

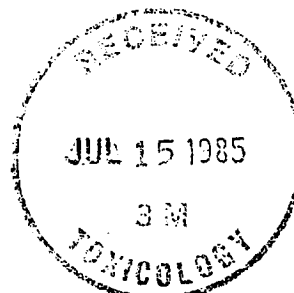
**HAZLETON**

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



JANINE GLEASON
MINNESOTA MINING & MANUFACTURING COMPANY
TOXICOLOGY SERVICES
ST. PAUL, MN 55101

SAMPLE NUMBER: 50503499

SAMPLE ENTERED: 05/15/85

REPORT PRINTED: 07/12/85

T-3752

PURCHASE ORDER NUMBER: T357842, REL. #513

ENCLOSED: ACUTE ORAL TOXICITY - METHOD, SUMMARY, PATHOLOGY
QAU REPORT
RAW DATA APPENDIX

SIGNED:

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

DATE

7-12-85

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: 50503499

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OECD ORAL SCREEN

Objective: To determine the acute oral toxicity produced when a test material is administered by oral gavage to rats according to the Organisation of Economic Cooperation and Development's Guidelines for Testing Chemicals, Section 401, Acute Oral Toxicity, adopted May 12, 1981.

Test Material: T-3752

Physical Description: Brown granular solid

Stability of Test Material: Sponsor has purity and stability determinations on file.

Test Animal: Young adult male and female albino rats of the Sprague-Dawley strain were procured, maintained 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 between 195 and 234 g were used for each dosage level. The study consisted of three dosage levels (0.20, 2.0 and 5.0 g/kg).

Preparation and Administration of Test Material: For each dose level, the appropriate amount of test material was mixed with corn oil and heated and stirred on a stir plate to a uniform suspension. The suspension was cooled to room temperature prior to dosing. An individual dose was calculated for each animal based upon its fasted body weight and administered by gavage. The dose volume was 15.0 ml/kg of body weight.

Observations: The animals were observed for clinical signs and mortality at 1, 2.5 and 4 hours following 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, at 7 days and at study termination or at death.

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.

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OECD ORAL SCREEN

(CONTINUED)

SUMMARY

Test Animal: Albino Rats - Sprague-Dawley strain

Source: Harlan Sprague-Dawley, Madison WI

Date Animals Received: 05/22/85

Temperature and Humidity of Animal Room: 19 to 24 Degrees C.;
42 to 60% Relative Humidity

Vehicle: Corn oil

Method of Administration: Oral Gavage

Date Test Started: 05/30/85

Date Test Completed: 06/20/85

Estimated Oral LD50*: Male - Between 0.20 and 2.0 g/kg of body weight

Female - Between 0.20 and 2.0 g/kg of body weight

Mortality Summary (Number of Deaths)

Dosage Level (g/kg)	Hours		Days										Total		
	0 - 4		1	2	3	4	5	6	7-14						
	M	F	M F	M F	M F	M F	M F	M F	M F	M F	M	F	Both		
0.20	0	0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0/5	0/5	0/10		
2.00	0	0	4 5	1 -	- -	- -	- -	- -	- -	- -	5/5	5/5	10/10		
5.00	0	0	4 5	1 -	- -	- -	- -	- -	- -	- -	5/5	5/5	10/10		

	Dosage Level (g/kg)	Average Body Weights (g)		
		Initial	Day 7	Terminal
Male	0.20	224	263	294
	2.00	212	---	---
	5.00	196	---	---
Female	0.20	201	209	219
	2.00	215	---	---
	5.00	211	---	---



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OECD ORAL SCREEN

(CONTINUED)

Clinical Signs

Hours					Days											
1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14

Dosage Level - 0.20 g/kg

Males

[illegible]

Females

[illegible]

Dosage Level - 2.00 g/kg

Males

[illegible]

Females

[illegible]



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(CONTINUED)

Clinical Signs (continued)

Hours					Days											
1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14

Dosage Level - 5.00 g/kg

Males

[illegible]

Females

[illegible]

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OECD ORAL SCREEN

(CONTINUED)

PATHOLOGY

Dosage Level: 0.20 g/kg of body weight Date Dosed: 06/06/85

Animal Number	Sex	Test Day		Necropsy Comments
		Died	Sacrificed	
C34524	M	-	14	No visible lesions.
C34518	M	-	14	No visible lesions.
C34504	M	-	14	No visible lesions.
C34510	M	-	14	No visible lesions.
C34509	M	-	14	No visible lesions.
C34465	F	-	14	No visible lesions.
C34499	F	-	14	No visible lesions.
C34466	F	-	14	No visible lesions.
C34464	F	-	14	No visible lesions.
C34473	F	-	14	Liver - hepatic anomaly at junction of median lobes, 8 x 5 mm, liver-like.



SAMPLE NUMBER: 50503499

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OECD ORAL SCREEN

(CONTINUED)

PATHOLOGY (continued)

Dosage Level: 2.00 g/kg of body weight

Date Dosed: 06/04/85

Animal Number	Sex	Test Day		Necropsy Comments
		Died	Sacrificed	
C34483	M	1	-	Red perinasal discharge; dark red, bilateral periocular discharge; perineum - moist, stained clear yellow.
C34480	M	1	-	Red perinasal discharge; perineum - moist, stained clear yellow; eye - white intraocular material.
C34481	M	1	-	Red perinasal discharge; dark red, bilateral periocular discharge; perineum - stained clear yellow.
C34477	M	1	-	Red perinasal discharge; perineum - moist, stained clear yellow;
C34512	M	2	-	Red perinasal discharge; perineum - moist with clear fluid; bilateral red ocular discharge; jejunum and ileum - contain dark brown material.
C34493	F	1	-	Perineum - stained yellow; small intestine - contains tan to yellow mucoid material.
C34463	F	1	-	Perineum - stained yellow; small intestine - contains tan to yellow mucoid material.
C34485	F	1	-	Perineum - stained yellow; jejunum - contains dark brown mucoid material.
C34469	F	1	-	Perineum - stained yellow; small intestine - contains tan to yellow mucoid material.
C34492	F	1	-	Perineum - stained yellow; small intestine - contains tan to yellow mucoid material.



SAMPLE NUMBER: 50503499

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OECD ORAL SCREEN

(CONTINUED)

PATHOLOGY (continued)

Dosage Level: 5.00 g/kg of body weight Date Dosed: 05/29/85

Animal Number	Sex	Test Day		Necropsy Comments
		Died	Sacrificed	
C34505	M	3	-	Stomach - contains dark brown semisolid material.
C34479	M	2	-	No visible lesions.
C34513	M	2	-	Stomach - contains dark brown semisolid material.
C34503	M	2	-	Stomach - multiple dark brown areas on glandular mucosa, up to 2 x 3 mm.
C34507	M	2	-	No visible lesions.
C34500	F	2	-	No visible lesions.
C34495	F	2	-	No visible lesions.
C34484	F	2	-	Upper thoracic cavity contains dark red, clotted material.
C34498	F	2	-	No visible lesions.
C34467	F	2	-	No visible lesions.

Deviation from the protocol: During the study period the temperature of the animal room ranged from 19 to 24 degrees C. This deviation is not considered to have had an effect on the validity of the study.

References: Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 401, Acute Oral Toxicity, adopted May 12, 1981.

QUALITY ASSURANCE STATEMENT

Acute Oral Toxicity Study in Rats

Study No. 50503499

The report as herein attached for the above-mentioned study has been reviewed by the assigned Quality Assurance Unit of Hazleton Laboratories America, Inc. It has been found to accurately identify and/or describe the authorized methods and standard operating procedures followed in the conduct of the study. Furthermore, the Quality Assurance Unit has conducted the following inspections of the testing facilities utilized in the conduct of this study and has submitted written reports of said inspections to the study director and/or management.

<u>Date of Inspection</u>	<u>Type of Inspection</u>	<u>Date Issued to Management</u>
5/21-23/85	Process Audit	5/23/85
7/12/85	Report Review	7/12/85

Diana E. Skalitzky
Diana E. Skalitzky
Inspector, Quality Assurance Unit

7/12/85
Date

ACUTE ORAL TOXICITY (LD₅₀) RECORD

Test Material T-3752 Vehicle CORN OIL RT No. 50503499
 Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 5-22-85
 Fasted: Date 6-5-85 Time 3:50 P.m. Tech. UMC Room No. 3

Sex



Dosage	Dose Time 10:00 a.m.								Tech.	Date	Scale Used:
0.20 (g/kg)											
Dose Volume 15.0 (ml/kg)											
Animal No./Ear Tag No. C3	4524	4501	4519	4504	4510	4522	4509		Sam	6-6	NA
Prefasted Body Weight (g)	NA								Sam	6-6	KT
Fasted Body Weight (g)	225	227	220	230	224	219	221		Sam	6-6	KTRON 15019
Actual Dose (ml)	3.4	3.4	3.3	3.5	3.4	3.3	3.3		Sam	6-6	NA
Day 7 Body Weight (g)	260	*	258	274	259	*	263		Sam	6-13	KTRON 15019
Day 14 Body Weight (g)	292	*	277	310	301	*	292		UMC	6-20	KTRON 15019
Doses Verified by									MP	6-6	NA

① Recording error 6-6-85 Sam
 ② Entry error 6-6-85 UMC



Dosage	Dose Time 10:15 a.m.								Tech.	Date	Scale Used:
0.20 (g/kg)											
Dose Volume 15.0 (ml/kg)											
Animal No./Ear Tag No. C3	4465	4499	4466	4464	4473	4471	4494		Sam	6-6	NA
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	200	200	200	201	205	202	200		Sam	6-6	KTRON 15019
Actual Dose (ml)	3.0	3.0	3.0	3.0	3.1	3.0	3.0		Sam	6-6	NA
Day 7 Body Weight (g)	212	198	210	207	220	*	*		Sam	6-13	KTRON 15019
Day 14 Body Weight (g)	220	217	210	213	235	*	*		UMC	6-20	KTRON 15019
Doses Verified by									MP	6-6	NA

MORTALITY (NO. DIED/NO. DOSED)



MORTALITY (NO. DIED/NO. LOSED)																														
Dose Level	Hours	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	
0.20g/kg	9/5	1/5	0/5	0/5	0/5	0/5	1/5	1/5	1/5	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	NA	0/5
0.20g/kg	9/5	1/5	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	NA	0/5
Technician	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	Sam	NA	MP
Date 1985	6/6	6/7	6/7	6/8	6/8	6/9	6/9	6/10	6/10	6/11	6/11	6/12	6/12	6/13	6/13	6/14	6/14	6/15	6/15	6/16	6/16	6/17	6/17	6/18	6/18	6/19	6/19	6/20	NA	4/26

NA - Not Applicable

Reviewed by MP Date 6-26-85

NA - Not Applicable

ACUTE ORAL TOXICITY (LD₅₀) RECORD

Test Material T-3752 Vehicle CORN OIL RT No. 50503499
 Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 5-22-85
 Fasted: Date 6-3-85 Time 3:00 pm Tech. CK Room No. 3
 1985

Sex

♂

Dosage	2.0 (g/kg)	Dose Time 10:45 a.m.							Tech.	Date	Scale Used:
Dose Volume	15.0 (ml/kg)								MP	6/4	NA
Animal No./Ear Tag No.	C3	4493	4478	4480	4482	4481	4477	4512			
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	205	200	208	203	211	213	221		MP	6/4	KTRON 15019
Actual Dose (ml)	3.1	3.0	3.1	3.0	3.2	3.2	3.3		Sam	6-4	NA
Day 7 Body Weight (g)	Dead 190	*	Dead 195	*	Dead 197	Dead 199	Dead 191.9				
Day 14 Body Weight (g)	Dead 158.5	*	Dead 163.85	*	Dead 163.85	Dead 163.85	Dead 163.85				
	3mc		3mc		3mc				Doses Verified by	MP	6-4
											NA

♀

Dosage	2.0 (g/kg)	Dose Time 11:00 a.m.							Tech.	Date	Scale Used:
Dose Volume	15.0 (ml/kg)								MP	6/4	NA
Animal No./Ear Tag No.	C3	4493	4473	4463	4485	4469	4492	4471			
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	205	205	206	234	218	211	200		MP	6/4	KTRON 15019
Actual Dose (ml)	3.1	3.1	3.1	3.5	3.3	3.2	3.0		Sam	6-4	NA
Day 7 Body Weight (g)	Dead 165.85	*	Dead 190	Dead 211	Dead 211	Dead 211	*				
Day 14 Body Weight (g)	189 MP	*	6-5-85 189 MP	6-5-85 201 MP	201 MP	200	*				
			3mc	3mc					Doses Verified by	MP	6-4
											NA

MORTALITY (NO. DIED/NO. DOSED)

Dose Level	Hours	Study Day														Total
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	
	0 - 4	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	am	pm	
2.0	0/5	4/5	4/5	1/5	NA											5/5
2.0	0/5	4/5	1/5	NA	NA											5/5
Technician	Sam	MP	Sam	Sam	NA											MMH
Date	1985 6/4	6/5	6/5	6/6	NA											6/26

NA - Not Applicable

* Doses calculated, but not administered

Reviewed by MMH Date 6-26-85 MMH

ACUTE ORAL TOXICITY (LD₅₀) RECORD

Test Material T-3752 Vehicle CORN OIL RT No. 50503499

Bulk Density NA (g/ml) Species Rat Source Harlan Date Received 5-22-85

Fasted: Date 5-29-85 Time 3:00 PM Tech. Sam Room No. 3

Sex

♂

Dosage	5.0 (g/kg)	Dose Time 11:45 a.m.							Tech.	1985 Date	Scale Used:
Dose Volume	15.0 (ml/kg)								Sam	5-30	NA
Animal No./Ear Tag No.	C3	4505	4479	4513	4503	4507	4512	4504			
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	196	197	195	196	195	196	196		Sam	5-30	KTRON 1348
Actual Dose (ml)	2.9	3.0	2.9	2.9	2.9	2.9	2.9		Sam	5-30	NA
Day 7 Body Weight (g)	DEAD 1785	DEAD CK	DEAD CK	DEAD CK	DEAD CK	*	*				
Day 14 Body Weight (g)	170g	5-31-85	5-31-85	5-31-85	5-31-85	*	*				
182g 181g 175g 176g								Doses Verified by	SO	5-30	NA

♀

Dosage	5.0 (g/kg)	Dose Time 12:00 p.m.							Tech.	1985 Date	Scale Used:
Dose Volume	15.0 (ml/kg)								Sam	5-30	NA
Animal No./Ear Tag No.	C3	4500	4495	4484	4498	4467	4485				
Prefasted Body Weight (g)	NA										
Fasted Body Weight (g)	208	215	210	210	213	230			Sam	5-30	KTRON 1348
Actual Dose (ml)	3.1	3.2	3.2	3.2	3.2	3.5			Sam	5-30	NA
Day 7 Body Weight (g)	DEAD CK	DEAD CK	DEAD CK	DEAD CK	DEAD CK	*					
Day 14 Body Weight (g)	5-31-85	5-31-85	5-31-85	5-31-85	5-31-85	*					
193g 200g 199g 194g 211g								Doses Verified by	SO	5-30	NA

MORTALITY (NO. DIED/NO. DOSED)

MORTALITY (NO. DIED/NO. DOSED)																																	
Dose Level	Hours	Study Day																												Total			
	0 - 4	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	5/5	1/5	0/5	1/5	NA																									2	NA	5/5	
5.0g/kg	9/5	3/5	0/5	NA	NA																										2	NA	5/5
Technician	Sam	CK	CK	Sam	NA																										2	NA	7/7
Date 1985	5/30	5/31	5/31	6/1	NA																										2	NA	6/26

NA - Not Applicable

* - Dosage calculated, but not administered

Reviewed by MD Date 6-26-85

STUDY TITLE: Acute Oral Toxicity

NT NO. 50503499

TEST MATERIAL. T-3752

SEX ♂

DOSEAGE LEVEL.

0.20 g/kg

ANIMAL/EAR TAG NO. C3-4524

HOURS		1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
STUDY DAY		1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE		6/4	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20
APPEARED NORMAL		✓	✓	✓	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Red Stained Face		—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Yellow Stained abdomen		—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Diarrhea		—	—	—	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
hypoaactive		—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																		
TECHNICIAN		SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	CK	CK	NY	NY	SM	SM
DATE	1985	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 ul - Sign Present, Ulight

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO.50503499

TEST MATERIAL. T-3752

SEX ♂

DOSEAGE LEVEL.

$$0.20 \text{ g/kg}$$

ANIMAL/EAR TAG NO. C3-4518

HOURS

HOURS																	
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHIKINJIN DATE	6/4	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20
APPEARED NORMAL	✓	NE	NE	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Diarrhea	—	✓	✓	✓	NE 10/10	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red stained face	—	—	—	✓	✓	NE 10/10	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
hypoaactive	—	—	—	✓	✓	✓	NE 3/1	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	CK	CK	FD	FD	SM	SM
DATE	1985 6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 ul - Sign Present, Ullight
 ① Entry error 6-8-85 JMC
 ② -

③ Entry error 6-10-85 smc

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral ToxicityRT NO. 50503499TEST MATERIAL T-3752SEX ♂DOSAGE LEVEL 0.20 g/kgANIMAL/EAR TAG NO. C3-4504

HOURS																		
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
SCHEDULED DATE	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20	
APPEARED NORMAL	✓	✓	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Hypoaactive	—	—	✓	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Red Stained Ice	—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Yellow stained abdomen	—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Diarrhea	—	—	—	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
DEATH																		
TECHNICIAN	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	CK	CK	NP	NP	SM	SM	
DATE	1985	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
sl - Sign Present, SlightNE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO.50503499

TEST MATERIAL. T-3752

SEX ♂

DOSEAGE LEVEL. 0.20 g / Kg

ANIMAL/EAR TAG NO. C3-4510

HOURS

HOURS																	
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCHEDULED DATE	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20
APPEARED NORMAL	✓	✓	✓	NG	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
hyperactive	—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red stained face	—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
yellow stained abdomen	—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Diarrhea	—	—	—	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	CK	CK	IP	IP	SMC	SMC
DATE	1985 6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 al - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

BT NO.50503499

TEST MATERIAL. T-3752

SNK ♀

DOSEAGE LEVEL. 0.20 g/kg

ANIMAL/EAR TAG NO. C3-4465

HOURS																		
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
SCHEDULED DATE	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20	
APPEARED NORMAL	NE	NE	✓	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Diarrhea	✓	✓	NE	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
hypoaactive	—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Red stained face	—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
DEATH																		
TECHNICIAN	SML	SML	SML	SML	SML	SML	SML	SML	SML	SML	SML	CK	CK	CP	CP	SML	SML	
DATE	1985	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 nt - Sign Present, slight

NE - Not Evident
NA - Not Applicable

STUDY TITLE:

REF NO. 50503499

TEST MATERIAL. T-3752

SEX ♀

DOSAGE LEVEL. 0.20 g/Kg

ANIMAL/EAR TAG NO. C3-4499

HOURS																	
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SICKING/D DATE	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
hypoactive	—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Yellow stained abdomen	—	—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																	
TECHNICIAN	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	CK	CK	MP	MP	SM	SM
DATE	1985 6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 al - Sign Present, Allight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

NT NO. 50503499

TEST MATERIAL. T-3752

SEX ♀

DOSEAGE LEVEL. 0.20 g/kg

ANIMAL/EAR TAG NO. C3-4466

HOURS

HOURS																		
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
SCHEDULED DATE	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20	
APPEARED NORMAL	✓	✓	✓	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Diarrhea	-	-	-	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Hypoaactive	-	-	-	-	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
Yellow stained abdomen	-	-	-	-	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	
DEATH																		
TECHNICIAN	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	SMC	CK	CK	MP	MP	SMC	SMC	
DATE	1985	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 ul - Sign Present, Ullight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

TEST MATERIAL. T-3752

SEX ♀

DOSEAGE LEVEL. 0.20 g/kg

ANIMAL/EAR TAG NO. C3-4464

		HOURS																
STUDY DAY		1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CHROMIUM DATE		6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20
APPEARED NORMAL		✓	NE	NE	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Diarrhea		—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Hypoactive		—	—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																		
TECHNICIAN		smc	smc	smc	smc	smc	smc	smc	smc	smc	smc	smc	smc	CK	CK	MP	MP	smc
DATE	1985	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 * - Sign Present, slight

NK - Not Evident
NA - Not Applicable

TEST MATERIAL. T-3752

STUDY TITLE:

Acute Oral Toxicity

SEM

DOSEAGE LEVEL

0.20 g/kg

ANIMAL/EAR TAG NO. C3-4473

HOURS

HOURS		1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
STIMULI DAY		6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20
SCHWIMMING DATE		✓	✓	✓	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
APPEARED NORMAL		✓	✓	✓	NE	NE	NE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Diarrhea		—	—	—	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Red stained face		—	—	—	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
hypoaactive		—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Yellow stained abdomen		—	—	—	✓	✓	✓	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
DEATH																		
TECHNICIAN		SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	CK	CK	MP	MP	SM	SM
DATE	1985	6/6	6/6	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20

✓ - Sign Present
 ✗ - Sign Present, Allight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

NT NO. 50503499

TEST MATERIAL. T-3752

SUM

DOSEAGE LEVEL

ANIMAL/EAR TAG NO. C3-4483

HOURS

✓ - **Виктор Рубин**

41 - Sign Present, Slight

NK - Not Evident

NA - Not Applicable

STUDY TITLES:

NT NO. 50503499

TEST MATERIAL. T-3752

SEE

DOBACH LEVEL

ANIMAL/EAR TAG NO. C3-4480

[illegible]

✓ - Sign Present
 x - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

RT NO. 50503499

TEST MATERIAL. T-3752

SEX ♂

DOZAGE I.V.VKL. 2.0g/Kg

ANIMAL/EAR TAG NO. C3-4481

[illegible]

✓ - Sign Present
sl - Sign Present, slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

KT NO. 50503499

TEST MATERIAL. T-3752

SEX

DOSEAGE LEVELANIMAL/EAR TAG NO. C3-4471**HOURS**

① Recording error 64.85 ✓

✓ - Sign Present
 x - Sign Present, slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

HT NO. 50503499

TEST MATERIAL. T-3752

• **♂**

DOSEAGE LEVEL. 2.0g/Kg

ANTHAL/EAR TAG NO. C3-4512

HOURS

✓ - Mike Grant

01 - Sign Present, slight

① recording error n^o 6-5-85

NR - Not Evident

NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO. 50503499

TEST MATERIAL. T-3752

SEX ♀

DOSAGE LEVEL 2.0g/kg

ANIMAL/EAR TAG NO. C3-4493...

[illegible]

① Recording error 6-4-85 ~~800~~ ✓.

✓ - sign present

01 - Sign Present, Slight

NR - Not Evident

NA - Not Applicable

STUDY TITLE:

NT NO. 50503499

TEST MATERIAL. T-3752

SLX

DOSAGE LEVEL. 2.0g/Kg

ANIMAL/EAR TAG NO. C3-4463

[illegible]

✓ - Sign Present
 al - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

NT NO. 5050 3499

TEST MATERIAL. T-3752

SEX ♀

DOSAGE LEVEL. 2.0g/Kg

ANIMAL/EAR TAG NO. C3-4485.

[illegible]

✓ - Sign Present
 ul - Sign Present, slight

NR - Not Evident
NA - Not Applicable

① Animal found dead in p.m. 6-5-85 Jmc

STUDY TITLES:

NT NO. 50503499

TEST MATERIAL. T-3752

♀

2.0g/Kg

ANIMAL/EAR TAG NO. C3-4469

HOURS

NK - Not Evident
NA - Not Applicable

STUDY TITLE:

HT NO. 50503499

TEST MATERIAL. T-3752

SUM

♀

DOSEAGE LEVEL

ANIMAL/EAR TAG NO. C3-4492

HOURS

[illegible]

✓ - Sign Present
 al - Sign Present, slight

NK - Not Evident
 NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

RT NO. 50503499

TEST MATERIAL. T-3752

SEX 

DOSEAGE LEVEL 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4505

HOURS

[illegible]

✓ - Sign Present
 si - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral ToxicityNT NO. 50503499TEST MATERIAL T-3752SEX ♂DOSAGE LEVEL 5.0 g/kgANIMAL/EAR TAG NO. C3-4479

HOURS														
STUDY DAY	1	2 1/2	4	1	2	3	4	5	6	7	8	9	10	11
SCHEDULING DATE	5/30	5/30	5/30	5/31	6/1	6/2	6/3	6/4	6/5	6/6	6/7	6/8	6/9	6/10
APPEARED NORMAL	✓	✓	NG	NA										
Hypoaactive	-	-	✓	NA										
DEATH				✓										
TECHNICIAN	Sam	Sam	Sam	CR										
DATE	1985 5/30	5/30	5/30	5/31										

✓ - Sign Present
sl - Sign Present, Slight

NR - Not Evident
NA - Not Applicable

TEST MATERIAL. T-3752

STUDY TITLE: Acute Oral Toxicity

SEX ☒ ♂

DOSEAGE LEVEL. 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4513

[illegible]

✓ - Sign Present
 ul - Sign Present, slight

NK - Not Evident
NA - Not Applicable

TEST MATERIAL. T-3752

STUDY TITLE: Acute Oral Toxicity

SEX ♂

DOSEAGE LEVEL. 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4503

HOURS

[illegible]

✓ - Sign Present
 n1 - Sign Present, Ulight

NE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

HT NO. 50503499

TEST MATERIAL. T-3752

SUM

DOSAGE LEVEL. 5.0 g/kg

ANTHAL/EAR TAG NO. C3-4507

[illegible]

✓ - Sign Present
 al - Sign Present, slight
 @ Recording error 5-30-85 mm

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO. 50503444

TEST MATERIAL. T-3752

5122

DOSEAGE LEVEL. 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4500

[illegible]

✓ - Sign Present
sl - Sign Present, Slight

NE - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO. 50503499

TEST MATERIAL. T-3752

SEX ♀

DOSEAGE LEVEL. 5.0 g/kg

ANTHAL/EAR TAG NO. C3-4495

[illegible]

✓ - Sign Present
 + - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

KT NO. 50503499

TEST MATERIAL. T-3752

SEX ♀

DOSEAGE LEVEL. 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4484

HOURS

[illegible]

✓ - Sign Present
sl - Sign Present, slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

NT NO. 50503499

TEST MATERIAL. T-3752

SNK ♀

DOSEAGE LEVEL. 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4498

HOURS

[illegible]

✓ - Sign Present
sl - Sign Present, Slight

NK - Not Evident
NA - Not Applicable

STUDY TITLE: Acute Oral Toxicity

HT NO. 50503499

TEST MATERIAL. T-3752

常盤宮

DOSEAGE LEVEL. 5.0 g/kg

ANIMAL/EAR TAG NO. C3-4467

HOURS

[illegible]

✓ - Sign Present
nl - Sign Present, slight

NE - Not Evident
NA - Not Applicable



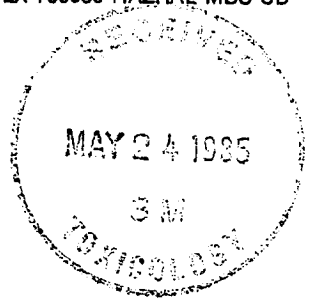
HAZLETON LABORATORIES AMERICA, INC.

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

PROTOCOL TP2069

Acute Oral Toxicity Study in Rats
(OECD Guidelines)

Study No. 50503499



for

3M

St. Paul, Minnesota

by

Hazleton Laboratories America, Inc.
Life Sciences Division
3301 Kinsman Boulevard
Madison, Wisconsin 53704

May 21, 1985

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PROTOCOL TP2069

Acute Oral Toxicity Study in Rats
(OECD Guidelines)

Study No.:	50503499
Study Location:	Hazleton Laboratories America, Inc. Life Sciences Division 3301 Kinsman Boulevard Madison, Wisconsin 53704
Test Material:	T-3752
Sponsor's Representative:	Janine Gleason
Study Director:	Steven M. Glaza
Proposed Timetable	
Starting Date:	Week of May 27, 1985
Completion Date:	Week of June 17, 1985
Final Report Date:	Week of July 15, 1985

OBJECTIVES

To determine the acute oral toxicity produced when the test material is administered by the oral route (gavage) to rats. All aspects of this study will conform to the Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 401, adopted May 12, 1981¹ and Principles of Good Laboratory Practice.² All procedures will be done according to Hazleton Laboratories America, Inc. (HLA) Standard Operating Procedures (SOPs) referenced in this protocol.

TEST MATERIAL

Test Material:	T-3752.
Physical Description:	Brown granular solid.
Purity and Stability:	Sponsor has purity and stability determinations on file.
Storage Conditions:	Store at room temperature.
Test Material Retention:	Any unused test material will be returned to the Sponsor 30 days after issuance of the final report.
Safety Precautions:	Laboratory personnel will take the normal necessary precautions in handling a substance of unknown toxicity. Laboratory clothing, latex gloves, safety glasses, and a particle mask approved for toxic dusts must be worn.

TEST SYSTEM

Animal Model

Young adult male and female albino rats (approximately 7 weeks of age) of the Sprague-Dawley strain will be obtained from Harlan Sprague-Dawley, Madison, Wisconsin. Rats will be selected at random from healthy animals that had been acclimated at HLA for at least 1 week. An adequate number of extras will be purchased in order that no animal in obviously poor health is placed on test. The weight variation in animals used on test will not exceed $\pm 20\%$ of the mean weight (i.e., mean = 250 g, range = 200 to 300 g).

Reason for Species Selection

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

Identification

Each animal will be assigned an individual animal number and ear tag which will accompany data collected from that animal throughout the study (OP-GENB 24).

Housing and Maintenance

The following environmental conditions will be maintained in the animal room used for this study (OP-TARC 230).

- o Temperature: $22^{\circ}\text{C} \pm 2^{\circ}$
- o Relative humidity: $50\% \pm 20\%$
- o Air change: At least 10 changes an hour of filtered 100% outside air
- o Light cycle: 12 hours light/12 hours dark

Temperature and humidity will be monitored throughout the study. Variations from prescribed environmental conditions will be documented.

Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals."³ Care will be taken to ensure that the animals are not disturbed for reasons other than data collection and routine maintenance. The animals will be individually housed in screen-bottom stainless steel cages held on racks, with absorbent pan liners in the urine- and feces-collecting pans. Pan liners will be changed at least three times each week.

Feed and water will be provided ad libitum. The diet will be Purina Rat Chow®. No contaminants are expected to be present in the feed or water which would interfere and affect the results of the study.

PROCEDURES

Experimental Design

Initially, a single dose of 5.0 g/kg will be administered to 10 animals (five males and five females). If no test material-related mortality is produced at this level, no further testing is required. If any mortality occurs at the 5.0-g/kg dose level, at the Sponsor's request, three or four geometrically spaced dose levels may be added. Each dose level will consist of 10 animals (five males and five females). Animals will be assigned to groups according to HLA Standard Operating Procedure OP-TOX 42.

Test Material Preparation and Administration

The test material will be suspended in an appropriate vehicle. Individual dosages will be calculated based upon the animal's body weight taken just before administration of the test material and administered by gavage.

Justification of Route of Administration

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

Observations

The animals will be observed individually for clinical signs and mortality at 1.0, 2.5, and 4 hours after test material administration. The animals will be observed daily thereafter for at least 14 days for clinical signs and twice daily (morning and afternoon) for mortality. The duration of observations may be extended when considered necessary. The time of death will be recorded as precisely as possible.

Individual body weights will be recorded just prior to study initiation and at 7 and 14 days following test material administration and at death. Changes in body weight will be calculated and recorded when survival exceeds 1 day.

Pathology

All test animals, whether dying during the study or sacrificed at termination, will be subjected to a gross necropsy examination and abnormalities recorded.

Report

The final report will contain a description of the test material, a description of how the study was conducted, response data for clinical signs, mortality and body weights by sex, a discussion of the data, and gross pathology findings.

Maintenance of Raw Data and Records

Original data or copies thereof will be available at HLA to facilitate auditing the study during its progress and prior to acceptance of the final report. When the final report is completed, all original paper data, as well as the final report, will be retained in the archives of HLA, Madison, Wisconsin (OP-GEN 44).

REFERENCES

1. Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals, Section 401, Acute Oral Toxicity, adopted May 21, 1981.
2. Organisation for Economic Cooperation and Development's Principles for Good Laboratory Practice, Annex 2, 1981.
3. DHEW Publications No. (NIH) 78-23 (1978).

PROTOCOL APPROVAL



Janine Gleason
Sponsor's Representative
3M



5/24/85

Date

Steven M. Glaza
Steven M. Glaza
Study Director
Group Leader, Acute Toxicology
Hazleton Laboratories America, Inc.

5-22-85

Date

(1107S/tji)