitum throughout the study, except for an overnight period just before test material administration when food, but not water, was withheld.

Reason for Species Selection: The rat is the animal classically used due to its small size, ready availability, and large amount of background data.

Method: Five male and five female rats weighing from 203 to 293 g were used for a single dosage level of 5.0 g/kg.

Preparation and Administration of Test Material: An individual dose was calculated for each animal based upon its fasted body weight and administered undiluted by gavage.

The dose volume of the test material was 4.63 ml/kg of body weight based upon an average bulk density of 1.08 g/ml.

Reason for Route of Administration: This is the method for administering a known quantity of test substance and has been the route of choice historically.



HAZLETON

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

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

SAMPLE NUMBER: 70100353

PAGE 3

SAMPLE: T-4016

ACUTE ORAL TOXICITY

(CONTINUED)

Observations: The animals were observed for clinical signs and mortality at 1, 2.5 and 4 hours after test material administration. The animals were observed daily thereafter for 14 days for clinical signs and twice daily for mortality.

All animals were weighed just before test material administration. Surviving animals were weighed again at 7 days and at study termination.

Pathology: At study termination surviving animals were euthanatized. Animals which died during the study or were euthanatized received a gross necropsy examination and all abnormalities were recorded.

**HAZLETON**

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

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

SAMPLE NUMBER: 70100353

PAGE 4

SAMPLE: T-4016

ACUTE ORAL TOXICITY

(CONTINUED)

SUMMARY

Test Animal: Albino Rats - Sprague-Dawley strain
 Source: Charles River Laboratories, Inc., Portage MI
 Date Animals Received: 12/22/86

Method of Administration: Oral Gavage

Date Test Started: 01/08/87

Date Test Completed: 01/22/87

Estimated Oral LD50: Male - Greater than 5.0 g/kg of body weight
 Female - Greater than 5.0 g/kg of body weight

	Dosage Level (g/kg)	Average Body Weights (g)			Mortality (Number Dead/Number Dosed)
		Initial	Day 7	Terminal	
Male	5.0	284	325	361	0/5
Female	5.0	209	224	234	1/5

Clinical Signs

	Hours			Days													
	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Males																	
Appeared Normal	4	4	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Hypoactivity	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Red-stained face	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Excessive salivation	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Females																	
Appeared Normal	3	3	3	2	4	4	4	4	4	4	4	4	4	4	4	4	4
Hypoactivity	1	1	1	2	1	1	0	0	0	0	0	0	0	0	0	0	0
Red-stained face	2	2	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0
Excessive salivation	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ataxia	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Emaciation	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Death	0	0	0	0	0	1*	0	0	0	0	0	0	0	0	0	0	0

* Found dead in p.m.

**HAZLETON**

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

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

SAMPLE NUMBER: 70100353

PAGE 5

SAMPLE: T-4016

ACUTE ORAL TOXICITY

(CONTINUED)

PATHOLOGY

Dosage Level: 5.0 g/kg of body weight

Animal Number	Sex	Test Day Died Sacrificed	Necropsy Comments
C66384	M	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66382	M	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66410	M	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66380	M	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66439	M	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66523	F	- 14	Stomach - contains dark-brown, firm, rubbery, porous material, ulcerated areas on nonglandular portion.
C66524	F	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66519	F	- 14	Stomach - contains dark-brown, firm, rubbery, porous material.
C66479	F	- 14	Stomach - contains dark-brown, firm, rubbery, porous material, ulcerated areas on nonglandular portion.
C66515	F	3 -	Stomach - contains dark-brown, firm, rubbery, porous material, and exhibited diffusely red areas on glandular portion, and ulcerated areas on glandular and nonglandular portions.

**HAZLETON**

LABORATORIES AMERICA, INC

Chemical & BioMedical Sciences Division

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

SAMPLE NUMBER: 70100353

PAGE 6

SAMPLE: T-4016

ACUTE ORAL TOXICITY

(CONTINUED)

References:

1. Hitch, R.K., "Acute Oral Toxicity Study," Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, U.S. Environmental Protection Agency Office of Pesticide and Toxic Substance Series 81-1, pp. 34-39, November 1982.
2. 21 CFR 59 (United States Food and Drug Administration's Good Laboratory Practices Regulations for Nonclinical Laboratory Studies).
3. DHHS Publication No. (NIH 85-23 1985) Guide for the Care and Use of Laboratory Animals.

ACUTE ORAL TOXICITY
Dose Administration/ Body Weight/ Mortality Record

Test Material: T-4016 Vehicle: N/A NIA No.: 70100353

Bulk Density: 1.08 (g/ml) Species: Albino Rat Source: Charles River Date Received: 12-22-86

Dose Level: 5.0 (g/kg) Tested: Date: 1-28-87 Time: 3:30pm Technician: JMC Room No.: 350

Strain: Franklin-Dawley Route of Administration: Oral gavage

Dose Volume	4.63 (ml/kg)	Sex:	Male/Female	Dose Time:	9:30am	Technician	Date	Scale Used
Animal No.	6400	6384	6383	6410	6380	6439	JMC	1/8
Pretested Body Weight (g)	N/A							MA
Tested Body Weight (g)	076	074	093	088	076	088	JMC	1/8
Actual Dose (ml)	1.3	1.3	1.4	1.3	1.3	1.3	JMC	1/8
Day 7 Body Weight (g)	273	344	344	349	320	337	SAM	1/5
Day 14 Body Weight (g)	321	366	400	348	368		BB	1/22
Dead Body Weight (g)								Ktron 15019

Dose Volume	4.63 (ml/kg)	Sex:	Male/Female	Dose Time:	9:35am	Technician	Date	Scale Used
Animal No.	6503	6524	6519	6494	6479	6515	JMC	1/8
Pretested Body Weight (g)	N/A							MA
Tested Body Weight (g)	019	007	003	010	006	009	JMC	1/8
Actual Dose (ml)	1.0	0.96	0.94	0.97	0.95	0.97	JMC	1/8
Day 7 Body Weight (g)	230	220	217	*	230	N/A	SAM	1/5
Day 14 Body Weight (g)	237	220	238	*	246	Found dead 1-11-87	BB	1/22
Dead Body Weight (g)						179		Ktron 15019

MORTALITY (NO. DIED/NO. DOSED)

Use Level	Sex	Study Day														Total													
		1		2		3		4		5		6		7			8		9		10		11		12		13		14
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
5.0g/kg	♀	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
5.0g/kg	♀	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
Technician		BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC	BB	JMC
Date	1987	1/8	1/9	1/10	1/11	1/12	1/13	1/14	1/15	1/16	1/17	1/18	1/19	1/20	1/21	1/22	1/23	1/24	1/25	1/26	1/27	1/28	1/29	1/30	1/31	2/1	2/2	2/3	2/4

MA - Not Applicable
* - Doseage calculated, but not administered
unused animal returned to stock

Reviewed by: JMC Date: 1-28-87

Entry error BB
1-22-87

Wrong date entered
1-23-87

Entry error
1-23-87

ACUTE ORAL TOXICITY

Individual Clinical Observations

Test Material: T-4016 Dose Level: 50g/kg HLA No.: 70100353

Animal Number	Male/Female	Pre dose	Hours			Study Day													
			1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C6-6384	Observations	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C6-6382	Hypocative	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Red thalipocative	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C6-6410	Observations	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C6-6380	Observations	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C6-6439	Observations	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Deaths		Technician	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8
Date		1987	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8	1/8

✓ = Sign present.
 SI = Sign present, slight.
 - = Not evident.

Reviewed By: JP
 Date: 1-23-87

① misspelled word 65 2-3-87

Individual Clinical Observations

HLA No.: 70100353

Dose Level: 5.0g/kg HLA No.: _____

Test Material: F-4016

① Died in PMW 1-11-87

✓ - sign present.

SI = Sign present, slight.

- = Not evident.

Reviewed By: 

Date: 1-23-87

[illegible]

① Misspelled words 5-2-3-87